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DEVELOPING SPEECH AND LANGUAGE THERAPY EDUCATION IN SOUTHERN VIETNAM IN COLLABORATION WITH INTERNATIONAL PARTNERS

Nguyen Thi Ngoc Dung*, Lindy McAllister**,
Sally Hewat***, Sue Woodward****

ABSTRACT

Background: There is a growing demand for rehabilitation, allied health services in developing countries. Governments and institutions seeking to develop new education programs for the workforce who can deliver these services are hampered by the lack of an appropriate academic and clinical workforce in the new discipline. Hospitals, universities and governments are partnering with overseas institutions and non-government organisations to provide the technical expertise and human resources needed to develop and deliver training and support the new workforce to develop services. This paper describes one such multi-agency partnership which has enabled the development of speech and language therapy training and service development in Vietnam. ***Findings:*** The paper describes the partners in this development and the governance arrangements needed for this successful and enduring partnership. The paper identifies challenges faced and provides recommendations for other organisations wishing to support the development of new allied health disciplines in low and middle income countries. ***Conclusions:*** International and multi-agency partnerships can be effective and enduring if all partners commit to good communication and proactive management of inevitable challenges and robust governance arrangements are in place.

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I. INTRODUCTION

An estimated 15.7% of the 95 million people[2] in Vietnam have a disability (Mont & Cuong, 2011) and Kane (1999) suggested that 17-27% of these have problems with 'hearing and speech'. The development and delivery of speech and language therapy (SALT) in Vietnam has until recently relied on expatriates travelling to Vietnam to provide services and training. The earliest known report (Landis & Pham, 1975) describes Landis, a speech and language therapist from the USA, providing "remedial speech services" in Vietnam for children with cleft lip and palate. SALT services have been provided since then by various visiting non-government organisations such as Smile Train[3], Project Vietnam[4], and Orthophonistes du Monde[5]. Training of teachers to deliver SALT has occurred in education settings (see for example Winterton, 1998, and in medical universities and hospitals (see for example Ducote, 2001; Cheng, 2010). Such training enabled staff at Hanoi Medical University to establish a three month course in paediatric speech therapy for existing health professionals in hospitals in Hanoi and

[2] http://countrymeters.info/en/Vietnam Accessed 18 March 2017
[3] http://www.smiletrain.org
[4] http://www.projectvietnam.org
[5] http://www.orthophonistesdumonde.fr/

surrounding areas. Recipients of short course training often called themselves speech therapists despite limited training in only a portion of internationally recognised SALT scope of practice.

There are now multiple drivers for growth in formal speech therapy education in Vietnam. These include internal drivers such as decreasing rates of poverty and increasing survival rates, and health, education and social policy reforms, including the Vietnamese government's National Plan of Rehabilitation Development (Ministry of Health, 2014) which specifically mentions the need to build a SALT workforce. Improved IT access allows people in need of assistance for themselves or family members with communication and swallowing disabilities to identify international rehabilitation trends in speech therapy services. These together have created a demand for speech therapy service developments in Vietnam across a number of sectors, including government hospitals and clinics, private clinics and schools. The Vietnamese government has also been very successful at responding to external drivers such as the Millenium Development Goals (United Nations Development Program, 2000[6]), and is actively engaged in meeting the Sustainable Development Goals (United Nations Development Program, 2015[7]). Services for people with disabilities, such as those delivered by speech and language therapists (SALTs), help governments meet these goals as well as the aims of the World Report on Disability (World Health Organisation, 2011).

Fulfilling the mandate for formal SALT education and services referenced in the "National Plan of Rehabilitation Development in the Period of 2014 to 2020" will prove a challenge because the qualified SALT workforce in VN is small and there are to the best of our knowledge no academics with clinical degrees (as opposed to research degrees) in speech therapy which would enable them to practice and teach across the scope of SALT. Leaders in the development of comprehensive SALT education in Vietnam (see for example McAllister, Woodward, Christie et al, 2010) acknowledged that for the present, offering formal programs in speech therapy requires partnerships with colleagues in countries with developed SALT education and services. Partnerships between clinicians and academics in Low and Middle Income Countries (LMIC) and High Income Countries have successfully established speech therapy education and services in many LMIC countries in Africa, Asia, South East Asia and South America (see International Journal of Speech-Language Pathology 2013, vol. 15, issue 1 for examples from nine such countries).

This paper describes one such partnership which has enabled the delivery of SALT education in Ho Chi Minh City (HCMC) Vietnam since 2010. This highly successful partnership between University of Medicine Pham Ngoc Thach (UPNT), the ENT Hospital HCMC, Trinh Foundation Australia and the University of Newcastle has produced to date 65 SALT graduates; 33 from two comprehensive 2 year post-graduate training programs and 32 graduates of a 10-month post-graduate paediatric speech therapy course. These

[6] http://www.unmillenniumproject.org/goals/
[7]http://www.undp.org/content/undp/en/home/sustainable-development-goals.html

graduates are actively involved in establishing and building speech therapy services in hospitals, schools and clinics across Vietnam. The paper describes the training programs undertaken to date, and the arrangements which govern, monitor and strengthen the partnership. The paper provides recommendations for universities in both high income and LMIC countries considering or engaged in partnerships to develop SALT.

II. A COLLABORATIVE INTERNATIONAL PARTNERSHIP FOR THE DEVELOPMENT OF SPEECH AND LANGUAGE THERAPY (SALT) EDUCATION IN HO CHI MINH CITY

This paper's first author (Dr Ngoc Dung, an ENT doctor) undertook an internship in France during which time she worked closely with SALTs and came to understand the value of SALT for patients. When she was Director of the ENT Hospital of HCMC, she asked visiting Australian SALTs in 2008 for assistance in providing training at her hospital to serve the growing need for people with voice, swallowing, hearing and speech impairments. A small group of Australian SALTs and orthodontists founded Trinh Foundation Australia (TFA) to meet this request, and a 6 week short course was run at the ENT Hospital of HCMC in 2009 for doctors, nurses and audiologists (see McAllister et al., 2010). Under Dr Dung's leadership the ENT Hospital of HCMC and TFA also cooperated to run a 2 year post-graduate training program (2010-2012); classes were held at UPNT and clinical training at the ENT Hospital. A subsequent 2 year SALT training program (2012-2014) and a 10-month course in paediatric SALT (2016-2017) were delivered during Dr Dung's tenure as Rector at UPNT. The implementation and success of these training programs required a very concerted and robust partnership between multiple organisations, as described below.

1. University of Medicine Pham Ngoc Thach

UPNT is a relatively recently established municipal university in HCMC. It offers degree courses in medicine, nursing, midwifery, physiotherapy, optometry and medical laboratory sciences, and non-degree level SALT courses. For the SALT courses, UPNT managed the recruitment and admission of the speech therapy students, payment of lecturers, and provided a Speech Therapy Office and administration support. The university's international office liaised with hospitals and clinics regarding clinical placements for the students, as well as liaised with other Vietnamese institutions, and government instrumentalities who oversight the program.

2. Trinh Foundation Australia

TFA is a small Australian non-government organisation which has had Certificates of Registration from PACCOM since 2009. The Australian Global Development Group has assisted TFA with satisfying all governance requirements for Australian Overseas Aid Organisations. TFA helped UPNT to establish a SALT office at the university and supplied laptops, printers, photocopiers, a library of key speech therapy texts, audio-visual and other resources for the training programs. TFA funds a SALT office/program manager at UPNT and interpreters and translators. In 2015, TFA ran an interpreter training program, with funding from a *Speech Pathology Association of Australia* development grant, in order to provide high quality interpreters and translators for teaching at UPNT, and for

other TFA activities such as running an extensive national continuing professional development (CPD) program for UPNT's SALT graduates and other interested staff in hospitals, schools and clinics, and developing SALT resources in the VN language. TFA supported the development of a Vietnamese/English glossary of speech therapy terms to assist with the provision of high quality translation and interpreting. The original 2 year training program curriculum outline was provided by TFA and extended and refined by successive long and short term volunteers teaching in the programs at UPNT 2012-2017. TFA now holds a culturally validated speech therapy curriculum and extensive teaching resources in both English and Vietnamese.

The SALT training programs at UPNT have been delivered with the support of the global SALT profession, primarily from within Australia. While the training programs use local Vietnamese staff whenever possible (e.g., to teach anatomy, physiology, developmental behavioural psychology and linguistics), there were no Vietnamese SALTs in Vietnam with clinical degrees in speech therapy (able to practice and teach speech therapy across the scope of practice). Therefore expertise for the speech therapy subjects was sourced from abroad. TFA enlisted the help of Australian Volunteers International, Australian Business Volunteers and more recently Scope Global to support long (12-24 month) and short-term assignments (1-3 month) of Australian SALTs to Vietnam (see McAllister, Woodward, Atherton, et al., 2013). In addition, TFA provided some financial assistance, as wells as pre-departure, in-country and return-to-Australia briefing and support to more than 110 volunteer lecturers and clinical educators for the training programs, as well as workshop presenters and clinical mentors for the program graduates. Evaluations of the contributions of these people from the perspectives of the Vietnamese SALT students and staff will appear in a related paper. The perspectives of volunteer clinical educators regarding their contributions appeared in Dung et al, 2016.

3.Australian Volunteers for International Development (AVID)

The Australian government funded Australian Volunteers for International Development (AVID) program initially through Australian Volunteers International and more recently Scope Global has placed six full time Australian SALTs on 18 to 24 months assignments to UPNT since 2010. This continued support is because of the close alignment between UPNT's goals, TFA's strategic plan and AVID's priorities in Vietnam for human resource development, as well as their focus on helping people with disabilities (see McAllister, Woodward, Atherton et al., 2013 for more detail). The roles of these volunteers at UPNT has been to coordinate the course and the associated clinical placements, support volunteer SALTs from Australia who came to lecture, supervise clinical education placements, provide CPD events, and mentor SALT graduates from UPNT.

4. University of Newcastle

During the delivery of the first 2 year training program, the University of Newcastle (UoN) supported an academic staff member on a short-term overseas study program to assist and provide academic mentoring for volunteer SALT co-ordinators based at UPNT, develop teaching and education resources, deliver specialist lectures and provide clinical and research

mentoring. Since 2011, a further 2 academic staff and 8 clinical educators and 47 final year SALT students from UoN have worked collaboratively with the university, TFA, SALT graduates and students of the SALT programs at UPNT to provide ongoing case conferencing, workshops, resource development, public education and community awareness activities regarding SALT, clinical supervision and mentoring. An outstanding graduate of the first 2 year program was offered a conjoint lecturer appointment a UoN in 2015 to further strengthen SALT clinical and research activities in Vietnam, foster further cross cultural understandings and mutual respect regarding SALT practices, and provide ongoing opportunities for shared education and research collaboration.

III. GOVERNANCE OF THE PARTNERSHIP

This partnership has sustained for almost 10 years by using principles of open and frequent communication, alignment of strategic goals and good governance. Formal MOUs govern the partnership between TFA, UPNT and UoN. The partners meet formally at least once a year at UPNT. These meetings usually include representatives of UPNT, TFA, UoN and AVI/Scope Global. The purpose of these meetings is to review progress towards agreed goals, revise plans and determine future steps forward. In between these formal meetings are hundreds of emails, skype calls and phone calls between representatives of the partners to solve any problems as they arise and make decisions about matters that arise. As in any partnership, honest communication, cultural sensitivity and respect have ensured the ongoing commitment of all partners to managing the inherent challenges in realising the shared goal of developing SALT in Vietnam.

IV. OVERVIEW OF THE SALT PROGRAMS AT UPNT ARISING FROM THE PARTNERSHIP

In this section we briefly describe the framework of the SALT training programs which prepared graduates to work clinically across the broad scope of practice of SALT; that is with people with language, speech, hearing, voice, stuttering and swallowing disabilities, using all available communication modalities including multi-modal communication (Augmented or Alternative Communication [AAC]). Students in the 2 year programs were trained to work with people of all ages, but students in the 10 month program were trained to work just with children from birth to 18 years. The graduates form the basis of a SALT workforce to provide teaching and clinical supervision for future degree programs in Vietnam. Students in the programs were mostly already practicing health professionals in Vietnam (nurses, physiotherapists and doctors) as well teachers, psychologists and social workers in more recent courses. In all programs, biopsychosocial constructs of disability, as utilised in the International Classification of Functioning, Disability and Health framework (ICF) (World Health Organization, 2010) were explicitly embedded throughout the curricula. Health promotion, research and advocacy were also built into the two-year courses. For more detail on the 2 year program see Atherton, Dung and Nhan (2013).

The SALT programs used alternating blocks of full time attendance at UPNT for

lectures, tutorials and clinical education sessions, and 2-3 month blocks of time for students to return to their workplaces, to implement what they had learned at UPNT, and undertake 2-4 week clinical placements. In earlier courses students were supervised by volunteer SALTs from Australia (see McAllister et al., 2016). More recently graduates of the 2 year programs have acted as supervisors. Where possible, lectures were delivered by Vietnamese academics (e.g., audiology, anatomy, physiology, linguistics, psychology) but because of there were no Vietnamese SALT academics available, lectures relating to all aspects of SALT were delivered by visiting Australian SALT academics supported by TFA. In the 10 month program, Vietnamese SALT graduates of the 2 year programs were involved in co-designing and co-teaching SALT subjects with visiting Australian SALT academics. This was done to ensure cultural relevance and, and to lay the groundwork for sustainability of such courses in the future, thereby reducing reliance on oversees SALT volunteers to come to Vietnam to teach.

V. CONCLUSION AND RECOMMENDATIONS FOR OTHER LOW AND MIDDLE INCOME COUNTRIES/UNIVERSITIES WISHING TO ESTABLISH SALT PROGRAMS AND SERVICES

We have sustained this successful and productive partnership described in this paper for almost a decade and have managed many challenges along the way. By involving Vietnamese academics, doctors and SALTs in ongoing curriculum design and teaching, we believe we have avoided post-colonial practice of imposing a 'western' curriculum on another country, a curriculum which may not account for that country's beliefs about health and disability and limited access to SALT services. This collaboration in curriculum development and teaching, together with ongoing provision of CPD, and clinical and research mentoring of SALT graduates lays the groundwork for sustainability of SALT education and service development. The partnership has by many measures been very successful: there are 65 SALT graduates to date establishing or working in an increasing number of speech therapy clinics across Vietnam[8]. The SALTs are engaging in research and practice innovations, are receiving CPD to further develop their capabilities and sustain SALT services, and are providing CPD and training about SALT to other professional groups, across Vietnam. New goals are emerging for the partnership as national agendas support future university degree level courses in speech therapy.

The partnership has identified a number of recommendations which we offer to others interested in developing similar partnerships to develop SALT education and services in LMIC. These recommendations apply to other health sectors also.

1. Have the international partners spend significant amounts of time in country, on a regular basis, to understand the cultural factors affecting the education and service development; provide them with cultural knowledge and brokers who can assist them to effectively work cross-culturally

[8] The 33 graduates from the 2 year programs have established sustainable SALT services, mostly in public hospitals, in HCMC, Hue, Hanoi, Vung Tau, Bau Loc and other southern provinces. Graduates of the 10 month program will supplement the workforce in these existing clinics and open new clinics in other locations.

2. Identify local champions and support them to lead the partnership and obtain buy in from local ministries, institutions and other organisations.

3. Focus in the early stages on building local workforce capacity to lead future stages of development and educate the public to obtain buy-in and support.

4. Focus on clinical training as well as knowledge transfer; local support will strengthen if local people can see the benefits to people from the new clinical services.

5. Ensure cultural relevance and acceptability of the curriculum; have local professionals involved in curriculum design, delivery and evaluation and use the feedback to improve cultural relevance of content and teaching.

6. Mentor and support local recipients of the new training to become lecturers, supervisors and researchers in the new profession.

7. Focus on building sustainability and independence of the local partners from the start of the partnership; recommendations 2-6 are all directed to ensuring sustainability and reduced reliance on international partners.

8. Create links with other non-government organisations working in country to ensure there is no duplication of training and wastage of human resource time and effort.

9. Build governance arrangements and communication protocols to ensure frequent and open communication to ensure the activities are meeting needs and goals in-country.

10.Be patient - time is needed to build cultural competence, understanding, a strong relationship.

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RÉSUMÉ:

DÉVELOPPER L'ENSEIGNEMENT DE L'ORTHOPHONIE DANS LE SUD DU VIETNAM EN COLLABORATION AVEC DES PARTENAIRES INTERNATIONAUX

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Contexte: Il y a une demande croissante pour la réadaptation et les services de santé connexes dans les pays en développement. Les gouvernements et les institutions qui cherchent à développer de nouveaux programmes d'éducation pour la main-d'œuvre qui peut fournir ces services sont entravés par le manque d'une main-d'œuvre académique et clinique appropriée dans la nouvelle discipline. Les hôpitaux, les universités et les gouvernements collaborent avec des institutions étrangères et des organisations non gouvernementales pour fournir l'expertise technique et les ressources humaines nécessaires pour développer et dispenser une formation et soutenir la nouvelle main-d'œuvre pour développer des services. Cet article décrit un tel partenariat multi-agences qui a permis le développement de la formation en orthophonie et en développement de services au Vietnam. **Résultats:** Le document décrit les partenaires de ce développement et les dispositions de gouvernance nécessaires pour ce partenariat réussi et durable. Le document identifie les défis rencontrés et fournit des recommandations à d'autres organisations souhaitant soutenir le développement de nouvelles

disciplines sanitaires dans les pays à revenu faible et intermédiaire. **Conclusions:** Les partenariats internationaux et multi-agences peuvent être efficaces et durables si tous les partenaires s'engagent à bien communiquer et à gérer de manière proactive les défis inévitables et si des dispositions de gouvernance solides sont en place.

EVALUATING THE EXPERIMENT'S RESULT OF TOOTH TRANSPLANTATION AFTER CRYOPRESERVATION

Nguyen Phan Hong An*, Tran Tuan Anh*, Tran Van Dang*,
Van Minh Nghieu*, Hoang Bao Duy**, Bui Thi Thu Hien**

ABSTRACT

Objective: Evaluating the experiment's result of tooth transplantation after cryopreservation. ***Subjects of the study:*** Implementation on rabbits. ***Methodology****:* experimental description. ***Result and discussion:*** after 8 weeks, gingival tissue's healing rate at good classification reaches 96.7% and complete healing with 100% after 12 weeks. The rate of teeth after transplatation at level 1 mobility increases gradually from 13.4% after 4 weeks of transplantation to 80% and 93.3% after 6 and 12 months of transplantation respectively. The rate of teeth mobility at level 2 gradually decreases from 63.3% to 20%. The *periodontal ligament* spaces on the digital periapical radiograph gradually narrow from 0,74±0,63mm (after 1 week) to 0,58±0,43mm (after 8 weeks) at ½ superior, and from 0,82±0,47mm (after 1 week) to 0,46±0,32mm (after 8 weeks) at ½ inferior. **Conclusion:** gingival tissue is a body part which has a high healing rate and becomes stable after 12 weeks. The mobility level of transplanted teeth after surgery decreases over time,in other words, transplanted teeth become firm again over time. The *periodontal ligament* spaces showed in radiograph has the signal of narrowing gradually after 8 weeks; the rate of transplanted teeth with medium and bad results tends to decrease. The shorter the storage time is, the higher the success rate with better result is.

Keywords: *Teeth storage, transplantation, experimental, rabbits*

I. INTRODUCTION

Nowadays, associated with the development of economy and society, life quality is also improved, as the result, the demands of ideal beauty becomes of more serious concern for people, especially the beauty of face and smile plays an important role in that ideal beauty. In order to have a nice smile, the dentition need to be aligned and adequate. However, not all of people has a full dentition, someloses teeth due to disease, accident or other reasons.There are many methods to replace the lost tooth to resolve this problem, in which, tooth implantation made of metal material such as titanium (implant) by Brånemark applied from 1950s to present is one of the most popular modern methods [1].

In Vietnam, technique of tooth implantation made of metal material such as titanium (implant) is popular [2]. Besides the dominant advantages, this method has a disadvantage of high cost, that's unsuitable for patients who have low income. In order to resolve this problem, there are some foreign

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and local scientist who suggested tooth transplantation lost tooth by the patient himself tooth which is located in other site with no or less function (wisdom tooth) [3], [4]. To reach the best result, this method requires carring out in only 1 surgery as fast as possible [5], [6]. However, in some cases, patients need more time to recover from other trauma (for example traumas after an accident...) before dental implant surgery for correcting aesthetic and chewing functions. Therefore, we need storage teeth in a long time for future transplantation. At present, there has not any study about the effect of cryopreservation on teeth for future transplantation and wheather this methods get the same result as other tissue transplantation. Hence, this study was carried out to provide new knowledge for dentistry as well as to help clinicians have more studied information in chosing effective treatment methods. However, studying in healing process after tooth transplantation is quite complicated; thus, we have not carried out on human yet because of morality in medical study and we had just carried out in experimentally with purpose: Evaluating the experiment's result of tooth transplantation after cryopreservation.

II. MATERIALS AND METHOD

2.1 Method: Descriptive experimental research.

2.2. Time and place of the study: This study was carried out from July 2016 to December 2017 at the laboratory, Clinical Medical Department, Binh Duong Medical College.

2.3 Subjects of the study: *Experimental rabbits (30 rabbits are equally divided into 3 groups)*

2.4. Selection criteria

- Buck rabbits, healthy, 3 months old
- The weight of each rabbit is from 1.8 to 2 kg

2.5 Exclusion criteria: Not meet the above selection criteria.

2.6 Research facilities:

- Rabbits were fed an experimental diet.
- It is ensured that each cage contains only one rabbit.
- Sterile surgical kits, endodontic kits
- High speed handpiece, Marathon electric drilling machine and bone cutter drill set
- Sterile gloves, surgical sutures
- NaCl 0.9%, betadine, alcohol 70%
- Thiopental, antibiotics,...
- Sterile dressings, experimental group record labels
- Three-layer sterile bags, cottons, bandages, gauzes …
- Refrigerators, Freezers (-85^{o}C).

2.7 Steps to conduct research:

- Prepare information slips and stick information to samples
- Gather information before surgery: teeth positions, periapical X-ray before surgery.
- Anaesthetize rabbits: use thiopental with a dose of 25mg/kg.
- Extract an inferior incisor from each rabbit (minimizing traumatic in alveolar bone and periodontal ligaments).
- Tooth canal filling.
- Preserve tooth samples in warm physiological saline, and then pack tooth samples in three layers of sterile material, from the inside out: Sterile cloth bag; Polyethylene (PE) bags which are thin, sterile and are sealed, containing tooth sample code information; thick PE bag. Transfer to laboratory for storage and disinfection by gamma irradiation at 25kGy and conduct cryopreservation at -85^{0}C according to standards of Asian Pacific Tissue Bankers Association [7][8]

+ After 04 weeks (Group 1); After 8 weeks (Group 2); After 12 weeks (Group 3), the samples are withdrawn and the receiving

positions (initial positions) are prepared with a drill bit and a rongeur.

+ Put transplanted teeth in the prepared alveolar

+ Adjust teeth to remove the premature contacts.

+ Teeth are fixed with metal wire and surgical bandages by Coe-Pak.

+ Postoperative care: antibiotics, pain relievers.

2.8 Criteria for evaluating results: The status of soft tissues healing over each certain time after transplantation; The attachment of transplanted teeth after cryopreservation over each certain time; Examine the *periodontal ligament* spaces on the digital periapical radiograph (mm).

2.9 Wide range of data processing: Data analysis is done by medical statistical algorithms on STATA 20.0 software to calculate frequency, percentage with qualitative variables; average, standard deviation with quantitative variables.

III. RESULT AND DISCUSSION

Table 3.1 *Results of the soft tissues healing over time*

Time	Good		Medium		Bad		Total
	Number	%	Number	%	Number	%	Number
1 week (1)	3	10,0%	25	83,3	2	6,7	30
4 weeks (2)	26	86,7%	3	10,0	1	3,3	30
8 weeks (3)	29	96,7%	1	3,3	0	0,0	30
12 weeks (4)	30	100,0%	0	0,0	0	0,0	30
p	p_{1-2} =0,000, p_{1-3}=0,000 p_{1-4}=0,000 (fisher's exact test) p_{2-3}= 0,353, p_{2-4}= 0,112 (fisher's exact test) p_{3-4}= 1,000 (fisher's exact test)						

Comment: This table shows that gingival tissue has a high and stable healing rate. Only after 1 week, its healing rate is quite good, accounted for 83.33%, in which 10% at good ranked. At this time, gingival tissue start to attach to the cervical and begin to work as a barrier to protect against bacteria and toxins that enter the under organizations which are still under healing process. And this is also the reason why most surgeons recommend that it is necessary to suture cervical teeth during the transplantation procedure.

Table 3.2 *The attachment of transplanted teeth after cryopreservation over time*

Time	Level 1		Level 2		Level 3		Total
	Number	%	Number	%	Number	%	Number
4 weeks (1)	4	13,4	19	63,3	7	23,3	30
8 weeks (2)	10	33,3	20	66,7	0	0	30
12 weeks (3)	17	56,7	13	43,3	0	0	30
6 months (4)	24	80	6	20	0	0	30
12 months (5)	28	93,3	2	6,7	0	0	30
p	p_{1-2} =0,005, p_{1-3}=0,000 p_{1-4}=0,000, p_{1-5}=0,000 (fisher's exact test) p_{2-3}= 0,069, p_{2-4}= 0,000, p_{2-5}=0,000 (χ^2 test) p_{3-4}= 0,052, p_{3-5}=0,001 (χ^2 test) p_{4-5}= 0,254 (fisher's exact test)						

Comment: The tooth mobility at level 1 increased within the time of transplantation, the difference between the evaluation tests is statistically significant ($p < 0.01$).

Table 3.2 shows that the mobility level of transplanted teeth after surgery decreases over time. In particular, the rate of teeth at level 1 mobility gradually increases from 13.4% after 4 weeks of transplantation to 80% after 6 months of transplantation. The rate of teeth at level 2 mobility gradually decreases from 63.3% to 20%. It shows that teeth at level 2 of mobility have gradually shifted to level 1 of mobility. It means that transplanted teeth gradually become firm again over time.

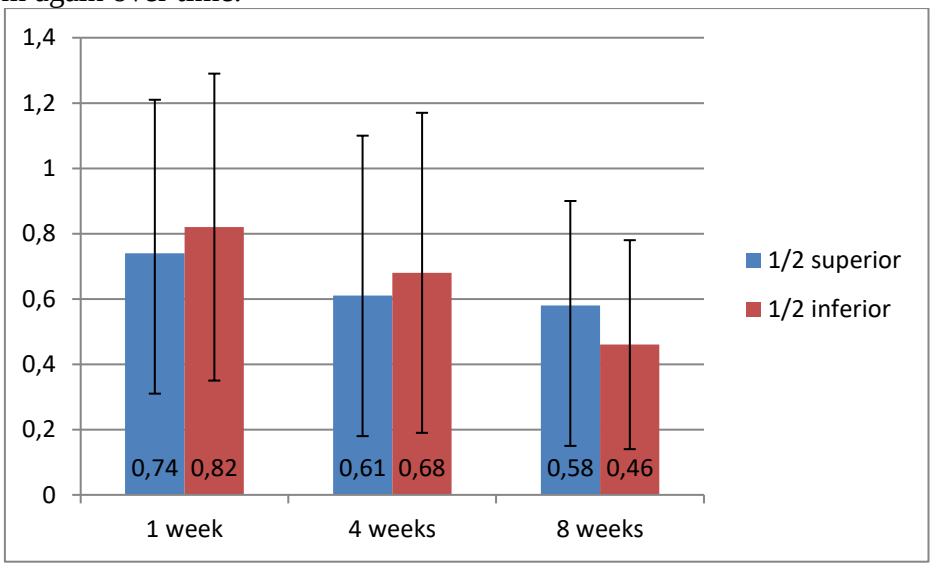

Chart 1: *Examine the periodontal ligament spaces on the digital periapical radiograph (mm)*

Comment: The *periodontal ligament* spaces has narrowing signs after 8 weeks in comparision with to one week after surgery. The difference is statistically significant.

Table 3.3*. Overall evaluation of transplantation results after cryopreservation over time*

Time	Good		Medium		Bad		Total
	Number	%	Number	%	Number	%	
4 weeks (1)	4	13,4	19	63,3	7	23,3	30
8 weeks (2)	10	33,3	20	66,7	0	0,0	30
12 weeks (3)	17	56,7	13	43,3	0	0,0	30
6 months (4)	24	80,0	6	20,0	0	0,0	30
12 months (5)	28	93,3	2	6,7	0	0,0	30
p	p_{1-2} =0,005, p_{1-3}=0,000, p_{1-4}=0,000, p_{1-5}=0,000 (fisher's exact test) p_{2-3}= 0,069, p_{2-4}= 0,000, p_{2-5}=0,000 (χ^2 test) p_{3-4}= 0,052, p_{3-5}=0,001 (χ^2 test) p_{4-5}=0,254 (fisher's exact test)						

Comment: The rate of transplanted teeth with good results on radiograph has been increasing over time while the rate of transplanted teeth with relative and bad results tends to decrease. The difference is statistically significant (p <0.01).

Table 3.4*: Relationship between storage time and transplantation results after 6 months*

Storage time	Good		Medium		Bad		Total
	Number	%	Number	%	Number	%	
4 weeks (1)	29	96,7	1	3,3	0	0,0	30
8 weeks (2)	27	90,0	3	10,0	0	0,0	30
12 weeks (3)	24	80,0	6	20,0	0	0,0	30

P	p_{1-2} =0,612, p_{1-3}=0,103 (fisher's exact test) p_{2-3}= 0,475 (fisher's exact test)

Comment: The shorter the storage time is, the higher the success rate with better results is (96.7%). However, with a 12-week storage period, results were not significantly different, and no bad results were found. Therefore, the shorter the storage time is, the higher the success rate with better results is.

IV. CONCLUSION

- Research result shows that gingival tissue is a body part which has a high and stable healing rate. Only after 8 weeks, its healing rate accounted for 96.7% and after 12 weeks, its healing rate accounted for 100%.

- The mobility level of transplanted teeth after surgery decreases over time. In particular, the rate of teeth at level 1 mobility gradually increases from 13.4% after 4 weeks of transplantation to 80% and 93.3% after 6 and 12 months of transplantation respectively. In contrast, the rate teeth at level 2 of mobility gradually reduces from 63,3% to only 20%. It means that teeth at level 2 of mobility have gradually shifted to teeth at level 1 of mobility, in other words, the transplanted teeth gradually become firm again over time.

- The *periodontal ligament* spaces showed in radiograph has narrowing signs after 8 weeks in comparison to one week after surgery. It also shows that the rate of transplanted teeth with good results on radiography has been increasing over time while the rate of transplanted teeth with relative and bad results tends to decrease.

- The shorter the storage time is, the higher the success rate with better results is.

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RÉSUMÉ:

ÉVALUATION DU RÉSULTAT DE LA TRANSPLANTATION DENTAIRE APRÈS CRYOPRÉSERVATION

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Objectif: Evaluation du résultat de la transplantation dentaire après cryopréservation. **Sujets d'etude:** Lapins. **Methode:** Descriptive. **Résultat et discussion:** Après 8 semaines, le tissu gingival guérit à une vitesse de bonne classification, le proportion étant 96.7%, et la guérison complète a été 100% au bout de 12 semaines. Le taux de mobilité dentaire niveau 1 augmente graduellement de 13.4% après 4 semaines, à 80% et 93% après 6 et 12 mois respectivement. Le taux de mobilite dentaire niveau 2 diminue de 63.3% a 20%. Les espaces des ligaments péridentaires sont retrouvés à la radiographie digitale périapicale rétrécis graduellement de 0.74±0.63mm (après 1 semaine) à 0.58±0.32mm (après 8 semaines) pour la moitié supérieure, et de 0.82±0.47mm (après 1 semaine) à 0.46±0.32mm (après 8 semaines) pour la moitié inférieure. **Conclusion:** Le tissu gingival est doté d'une guérison rapide, et qui se stabilise après 12 semaines. La mobilité des dents transplantées diminue avec le temps, autrement dit, les dents transplantées sont devenues fermes avec le temps. Les espaces des ligaments péridentaires sont graduellement rétrécis à la radiographie après 8 semaines; les résultats moyens et mauvais ont tendance à diminuer. Plus la durée de la préservation est courte, meilleure est le taux de succès, et meilleur est le résultat.

Mots clés: ***Cryo****préservation dentaire, transplantation expérimentale, lapins d'expérimentation.*

FLOW DIVERTER STENT IN THE TREATMENT OF CHALLENGING CEREBRAL ANEURYSMS: SUMMARY SERIES AT BACH MAI HOSPITAL AND HA NOI MEDICAL UNIVERSITY HOSPITAL

Nguyen Thai Binh*, Vu Dang Luu*, Pham Minh Thong*

ABSTRACT

Background and Purpose: The purpose of this study is to report our experience with challenging cerebral aneurysms, results in treatment with the flow-diverter stent and follow up. ***Methods:*** A consecutive series of 130 patients, with 134 procedures were performed in Bach Mai hospital and Hanoi Medical University Hospital from January 2012 to April 2017. 143 diversion devices (Pipeline, FRED and SILK) were used. Aneurysms morphology, stent patency and cerebral parenchyma before and after intervention were analyzed by DSA, MSCT and MRI images. Follow up data after 3-6 months and 12 months were recorded. ***Results:*** The study includes 130 patients (female/male ratio 3,32). Challenging intracranial aneurysms of internal carotid artery are mostly common (92,6%), especially in cavernous (35,1%) and in para-ophthalmic (40,3%) segments. 83 (61,9%) had wide-neck aneurysms and 16 (11,9%) had multiple aneurysms and only 5 (3,7%) had blister-liked aneurysms. Endovascular treatment was successfully performed in 94,8%. In 3 patients, the stent could not be delivered. Mortality and morbidity rates were 1,5% and 3,7% respectively. MRI and MSCT follow-up at 3 months showed complete occlusions and incomplete occlusions of aneurysms in 75,4% and 17,5%, respectively. 3 patients experienced a thromboembolic event (4,3%). ***Conclusions:*** Challenging intracranial aneurysms of cavernous and para-ophthalmic segments of internal carotid artery are mostly common with wide-neck and multi aneurysms. Deployment of flow diverter stent is safe and effective with high rate of successful and low procedural complications.

Key words: *Challenging intracranial aneurysms, flow-diverter stent*

I. BACKGROUND AND PURPOSE

Cerebral aneurysm is a relatively common disease (2.3 to 5% of the population) [1], tends to increase in Viet Nam, causing high mortality risk (40-45 %) or severe sequelae for patient, family and society [2]. The risk of rupture is proportional to the diameter of the aneurysm, about 6% per year for the giant aneurysms (> 25 mm) [3, 4]. Treatment of cerebral aneurysms has made significant progress in the last decade with the new materials. With complicated bulge forms such as giant aneurysm, wide - neck aneurysm, blister-like aneurysm, recurrent side-wall aneurysm, fusiform aneurysm, multiple aneurysm, endovascular treatment with coiling or surgical clipping are both difficult with high complications as well as recurrence after treatment, while occlusion the parent artery is not possible in most of cases. Deploying the flow-diverter stent is an effective alternative that has been widely used around the world.

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Kallmes et al. (2007) reported an experimental study using stent Pipeline NED in rabbits [5], the stent reduces the flow resulting from aneurysm thrombosis but preserves the parent artery and lateral branches. The next generation of flow diverter stents covers about 30-35% of the wall area, but can be fully resettable and redeployed if necessary. Many studies in the world have shown that this method has a very high success rate, about 93-95% [6-9], with low complications rate, about 2.3-5.6%.

In Vietnam, flow diverter stents were first used in 2009 in the Department of radiology - Bach Mai Hospital. We summarize the results of this method from 2012 to present with 137 patients treated at Bach Mai Hospital and Hanoi Medical University with two objectives:

1.To describe the characteristics of challenging cerebral aneurysm treated with flow diverter stents.

2.To evaluate the early results of stenting method.

II. MATERIALS AND METHODS

1. Patients selection:

• This retrospective and prospective study included 130 patients (1) > 18 years. (2) have complicated un-ruptured or ruptured challenging aneurysms (has been treated through acute stage). (3) Being treated with flow diverter stent in the Department of Radiology - at Bach Mai Hospital and Hanoi Medical University Hospital from January 2012 to April 2017.

• Exclusion criteria: (1) Patients should not take the dual anti-coagulant medication exactly according to the regimen. (2) Neurointerventionists who have experience less than 5 years. (3) The patient did not agree to participate in the study.

2. Methods:

Retrospective and prospective study. Select patients into study with convenient sample size from January 2012 to April 2017 at Bach Mai Hospital and Hanoi Medical University Hospital. Research facilities include: Digital subtraction angiography system Phillip Allura Xper. MS CT (64 slides or more) and 1.5T magnetic resonance imaging. Flow diverter stents: Pipeline (Covidien), FRED (Microvention) or Silk (Balt) were used.

3. Procedure and follow up:

Patients were evaluated cerebral aneurysms by CT scan or MRI.

3-5 days before procedure, patients were given dual anti-platelet medications (Clopidogrel 75 mg / day and Aspirin 100 mg / day). Heparine bolus 2500 UI and maintain 500-1000 UI /h before and intra procedure.

Technical success criteria are stent fully opened and covered at least 4mm before and after the aneurysm.

Patients were given dual anti-platelet therapy for 3 months and maintained aspirin 100mg / day for the next 9 months.

Imaging characteristics in CT Angio or MRAngio or DSA angiogram of the patients were recorded.

- Morphology of the aneurysms, technical success rate, changes of degree of angiographic filling and contrast stasis before and after aneurysm stenting, early and late complications, imaging of cerebral arteries, parenchyma and aneurysms after 3 months, and 6-12 months of intervention.

III. RESULTS

The study included 134 procedures of 130 patients (two patients have aneurysms of

bilateral internal carotid arteries and one cases of vertebral aneurysm treated in 3 procedures.

Characteristics of group: The ratio of female/male was 3.32. The median age of group was 50, range from 22- 76 years old.

Imaging of challenging aneurysms on DSA:

- **Size:** Diameter average: 6.6mm (± 5.3), with a minimum diameter of 1.7mm, maximum diameter 28mm, aneurysm high average: 7.2 mm (± 6.3), of which the smallest 2mm, the biggest 39mm. The neck diameter average is about 5.1 mm. The dome/neck ratio is 1.4.

Table 1: *Type of challenging aneurysms*

Morphology	N	%
Wide - neck aneurysms (<10mm)	83	61,9
Large aneurysms (>10mm)	12	9,0
Giant aneurysms (>20mm)	12	9,0
Multiple aneurysms	16	11.9
Blister-like aneurysms	5	3.7
Fusiform aneurysms	6	4.5
Total	134	100

- **Localization:** Challenging aneurysms commonly located in the cavernous segment and the para-ophthalmic segment or multi locations, respectively 35.1%, 40.3%, 11.9%.

Table 2: *Localization of the aneurysms*

Localization		N	%
Carotid artery	Cavernous segment	47	35,1
	Para-ophthalmic segment	54	40,3
	Posterior communicating segment	3	2,2
	Anterior Choroid segment	1	0,7
	Terminus segment	3	2,2
	Multiple localization	16	11,9
Vetebro-basilar artery	V4 segment of Vertebral Artery (*1 or multiple aneurysms*)	9	6,7
	P1 Segment of posterior cerebral artery	1	0,7
	Total	134	100

- **Technical features:** 143 stents were used, of which 121 cases treated with single stents, 9 cases with 2 stents and 4 cases with combined stent and coil.

Stent Pipeline was most commonly used with 121 stents, accounting for 84.6%. Stent FRED applied to 21 cases accounted for 14.7%. Silk stent is new in the market, was deployed in one case. Average stent diameter 4.3 mm (± 0.38), mean stent length: 21.6 mm (± 4.6)

Technical success rate: 129 procedures, accounting for 96.3%, with good results reaching 85.8%. 7 stent were not fully open, needed to ballooning. 2 cases had distal stent displacement lower than expected but still covered the neck of the aneurysms, 5 cases existed

endoleak. Failure rates accounted for 3.7% due to not open stents, treated by coils; displacement of the stent into the aneurysm or obstruction of the stent.

Table 3: *Technical features*

		N	%	Total
Success	Stent fully open in good position	115	85.8	n=129 %=96.3
	Stent not fully open	7	5.2	
	Displacement but still covered the neck of the aneurysms	2	1.5	
	Endoleak	5	3.7	
Unsuccessful	Stent not open	1	0.7	n=5 %=3.7
	Displacement of the stent into the aneurysm	2	1.5	
	Obstruction of the stent	2	1.5	

Table 4. *Degree of angiographic filling of the aneurysms immediately after stenting (The O'KM scale classification)*

Filling grade	n	%
A: Total filling (>95%)	111	83.5
B: Subtotal filling (5-95%)	15	11.3
C: Entry remnant (<5%)	5	3.8
D: No filling (0%)	2	1.5
Total	133	100.0

The majority of aneurysms immediately after stenting had a filling grade of A occupying 83.5 %. Cases of complete occlusion of the aneurysm right after intervention due to coil and stent placement.

- **Treatment results:**

Table 5: *Results of aneurysms obstruction right after intervention, after 3 months and 6-12 months (Roy - Raymond's Classification):*

Filling grade	*After 3 months*		*After 6-12 months*	
	N	%	N	%
A: Total filling (>95%)	55	82.1	57	95
B: Subtotal filling (5-95%)	12	17.9	3	5
C: Entry remnant (<5%)	0	0	0	0
Total	67	100%	60	100

In 134 cases, there were 17 new cases that were not checked. 67 cases follow-up after 3 months and 60 cases follow-up after 6 - 12 months. The remaining cases were lost connection. Total occlusion rates were 82.1% after 3 months and 95% after 6-12 months.

Table 6: *Mild and severe complications*

	N	%
Spasm	10	7.5
Dissection	3	2.2
Ischemic Stroke	3	2.2
Dead	2	1.5
Total	18	13.4

The incidence of severe complications accounted for 8/134 cases (6%), including dissection: 3 cases, cerebral infarction: 3 cases, and death: 2 cases (Subarachnoid hemorrhage

grade 4 according to Fisher's Classification after 2 weeks and due to aneurysm rupture, stent obstruction).

IV. DISCUSSION

1. Characteristics of patient groups:

Our sample included 130 patients with a female / male ratio of 3.32, and an average age of 50, consistent with foreign authors [10, 11], cases of cerebral aneurysm <18. ? The age should not be indicated for the flow diverter stent but should be treat by other methods because the artery has not yet been not fully developed.

2. Morphology of challenging aneurysms:

Localization: we found that most common locations of challenging aneurysms were the cavernous and para-ophthalmic segments, otherwise multiple aneurysms at different segment of internal carotid artery, accounting for 35.1%, 40.3% %, 11.9%. On the other hand, there was quite rare aneurysm located in the lower segments of internal carotid artery because this segment runs inside the petrous bone and its wall is thicker. In many cases, the aneurysms had some branches, so it was quite difficult to preserve these branches with coiling. The wall of stents is mesh designed to ensure not to slow down the flow of these branches [12].

Dimensions: Average diameter of aneurysms was 6.6mm (± 5,3), in which the smallest was 1.7mm, the largest was 28mm. Average height of aneurysm was 7.2 mm (± 6,3), of which the largest was 39mm, the smallest was 2mm, the average neck diameter was about 5.1mm, similar to Nelson's study [11].

Morphology: The incidence of wide-neck aneurysms <10 mm, > 10 mm, and > 20 mm, are 64.2%, 9% and 9%, respectively, these aneurysms have high rate of revascularization as well as high ability to migrate coil. Although the balloon-assisted coiling method could be performed, however, in many cases this method was difficult to perform if needing to preserve the branches arising from the wall of the aneurysm. Small aneurysms of <3mm in diameter or multiple aneurysms on a parent artery were also inconvenient for coiling. In five patients with blister-like aneurysms, one patient had subarachnoid hemorrhage treated through out acute phase, was successfully reconstructive treated with stent and coil. Although blister-like aneurysms have small size (<3mm), but they have very fragile wall due to dissection. In contrast, the giant one can hardly be completely packing by coil, but the combination of coil and stent can make progress blood clotting intra-aneurysmal and reduces the risk of displacement of stent into sac.

3. Technical characteristics:

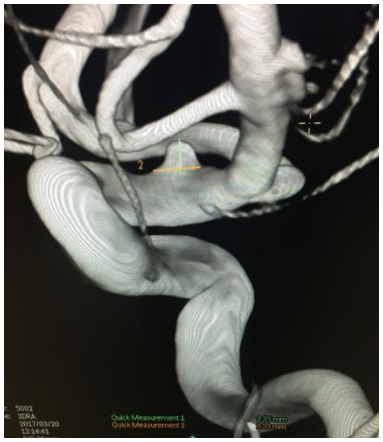
The average diameter of the stent used was 4.3mm (± 0.38), mean stent length: 21.6mm (± 4.6). The size of the stent depends on the diameter of the damaged arteries and is sizing based on software of the angiogram. If the stent is too large for the vessel, it will not open like design leading to thrombus formation earlier in the aneurysm. If the stent is smaller than the diameter of the vessel, there is a risk of leaking or displacement. The technical success rate was 129 cases, accounting for 96.3%, consistent with similar studies [11]. 5 unsuccessful cases accounted for 3.7% due to the stent did not open, displacement of the stent to the sac or stent obstruction. The stent did not fully open in 5.2% of cases and needed to ballooning with good results. The cases of

stent mildly migrated but still completely covered the aneurysm neck or dissection without symptoms did not need to do more but needed to follow up the progressing. Two cases of giant aneurysms had obstruction of stent. Navigation the giant aneurysm was very difficult because of turbulent flow; some solutions had been applied as a wire-loop technique or used solitaire stent or snared to fixe the top of micro catheter... [13].

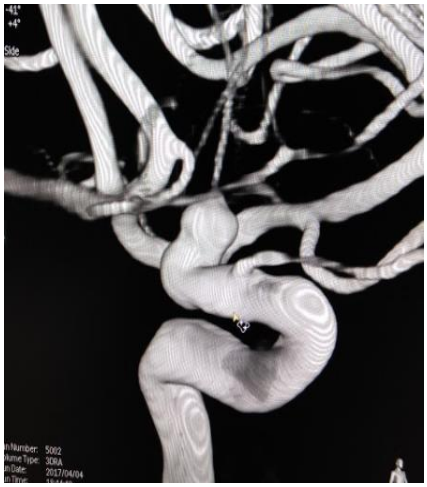
Right after deploying the stent, A1, A2, A3 grades of angiographic filling according to the OKM scale were seen in majority with 111 cases, accounting for 83.5%, highly in the aneurysm less than 10mm. In contrast, the giant aneurysms had grade higher according to thrombosis [9]. In two cases, the aneurysms obstruction was seen immediately after procedure due to coil and stent combination. We applied the OKM classification to compare the dynamics of flow in the aneurysm before and right after the stenting, but it did not replace the Roy-Raymond classification [14].

a.

b.



c.



d.

e.

f.

Figure 1: *Male patient, 49 years old, admitted to hospital with headache, GSC: 15. CT-scan images show subarachnoid hemorrhage of two hemispheres (a), and after 2 weeks (b). DSA image show a blister-like aneurysm of anterior choroidal segment of the right internal carotid artery (c, d). Good results with entry remnant filling (grade C) after coiling and deploying 1 stent Pipeline.*

4. Outcome and Complications:

CT Angio and MRAngio of 67 cases were recorded after 3 months follow up. The rate of aneurysm complete occlusion, stent patency and normal cerebral parenchyma accounted for 82.1%, consistent with Lubicz's study [15], and increased after 6-12 months to 95%. The rate of aneurysm uncompleted occlusion, stent patency and normal cerebral parenchyma accounted for 17.9%, seen commonly in large aneurysms > 10 mm, but the overall size of the aneurysms decreased. Small one (<10 mm) tend to disappear rather than thrombosis, as observation on images. CT-Scan had higher resolution than MRI in evaluating stent patency, stenosis, as well as better observation to size the remnant part. In fact, MRI is superior in the diagnosis of cerebral infarction. No cases of rupture have been reported later if technique was successful. This was the advantage of this method compared to coiling or surgical methods.

Giant sac had a high risk of rupture if one tip of the stent displaced into the aneurysm leading to hemorrhage. In our study, a patient with a giant aneurysm have ruptured into cavernous sinus after placement of the stent. After blocked by a detachable silicone balloon occlusion, then dilated stent, angiogram showed good circulation flow, however, there was widespread left hemisphere ischemic stroke with hemorrhagic transformation leading to death. This was the case where the shortened stent is tipped into the aneurysm leading to hemodynamics disturbances and rupture, long time of intervention lead to the formation of clots intra-stent. In case of a fusiform aneurysm of V4 vertebral artery, shortened stent resulted in the head of the stent came down into the aneurysm, needing to place 1 supplementary stent, follow up shown good results.

V. CONCLUSION:

Challenging aneurysms accounts for the high incidence in the carotid artery at the cavernous and anterior choroid segments, the most commonly types were wide-neck and multiple sacs in one parent artery. Applying the flow diverter stent was a safe and effective treatment with high success rate (96.3%) and low complication (3.7%). Imaging follow-up was important to evaluate the state of aneurysm, parent vessel and cerebral parenchyma allows to make decisions for the patient. CT-Scan allowed better assessment of the aneurysm as well as the stent than MRI, but low sensitivity to small cerebral infarct lesions.

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RÉSUMÉ:

UTILISATION DU STENT VISANT A DEVIER LE FLOT SANGUIN DANS LE TRAITEMENT DES ANÉVRYSMES CÉRÉBRAUX DEFIANTS: RÉSUMÉ DES SERIES DE L'HÔPITAL BACH MAI, ET DE L'HOPITAL DE L'UNIVERSITÉ DE MÉDECINE DE HANOI

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Le but de cette étude est de rapporter notre expérience sur les anévrysmes cérébraux défiants, les résultats du traitement par le stent visant à dévier le flot sanguin, et son suivi.

Méthode: 130 patients consécutifs, soumis à 134 procédures sont suivis à l'hôpital Bach Mai, et l'hôpital de l'Université de Medécine de Hanoi, de Janvier 2012 àAvril 2017. Les stents suivants on été utilisés: Pipeline, Fred, et Silk. La morphologie des anévrysmes, l'intégrité du stent, et le parenchyme cérébral avant et après l'intervention, ont été analysés par DSAA, MSCT, et MRI. Les données après 3-6 mois et 12 mois ont été enregistrées.

Résultats: L'étude recrute 130 patient (F/H: 3.32). Les anévrysmes cérébraux défiants de la carotide interne sont les plus fréquents (92.6%), en particulier les anévrysmes caverneux (35.1%), et ceux des segments paraophtemiques (40.3%), 83 (61.9%) sont des anévrysmes à large entrée, et 16 cas d'anévrysmes multiples (11.9%), et seulement 5 (3,7%) sont des anévrysmes prenant le forme d'ampoules. Le traitement endovasculaire a été effectué avec succès chez 94.8. Le stent n'a pu être utilisé chez 3 patients. Le taux de mortalité et de morbidité ont été de 1.5% et 3.7% respectivement. Le suivi par MRI et MSCT en 3 mois a montré l'occlusion complète, et imcomplète des anévrysmes chez 75.4% et 17.5% respectivement. L'accident thromboembolique (4.3%) est survenu chez 3 patients.

Conclusions: Les anérvrysmes cérébraux a grand défi, caverneux, et des segments paraophtalmiques de la carotide interne sont fréquents sous forme d'entrée large et d'ampoules. Le déploiement du stent visant à dévier le flot sanguin est à risque minime, efficace, et comporte peu de complications liées a la procédure.

SURVEY OF URINE NEUTROPHIL GELATINASE - ASSOCIATED LIPOCALIN IN PATIENTS WITH ACUTE KIDNEY INJURY

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ABSTRACT

Objective: To evaluate the diagnostic, severity classification and prognostic value of urinary neutrophil gelatinase-associated lipocalin (uNGAL) in patients with Acute Kidney Injury (AKI) admitted to the emergency department (ED). ***Subjects and methods:*** Overall, there were 101 patients who actively participated in this study. These patients were admitted to the ED of Trung Vuong Hospital, Ho Chi Minh city and fulfilled the KDIGO criteria of AKI. A total of 40 healthy controls were comprised of the control group. The uNGAL examination procedure had been perfomed on all 96 patients (5 of the patients were excluded due to having anuria) and in the control group. ***Results:*** Average urinary NGAL level of AKI group (412.26 ng/ml) was significantly higher than the control group (10.74 ng/ml) with $p < 0.001$. All of AKI patients (100%) in our study had shown an increment in their urinary NGAL concentrations. The concentration of urinary NGAL had increased significantly along with the stage of AKI with $p < 0.001$. The uNGAL levels were higher among the non-survivors than in survivors ($p < 0.001$). Using uNGAL as the cutoff value at 503.16 ng/mL to estimate the mortality rate among AKI patients had concluded the sensitivity of 72.2%, the specificity of 73.19%, and the AUC of 0.840. ***Conclusion:*** Urinary NGAL is valuable for the diagnosis, severe classification, and prognostication of acute renal failure patients in the ED.

Keywords: *AKI, urine NGAL.*

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I. INTRODUCTION

Acute kidney injury (AKI) is defined as an abrupt or rapid decline in renal filtration function. This condition is usually marked by a rise in serum creatinine concentration or by azotemia. Acute kidney failure can occur for various reasons. The most common reasons are: acute tubular necrosis, severe or sudden dehydration, toxic kidney injury from poisons or certain medications, autoimmune kidney diseases, such as acute nephritic syndrome and interstitial nephritis, urinary tract obstruction [1]. The diagnosis of AKI is usually based on either an elevation of serum creatinine or the detection of oliguria. Unfortunately, creatinine examination results could be both a delay factor as well as an unreliable indicator of AKI occasionally. Moreover, after getting a kidney injury, the BUN or creatinine levels among patients may be perceived as normal, hence the only sign of a kidney injury is the decrement in urine production. Therefore, the lack of early biomarkers has crippled our ability to performed valuable therapies upon AKI patients in time.

Neutrophil gelatinase-associated lipocalin (NGAL) is a protein, belonging to the lipocalin superfamily. NGAL was initially found in activated neutrophils, in accordance with its role as an innate antibacterial factor. However, it subsequently appeared that many other types of cells, including those kidney tubule, may produce NGAL in response to various injuries. The increase in NGAL production and release from tubular cells after harmful stimulating of various kinds may have been the self-defensive mechanism based on the activation of specific iron-

dependent pathways, which in all probability also represent the mechanism through which NGAL promotes kidney growth and differentiation [2].

Several studies have shown uNGAL, a marker of renal tubular inflammation rather than glomerular filtration, and can be used as the marker for early diagnosis and prognosis of AKI in ICU patients [3],[4]. In Vietnam alone, numerous studies on the role of NGAL in AKI patients have been implemented recently. One as such was the thesis of Ta Anh Tuan (2012) which referred to the urinary NGAL concentration in severe kid patients with AKI [5]. However, the shortage of studies on the role of urinary NGAL in early diagnosis and prognosis AKI in adult patients is apprehensive. Therefore, we conducted this research for the aim "Evaluation the diagnostic, severity classification and prognostic value of urinary uNGAL in patients with AKI in the ED".

II. SUBJECTS AND METHODS

1.1.Subjects

* The study was conducted with a study group of 101 AKI patients admitted to the emergency department, Trung Vuong Hospital, Ho Chi Minh city from 12/2013 to 01/2017 and a control group of 51 healthy people.

* Excluding criteria: Patients with chronic kidney failure who did not fit with diagnostic criteria, did not do enough test results or did not agree to participate in the study.

* Because of 5 cases with anuria, we only studied on uNGAL concentration of 96 AKI patients.

1.2. Methods

* Study design: A prospective, cross-sectional descriptive study

* Urinary NGAL measurement: 24-hour urine was collected. After that, the volume of urine before collecting 1 ml sample for testing purpose. uNGAL the by the sandwich ELISA method using NGAL monoclonal antibody in the NGAL kit. After that, the sample will be analyzed by Architect System of Abbott, America to measure uNGAL concentration.

1.3.*Diagnostic criteria:* KDIGO (Kidney Disease Improving Global Outcomes) definition and classification of AKI [6]

* Diagnostic criteria for AKI: Serum creatinine increase ≥ 0.3 mg/dl (26.5 µmol/l compared to basic creatinine within 48 h or urine volume < 0.5 ml/kg BW/hour at least 6 hours.

* AKI degree:

- AKI degree 1: Serum creatinine < 220.0 µmol/l

- AKI degree 2: Serum creatinine from 220.0 - 353.6 µmol/l

- AKI degree 3: Serum creatinine ≥ 353.6 µmol/l

1.4.Statistical analysis: Statistical analyses were conducted using SPSS 23.0

III. RESULTS AND DISCUSSIONS

Table 1. *Urine NGAL concentration in study group*

Index		Control group (n=51)	Study group (n=96)	p
Urinary NGAL (ng/ml)	$\overline{X}$ ± SD	10.74 ± 5.18	412.26 ± 324.91	< 0.001
	Max	20.28	1292.38	
	Min	3.32	69.63	

The average concentration of urinary NGAL in our study group was 412.26 ng/ml which was significantly higher than in control group (10.74 ng/ml) with p < 0.001. The maximum and minimum concentration of urinary NGAL was 1292.38 and 69.63 ng/ml respectively. With the reference range of urinary NGAL from 0.38 to 21.1 ng/ml, all of the AKI patients (100%) had urinary NGAL elevation. Elevation of urinary NGAL common in AKI patients. All studies confirmed that 100% of patients with AKI had increased uNGAL [7],[8]. Mohamud Egal et al found that NGAL was a predictor for AKI in the univariate and multivariate analysis; cutoff value for AKI was 250 ng/ml for urinary NGAL (PPV 58%; NPV 78%). The study of Ramprasad Matsa concluded that uNGAL were significantly higher in the patients who developed AKI (436 ng/mL) compared to the non-AKI patients 342 ng/mL, p < 0.001.

Table 2. *Relation between Urine NGAL concentration and stage of AKI (n = 96)*

AKI Stages (KDIGO)	n	%	Urine NGAL (ng/ml)
1	68	70.8	230.58 ± 146.29
2	21	21.9	796.92 ± 147.77
3	7	7.3	1023.20 ± 179.70
pANOVA			< 0.001 p1-2, p1-3 < 0.001, p2-3 = 0.002

According to the KDIGO classification, the stage 1 AKI in our study made up the highest proportion (70.8%). Stage 2 and 3 occupied smaller proportion (21.9% and 7.3% respectively). Our results also pointed that patients' uNGAL concentrations at the time of admission were significantly related to their KDIGO stage (p < 0.001). This result was similar to the study of Geus H.R. [9] and Royakkers A.A. [10] when research on the relation between uNGAL and RIFFLE stage. Moreover, the author found that uNGAL adds significant accuracy to the prediction of the development of severe AKI in combination with eGFR alone or with other clinical parameters and has an interesting predictive value in patients with normal serum creatinine [9].

Table 3. *Correlation between Urine NGAL and mortality in AKI patients*

Outcome	n	%	Urine NGAL (ng/ml)
Survivors	70	72.92	356,72 ± 284,25
Nonsurvivors	18	18.75	735,79 ± 330,55
P			< 0.01

In our study, uNGAL levels were significantly higher in nonsurvivors than in survivors (p < 0.001). The average concentration of urinary NGAL in the survivors group was 356,72 ng/ml while the level of uNGAL in the non-survivors group was 735,79 ng/ml. We used the receiver operating characteristic (ROC) curve to determine the value of urine NGAL in the diagnosis of mortality in AKI patients. The results showed that uNGAL at 503.16 ng/ml had a sensitivity of 72.2% and specificity of 73.19%, area under the curve of 0.840, p < 0.01. When comparing the results with other authors, we found that there was a correlation in the assessment of uNGAL values in predicting of mortality in AKI patients. Matsa R. et al. [8] concluded that uNGAL levels were significantly higher in the patients who died (52.5 ng/ml versus 190 ng/ml).

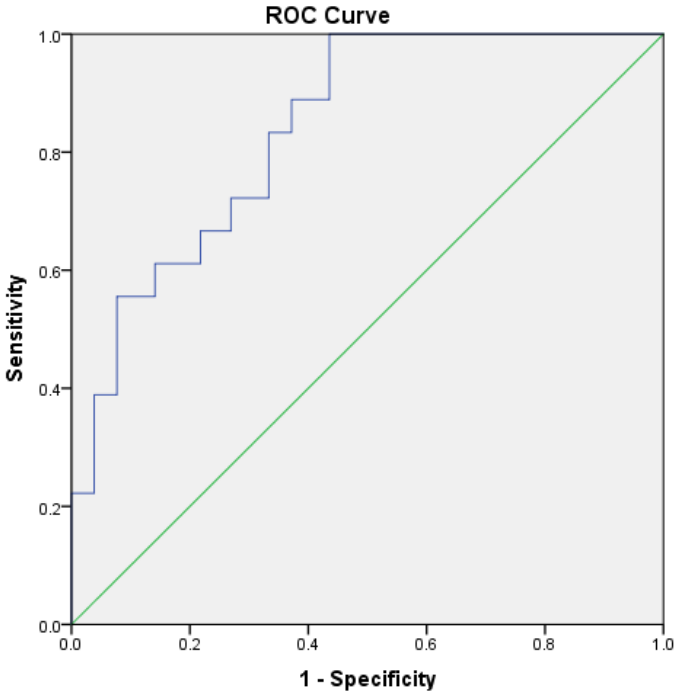

Chart 1. *ROC curve of uNGAL level for predicting mortality in AKI patients*

- *AUC = 0,840 (p < 0,001)*
- *Cut-off: 503,16 ng/ml.* Sensitivity: 72.2%. Specificity: 73.19%

IV. CONCLUSIONS

In our study, average urinary NGAL level of AKI group (412.26 ng/ml) was significantly higher than the control group (10.74 ng/ml) with p < 0.001. All of AKI patients (100%) in our study increased urinary NGAL concentration. The concentration of urinary NGAL increased significantly along with stage of AKI with p < 0.001. uNGAL levels were higher in nonsurvivors than in survivors (p < 0.001). Using a uNGAL cutoff value of 503.16 ng/mL for predicting mortality in AKI patients, the sensitivity was 72.2%, specificity was 73.19%, the AUC was 0.840.

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RÉSUMÉ:

VALEUR DIAGNOSTIQUE ET PRONOSTIQUE DE LA LIPOCALINE ASSOCIÉE À LA GÉLATINASE DANS LES CELLULES NEUTROPHILES URINAIRES DU PATIENT AVEC LÉSION URINAIRE AIGUE

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Objectif: Evaluer le diagnostic, la classification de sévérité, et la valeur pronostique de la Lipocaline associée à la gélatinase dans les cellules neutrophiles urinaires (uNGAL) chez les patients avec lésion rénale aigue (AKI) admis au department des urgences (ED).

***Sujets et méthode*:** Il y avait en tout 101 patients qui avaient participé activement à l'étude. Ces patients ont été admis dans l'ED de l'hôpital Trưng Vương, ville de HCM, répondant aux critères d'AKI suivant KDIGO.

Un total de 40 volontaires en bonne santé ont été recrutés pour le groupe contrôle. L'examen pour uNGL a été fait sur 96 patients (5 ont été exclus pour cause d'anurie), et sur le groupe contrôle.

Résultats: La moyenne de uNGAL chez le groupe avec AKI (412.26 ng/ml) est sensiblement supérieure au groupe de contrôle (10.74ng/ml), avec $p < 0.001$. Tous nos patients avec AKI (100%) de notre étude avaient montré une nette augmentation de concentration de leur NGAL urinaire. Cette concentration augmentait suivant le degré de AKI avec $p < 0.001$. Les uNGAL etaient chez les non - survivants supérieures aux survivants ($p < 0.001$). Le uNGAL de 503.16/ng/ml étant choisi comme valeur de référence (cutoff value), dans l'estimation de la mortalité chez les patients avec AKI, la sensivité sera de 72,2% la spécificité 73.19% et la région sous la courbe (AUC) 0.849.

Conclusion: uNGAL est utile pour le dagnostic, la classification de sévérité, et le pronostic de l'insuffisance rénale aigue des patients dans les ED.

Mots cles: *AKI, uNGAL*

CEREBRIFORM NEVUS: A RARE DISORDER

Nguyen Nham Quynh Anh*, Nguyen Roan Tuat*, Thai Duy Quang*

ABSTRACT

We present a case of cerebriform nevus in an 6 year-old girl. The lesion had been present since birth and had gradually increased in size, and good result obtained with total excision and local flap coverage. Since it carries the risk of malignant melanoma or infection, the lesions may be aesthetic problems. there is importance of early diagnosis, regular follow-up and management of this rare condition. The cerebriform nevus is a benign tumor, which may appear at birth or at an early age. Its located on the scalp, and its external appearance is similar to that of the brain.

I. CASE REPORT

A 6 years old girl presented to our plastic surgery department with a swelling on of the scalp which was present since birth and was gradually progressive. The patient also gave the history of hair loss in the area of swelling since birth. There was no family history of the similar disorder.

On dermatologic examination, there was 4x4 cm mass which confirmed to the left half of the scalp involving left occipital (fig1). It was non tender and soft to firm in consistency. There was congenital, raised, yellowish, colored plaques with fibroelastic consistency, with deep folds in the lowermost part of the swelling in parietal and occipital regions. There were mild scaling and atrophy of skin along with alopecia over swelling.

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Pediatric examination: Routine blood investigations were normal. There were no cardiac or ophthalmic changes. Neuropsychomotor development was normal. CT scan of the head showed infiltration of the lesion in the subcutaneous fat with bone involvement

The histopathologic examination revealed acanthosis, hyperkeratosis, papillomatosis and follicular plugging in the epidermis. the upper dermis showed underdeveloped hair follicles with sebaceous glands There was dilatation of the emtry hair follicles, surrounded by nests of nevus cells with apparent pigmentation has deeper parts of the lesion with increased collagen fiber. The hair follicles and sebaceous glands surrounded by nevus cells without atypia (fig3)

II. DISCUSSION

Cerebriform intradermal nevus is a rare disorder that usually presents at birth or early life that is also called pseudo or sencondary cutis verticis gyrata. Clinically CIN is characterized by a well demarcated cerebriform skin surface, usually on the parietal area of the scalp. CIN shows as an asymmetric, skin colored, and of alopecia or sparse hair within the lesion is common with folds accompanied by thickening of the skin. Patients with CIN usually have normal intelligence. A higher incidence of the disease is reported in females. Pruritus, burning sensation and pain may occur. On histological examination, intradermal nevus cells are seen throughout the full thickness of the dermis. Neuroid transformation may be seen in the deeper parts of the lesion with increased collagen fibers. Hair follicles can either be normal or atrophic. No systemic diseases have been reported to be associated with CIN. Some researchers consider giant congenital melanocytic nevi and CIN to be related conditions and they believe that CIN is a rare form of congenital melanocytic nevi because of histopathological similarities. However, other authors suggest that CIN is a separate disorder which is usually not pigmented with a few nevus cell nests at the dermoepidermal junction, and of alopecia or sparse hair within the lesion is common. Surgical excision and plastic reconstruction are frequently performed because of the risk of malignant transformation and aesthetic reasons. When they are not possible, close follow-up is mandatory. Each individual case requires a specific decision of whether to excise the lesion surgically or follow a wait-and-see policy. Because of the possibility of

progression to melanoma, follow-up of the patients with congenital nevus is essential.

III. CONCLUSION

Cerebriform nevus is one of the rare causes of cutis verticis gyata. Apart from its cerebriform appearance, the major part of the surface of the scalp was smooth. Because of the risk of malignant transformation, complete excision before puberty is often recommended

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RÉSUMÉ:

LE NAEVUS CÉRÉBRIFORME: UNE MALADIE RARE

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Nous présentons un cas de naevus cérébriforme chez une enfant de 6 ans. La lésion a été retrouvée dès la naissance, et s'était développée en grosseur, et le résultat de l'excision totale et de couverture avec un pan de tissu local a été satisfaisant. Comme la lésion comporte le risque de transformation en mélanome malin ou d'infection, en plus des problèmes esthétiques, l'importance est grande du diagnostic précoce, du suivi régulier, et du traitement de cette maladie rare. Le naevus cérébriforme est une tumeur bénigne, faisant son apparition dès la naissance ou le jeune aghe, il est localize sur le scalp, et son apparence rappelle le cerveau.

THE VALUE OF ORTHOPANTOMOGRAPHY AND CONE BEAM COMPUTED TOMOGRAPHY IMAGING IN MANDIBULAR THIRD MOLAR SURGERY

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ABSTRACT

Objective: To compare the accuracy of orthopantomography (OPG) with cone beam computed tomography (CBCT) imaging in defining the dimensions and shapes of mandibular third molars. ***Materials and method:*** the sample consisted of 60 mandibular third molars of patients examined and treated for surgical extraction at the Department of Oral Surgery, Hanoi National Hospital of Odonto-Stomatology, from August 2014 to August 2015. Tooth measurements were obtained on OPG and CBCT films and then clinically, following tooth removal. ***Results:*** The mean root lengths measured on radiographs were: 9,5 ± 1,9mm for OPG and 10,2 ± 1,1mmfor CBCT. The mean differences as compared to measurements done clinically were: -1,0 ± 2,1mm for OPG and -0,5 ± 1,5mm for CBCT. The mean tooth lengths measured on radiographs were: 16,5 ± 2,5mm for OPG and 16,8 ± 1,3mm for CBCT. The mean differences as compared to direct measurements (17,7 ± 1,1mm) were: -0,6 ± 2,1mm for OPG and -0,6 ± 1,0mm for CBCT. The mean of largest root widths measured on radiographs were: 9,3 ± 8,9mm on OPG and 8,6 ± 1,1mm on CBCT. The mean differences as compared to direct measurements (8,7 ± 2,0mm) were 1,8± 13,8mm for OPG and -0,1 ±1,5mm for CBCT. There was a concordance in roots number between clinical inspection with CBCT imaging but not with OPG. Concerning root shapes, convergent roots were found in 49% cases and divergent roots in 21.51% ones. Straight shaped roots were more prevalent (63.44%) than curved shaped roots (35.48%). Clubbed shaped roots were found in only one case (1.08%). The rates of complications associated with different malpositions were: 66,67% for mesioangular, 55,56% for vertical and 33.33% for distoangular. The rates of complications associated with malpositions asclassified according to Pell and Gregory(1933) were: 65,52% for Class A, 85,19% Class Band 62,5% for Class C. ***Conclusion:*** There was some discrepancy between measurements done on both radiography imaging with direct measurements. CBCT imaging demonstrated a higher accuracy over OPG in defining the sizes and shapes of mandibular third molars and therefore would a better investigation method to be used in their surgical removal.

Keywords: *Mandibular third molar, Orthopantomography, Cone beam computed tomography*

I. INTRODUCTION

The impacted mandibular third molar (MTM) is often the cause of local and systemic disturbanceswhich may sometimes lead to severe complications. This is partly related to the morphology and site of eruption of this particular tooth. Careful clinical examination and radiographic investigation are thus required for the treatment planning and surgical removal of MTM.

Radiographic imaging commonly used to assist in MTM removal are orthopantomograms (OPG) and Cone beam computed tomograms (CBCT). OPG provides useful information for the diagnosis and surgical treatment, however it lacks of

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accuracy in assessing the position, morphology and orientation of the tooth crown as well as the number and size of the dental roots. Besides supplementing to OPG limitations, CBCT allows an accurate estimation of anatomic stuctures related to MTM such as the second molar distal bony septum and the mandibular canal. The aim of this study was to compare some MTM morphological and dimensional parameters assessed on OPG and CBCT with measurements done clinically following tooth removal.

II. SUBJECTS AND METHOD

2.1 Subjects: this study was conducted on patients who presented at Hanoi National Hospital of Odonto- Stomatology, from August 2014 to August 2015.

***** Selection criteria:

- Patients requesting MTM extraction
- Patients accepting radiographic investigation with OPG and CBCT

* Exclusion criteria:

- Patients suffering from systemic conditions: allergy, cardiovascular diseases, diabetes, blood dyscrasias
- Non-cooperative patients
- Patients refusing X-ray radiography

2.2 Method: Cross-sectional study

*Sample size: according to sample size calculation for cross sectional study, n= 58.

The number of MTM included in the study was: 60

*Instruments and devices: electronic precison caliper with positioning indication, Mitutoyo, Japan, the resolution was of 0,02mm

2.2.1. Research process:

- Step 1: clinical examination and information recording
- Step 2: assessment of clinical signs and symptoms: swelling, trismus, pain …
- Step 3: intraoral measurement with caliper to evaluate: tooth position, its inclination to the second molar, the distance from the occlusal face of the second molar to the most superior convex point of MTM, the distance between the most mesial convex point of MTM crown to the ramus gingival border (internal turning point of the ramus and mandibular body)
- Step 4: radiograph taking and evaluation of morphological parameters on OPG and CBCT
- Step 5: MTP extraction and measurement by direct clinical examination
- Step 6: data processing with SPSS 16.0

Comparison test of ratios and Fisher exact test (in case of frequency < 5) were applied for statistical analysis. The significant value was set at $p < 0,05$.

2.2.2 Variables

Independent variables: age and gender

Dependent variables: MTM position, distance from MTM to related anatomical structures.

III. RESULTS AND DISCUSSION

The comparison between OPG, CBCT imaging and clinical examination following surgical extraction issued the following results.

3.1. Crown length of MTM (CL)

Table 3.1: *Mean crownlength of MTM*

	OPG		CBCT		Clinical examination		p
	n	Crown length (mm)	n	Crown length (mm)	n	Crown length (mm)	
38	34	7,3 ± 0,9	34	6,7 ± 0,9	34	6,9 ± 0,6	> 0,05

48	26	7,3 ± 1,1	26	6,5 ± 0,7	26	7,3 ± 0,7	> 0,05
Total	60	7,3 ± 1,0	60	6,6 ± 0,8	60	7,0 ± 0,6	> 0,05

Table 3.2: *Mean difference between OPG imaging, CBCT imaging and clinical examination*

MTM	CL difference between OPG and clinical measurements		CL difference between OPG and clinical measurements		p (Wilcoxon signed-rank test)
	n	Δ (mm)	n	Δ (mm)	
38	34	0,4 ± 1,1	34	-0,1 ± 0,9	< 0,05
48	26	0,2 ± 1,5	26	-0,3 ± 0,6	< 0,05
Total	60	0,3 ± 1,3	60	-0,2 ± 0,9	< 0,05

The mean crown length measured on OPG was: 7,3 ± 1,0mm on BCT, it was: 6,6 ± 0,8mm. The differences as compared to visual examination were 0,3 ± 1,3mm and -0,2 ± 0,9mm respectively for OPG and CBCT. The higher accuracy of CBCT over OPG was statistically significant with P < 0.05.

3.2. Mesiodistal crown width of MTM (MDCW)

Table 3.3. *Mean Mesiodistal crown width*

MTM	OPG		CBCT		Clinical examination		p
	n	MD crown width (mm)	n	MD crown width (mm)	n	MD crown width (mm)	
38	34	11,2 ± 1,8	34	11,4 ± 1,0	34	11,6 ± 1,1	> 0,05
48	26	11,6 ± 1,2	26	11,2 ± 1,2	26	12,2 ± 1,3	> 0,05
Total	60	11,3 ± 1,6	60	11,3 ± 1,0	60	11,8 ±1,2	> 0,05

Table 3.4: *Difference in mesiodistal crown width between OPG, CBCT imaging and clinical examination*

MTM	MDCW difference between OPG and clinical measurements		MDCW difference between CBCT and clinical measurements		p
	n	Δ (mm)	n	Δ (mm)	
38	34	-0,7 ± 2,4	34	-0,4 ± 0,7	> 0,05
48	26	-0,6 ±1,2	26	-0,6 ± 0,4	> 0,05
Total	60	-0,7 ± 0,2	60	-0,4 ± 0,6	> 0,05

The mean mesiodistal crown width measured on radiographs was 11,3 ± 1,6 mm on OPG and, 11,3 ± 1,0 mm on CBCT. The difference with clinical measurements was: -0,7 ± 0,2mm with OPG and -0,4 ± 0,6mm with CBCT. The difference in accuracy between the two radiographic imaging as compared to visual examination was not statistically significant with P > 0.05.

3.4. Rooth length of MTM (RL)

Table 3.5: *MTM root length*

MTM	OPG		CBCT		Clinical examination		p
	n	Root length (mm)	n	Root length (mm)	n	Root length (mm)	
38	34	9,5 ± 2,2	34	10,1 ± 1,2	34	11,1 ± 0,9	< 0,05

48	26	9,5 ± 1,3	26	10,4 ± 1,1	26	9,9 ± 1,6	< 0,05
Total	60	9,5 ± 1,9	60	10,2 ± 1,1	60	10,7 ±1,3	< 0,05

Table 3.6: *Difference in mean root length between OPG, CBCT imaging and clinical examination*

MTM	RL difference between OPG and clinical measurements		RL difference between OPG and clinical measurements		p
	n	Δ (mm)	n	Δ (mm)	
38	34	-1,2 ± 2,5	34	-0,9 ± 1,5	< 0.05
48	26	-0,5 ± 0,8	26	0,4 ± 0,6	< 0.05
Total	60	-1,0 ± 2,1	60	-0,5 ± 1,5	< 0.05

The mean root length measured on OPG was 9,5 ± 1,9mm, on CBCT it was 10,2 ± 1,1mm. The differences with direct measurements were:-1,0 ± 2,1mm for OPG and -0,5 ± 1,5mm for CBCT. The higher accuracy of CBCT over OPG was statistically significant with P < 0.05.

3.5. Total tooth length

Table 3.7. *MTM total tooth length*

MTM	OPG		CBCT		Clinical evaluation		P
	n	Tooth length (mm)	n	Tooth length (mm)	n	Tooth lenth (mm)	
38	34	16,6 ± 2,5	34	16,8 ± 1,2	34	18,0 ± 0,9	< 0,05
48	26	16,4 ± 2,6	26	16,8 ± 1,4	26	17,1 ± 1,1	< 0,05
Total	60	16,5 ± 2,5	60	16,8 ± 1,3	60	17,7 ± 1,1	< 0,05

Table 3.8: *Difference in mean tooth length between OPG, CBCT imaging and clinical examination*

MTM	TL difference between OPG and clinical measurements		TL difference between CBCT and clinical measurements		p
	n	Δ (mm)	n	Δ (mm)	
38	34	-0,7 ± 2,2	34	-0,9 ± 1,1	> 0,05
48	26	-0,7 ± 2,2	26	-0,07 ± 0,5	> 0,05
Total	60	-0,6 ± 2,1	60	-0,6 ± 1,0	> 0,05

The overall mean tooth length measured clinically was 17,7 ± 1,1mm. On OPG, it was 16,5 ± 2,5mm and on CBCT, it was 6,8 ± 1,3mm. The mean difference between visual examination was -0,6 ± 2,1mm with OPG and -0,6 ± 1,0mm with CBCT. Though CBCT demonstrated higher accuracy over OPG, the difference was not statistically significant with P > 0,05.

3.6. The number of MTM roots (RN)

Table 3.9: *MTA roots number*

MTM	OPG		Clinical examination		CBCT		p
	n	Mean roots number	n	Mean roots number	n	Mean roots number	
38	34	1,9± 0,3	34	2,0 ± 0,2	34	1,9 ± 0,2	

48	26	2,0 ± 0,0	26	2,1 ± 1,3	26	2,0 ± 0,2	
Total	60	2,0 ± 0,2	60	2,1 ± 0,3	60	2,0 ± 0,2	

Table 3.10: *Difference in roots number between OPG, CBCT and clinical examination*

MTM	RN difference between OPG and clinical examination		RN difference between CBCT and clinical examination		p
	n	Δ (mm)	n	Δ (mm)	
38	34	-0,2 ± 0,4	34	-0,1 ± 0,3	< 0,05
48	26	-0,1 ± 0,3	26	0,0 ± 0,0	< 0,05
Total	60	-0,2 ± 0,4	60	-0,1 ± 0,3	< 0,05

There was a difference in root number between clinical examination with OPG but not with CBCT

3.7. The largest root width of MTM (LRW)

Table 3.11: *Largest root width of MTM*

MTM	OPG		CBCT		Clinical examination		P
	n	Root width	n	Root width	n	Root width	
R38	34	8,2 ± 1,4	34	8,6 ± 0,9	34	9,1 ± 1,2	< 0,05
R48	26	10,6 ± 13,3	26	8,5 ± 1,2	26	7,6 ± 2,9	< 0,05
Chung	60	9,3 ± 8,9	60	8,6 ± 1,1	60	8,7 ± 2,0	< 0,05

Table 3.12: *Difference in largest root width between OPG, CBCT and clinical examination*

MTM	LRW difference between OPG and clinical examination		LRW difference between CBCT and clinical examination		P
	n	Δ (mm)	n	Δ (mm)	
38	34	-1,1 ± 1,0	34	-0,4 ± 0,5	< 0,05
48	26	0,9 ± 1,1	26	0,7 ± 2,7	< 0,05
Total	60	1,8± 13,8	60	-0,1 ±1,5	< 0,05

The mean largest root width measured clinically was 8,7 ± 2,0mm, on OPG it was 9,3 ± 8,9mm and on CBCT, 8,6 ± 1,1mm. The difference between clinical measurementswere: 1,8± 13,8mm for OPG and -0,1 ±1,5 for CBCT. The higher accuracy of CBCT imaging as compared to OPG was statistically significant with P < 0,05

3.8. Root morphology of MTM

Concerning root shapes, convergent roots were found in 49% cases and divergent roots in 21.51% ones. Straight shaped roots were more prevalent (63.44%) than curved shaped roots (35.48%). Clubbed shaped roots were found in only one case (1.08%).

Table 3.13: *Difference in root morphology between clinical examination and OPG, CBCT imaging*

Root morphology	OPG vs clinical examination		CBCT vs clinical examination	
	n	%	n	%
Concordance	16	51.6	23	74.2
Nonconcordance	15	48.4	8	25.8
Total	31	100	31	100

The rates of complications associated with different malpositions were noted as: 66,67% for Mesioangular, 55,56% for Vertical and 33.33% for Distoangular. The rates of

complications associated with malposition classified according to Pell and Gregory (1933) were: 65,52% for Class A, 85,19% Class B and 62,5% for Class C.

IV. CONCLUSION:

There was some discrepancy between measurements done on both OPG and CBCT imaging and direct measurements. CBCT imaging demonstrated a higher accuracy over OPG in defining the sizes and shapes of mandibular third molars and therefore would a better investigation method to be used in their surgical removal.

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RÉSUMÉ:

VALEUR DE L' IMAGERIE ORTHOPANTOMOGRAPHIQUE ET TOMOGRAPHIQUE À FAISCEAU CONIQUE DANS LA CHIRURGIE DE LA DENT DE SAGESSE INFÉRIEURE

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Objectif: Comparer la précision de l'imagerie orthopantomographique (OPG) et celle de l'imagerie tomographique par faisceau conique (CBCT) dans la détermination des dimensions et formes de la dent de sagesse inférieure. ***Matériel and méthode****:* l'échantillon est composé de 60 dents de sagesse inférieures de patients venant pour consultation et traitement chirurgical au Département de Chirurgie Buccale de l'Hôpital National d'Odonto-Stomatologiede Hanoi, d' Août 2014 à Août 2015. Les mesures ont été réalisées sur les clichés OPG and CBCT puis par examen visuel en clinique sur dents extraites. ***Résultats****:* la longueur moyenne des racines dentaires mesurées sur les clichés radiographiques était de**:** 9,5 ± 1,9mm sur OPG et 10,2 ± 1,1mm sur CBCT. La différence moyenne avec les mesures directes était de: -1,0 ± 2,1mm pour OPG et -0,5 ± 1,5mm pour CBCT. La longueur dentaire moyenne mesurée sur clichés radiographiques était de 16,5 ± 2,5mm sur OPG and 16,8 ± 1,3mm sur CBCT. La différence moyenne avec les mesures directes(17,7 ± 1,1mm) était de: -0,6 ± 2,1mm pour OPG et -0,6 ± 1,0mm pour CBCT. La plus grande largeur radiculaire

moyenne était de: 9,3 ± 8,9mm surOPG et 8,6 ± 1,1mm sur CBCT. La différence moyenne avec les mesures directes(8,7 ± 2,0mm) était de 1,8± 13,8mm pour OPG et-0,1 ±1,5mm pour CBCT. Il y avait concordance sur le nombre de racines entre l'examen clinique et l'imagerie avec CBCT mais pas avec OPG. Concernant les formes radiculaires, les racines convergentes ont été trouvées dans 49% des cas et les raciness divergentes dans 21.51%. Les racines droites étaient prévalentes (63.44%) par rapport aux racines courbées (35.48%). Les racines en "baguette de tambour" on téte notées dans un seul cas (1.08%). La fréquence des complications associées avec les différentes malpositions était de: 66,67% pour la mésioversion, 55,56% pour l' impaction verticale et 33.33% pour la distoversion. La fréquence des complications associées avec les malpositions classées selon Pell et Gregory (1933) était de: 65,52% pour la Classe A, 85,19% pour la Classe Bet 62,5% pour la Classe C. ***Conclusion:*** l'étude a montré une différence entre les mesures faites sur les clichés radiographiques et celles faites sur dents extraites. L'imagerie par CBCT a démontré une précision supérieure à celle par OPG dans la détermination des dimensions et formes des dents de sagesse inférieure et peutêtre ainsi être considérée comme une méthode d'investigation de choix dans la chirurgie de dent de sagesse inférieure.

***Mots clés**: Dent de sagesse inférieure, Orthopantomographie, Tomographie volumétrique à faisceau conique*

CLINICAL FEATURES AND CT SCAN IMAGING OF ECTOPIC TEETH IN NASAL AND PARANASAL SINUSES

Pham Thi Bich Dao*

ABSTRACT

The objective of the study was to describe the clinical features and CT scan imaging of ectopic teeth erupted in nasal and paranasal sinuses in relation with the indications for their surgical removal in order to add evidence to the diagnosis and management of this rare pathology. The sinonasal symptoms presented by the patients were: unilateral headache and facial pain (96.8%), stuffy nose on one side (54.8%), runny nose on one side (51.6%), nasal bleeding and swelling on one side (6.4%). Ectopic teeth were found in the nasal cavity in 12.9% cases, in the frontal sinus in 61,3% cases, in the maxillary sinus in 19.4% cases and in the ethmoid sinus in 6.4% cases. CT scan imaging detected one tooth in 83.9% cases, odontomas in 12.9% cases and multiple teeth in 3.2% cases. Clinical examination found missing upper tooth in 6.4% cases. In the nasal cavity, the frontal and maxillary sinuses, the mean size of the ectopic teeth was normal or bigger than normal, while in the ethmoid sinus it was smaller than normal.

Key words: *Ectopic teeth, sinuses, odontoma, nose bleeding/ epistaxis, missing teeth*

I. INTRODUCTION

In 1925, Abercombie reported the case of an English patient with persistent sanious purulent discharge on one side of the nose who was cured following the removal of an ectopic tooth making eruption in the floor of the nasal cavity [1]. In 1967, Tabib R. used the Jacques approach to remove an ectopic tooth in the frontal sinus of a patient [2]. Ectopic eruption is a disturbance in which the tooth makes eruption out of the dental arch such as in the nasal cavities or paranasal sinuses where it can cause various clinical manifestations. Tooth germs are formed during the sixth to tenth week of the embryo, they develop in the jaw bones and follow a normal course to make eruption on the dental arch. If, for any reason, this course is abnormal, they will become ectopic teeth [3]. The main manifestations of ectopic tooth in the nose and paranasal sinuses are: pain, especially if the tooth blocks the path of drainage of the sinus, and persistent sanious purulent discharge on one side which is resistant to conventional sinusitis treatment. The clinical diagnosis for patients presenting such symptoms should be supported by CT imaging of the sinus region. Radiographic imaging will confirm the presence of a toothlike structure, of the same radiopacity as bone, located in the middle of the sinus or next to the sinus wall. In case the ectopic tooth is located at the ostium of the sinus, it will block its drainage and clinical manifestations will be more severe. Ectopic toothlike structures could be seen as one tooth, an odontoma or multiple teeth [5]. Histopathological examination often shows that these structures are mainly composed of enamel tissue [6]. The asymptomatic ectopic teeth, which are accidently detected during other examination or treatment, do not have indication for removal, while the symptomatic ones undoubtedly need to be

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surgically removed [7]. This clinical study was conducted to describe the clinical features and CT scan imaging of ectopic teeth, erupted in nasal and paranasal sinuses along with their surgical removal implications in order to add evidence to the diagnosis and management of this rare pathology.

II. SUBJECTS AND METHOD

1. Subjects: patients with ectopic teeth in nasal and paranasal sinuses consulting at the National Hospital of Otolaryngology, Hanoi. The selection criteria were: patients with confirmed diagnosis of ectopic teeth in sinuses, presenting clinical sinonasal manifestations, having CT scan, accepting to undergo surgical removal and histopathological examination. The exclusion criteria were: surgical sample not confirmed as tooth by histopathological examination, patients refusing to join the study.

2. Method:

* Study design: Cross sectional study

* Study sample: 31 patients presenting at the National Hospital of Otolaryngology with confirmed diagnosis of ectopic teeth, from November 2011 to November 2015

* Positive diagnosis was based on: recurrent sinusitis on one side, pain on the same side of the head and face; purulent and sanious, sometimes bloody, nasal discharge; CT scan imaging showing toothlike radiopaque structure; upon surgical removal, odontoid structure resembling incomplete tooth with the presence of enamel substance as evidenced by histopathological examination.

* Data processing and analysis: statistical analysis was performed with SPSS 20.0 and the results presented as ratios and percentages.

* Ethical considerations: the patients volunteered to join the study and were free to leave the study at any time. All personal information were kept strictly confidential.

III. RESULTS

1. Clinical features

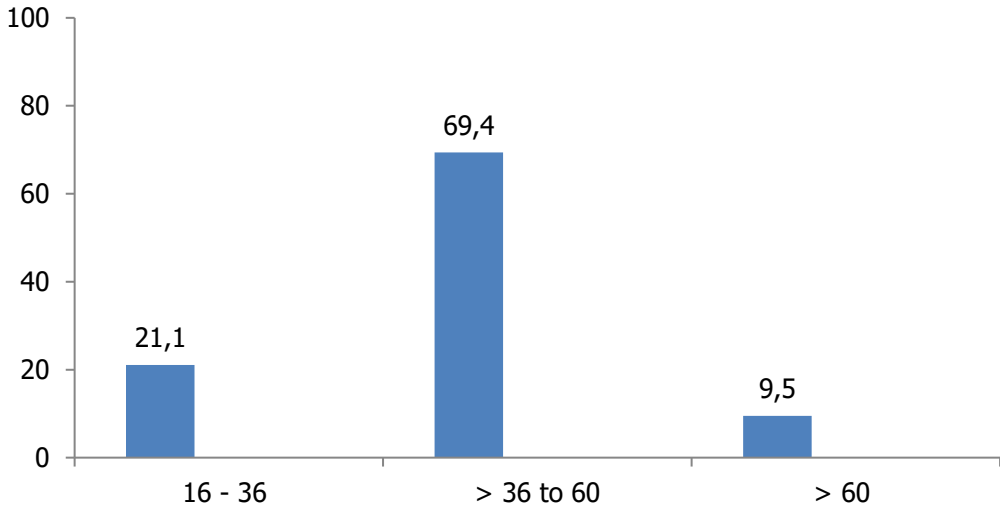

Chart 1. *Distribution of ectopic teeth according to age groups*

Ectopic teeth were most often found in the age group from 36 to 60 (69,4%), then from 16 to 36 (21,1%), and beyond 60 (9,5%).

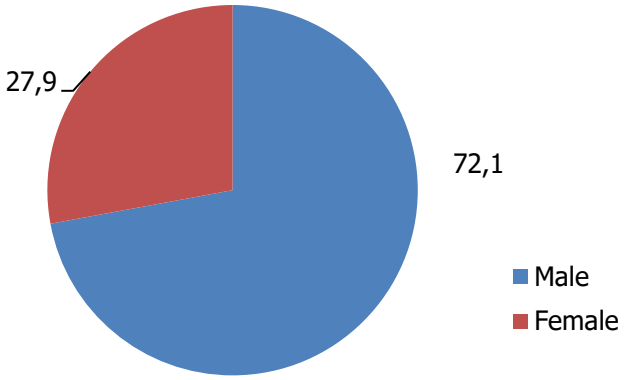

Chart 2. *Distribution of ectopic teeth according to genders*

Ectopic teeth were more prevalent in male (72,1%) than in female (27,9%).

Table 1. *Clinical signs and symptoms of ectopic teeth*

Clinical manifestations	n	%
Headache and facial pain	30	96,8
Stuffy nose on one side	17	54,8
Runny nose on one side	16	51,6
Facial swelling	2	6,4

Among the common complaints, headache and facial pain on one side was most prevalent (96,8%) , followed by stuffy nose on one side (54,8%), runny nose on one side (51,6%) and facial swelling on the same side (6,4%). Missing tooth on the upper dental arch was reported in only 2 cases (6,4%).

Pain was reported in 100% cases, when the ectopic tooth was located at the sinus ostium, blocking its drainage and in 50% cases when it was located at the sinus floor. Nasal purulent discharge was found in 100% cases with ectopic teeth making eruption close to sinus ostia. Purulent and bloody discharge was found in 100% cases of ectopic teeth in the nsasal cavity and 76% in paranasal sinuses, when they were located close to the ostium.

2. Morphological features of ectopic teeth on CT scan imaging

Table 4. *Morphological features of ectopic teeth as disclosed on CT scan*

Morphological features Location	One tooth	Odontoma	Multiple teeth	Total
Frontal sinus	16 (84,2%)	1 (5,3%)	2 (10,5%)	19 (100%)
Maxillary sinus	2 (33,3%)	4 (66,7%)	0 (0%)	6 (100%)
Ethmoidal sinus	2 (100%)	0 (0%)	0 (0%)	2 (100%)
Nasal cavity	4 (100%)	0 (0%)	0 (0%)	4 (100%)
Total	24 (77,4%)	5 (16,2%)	2 (6,4%)	31 (100%)

The image of one tooth was seen on CT scan in 77,4% cases and that of multiple teeth in 6,4%. The ectopic teeth in frontal, maxillary sinuses and nasal cavities were approximately of the same size as normal teeth, while those in the ethmoid sinus were a little bit smaller (1005).

The distribution of ectopic teeth in this sample was: 19 in Frontal sinus (61,3%), 6 in maxillary sinus (19,4%), 4 in nasal cavity (12,9%) and 2 in ethmoid sinus (6,4%).

IV. DISCUSSION

Ectopic eruption of teeth in a region other than the oral cavity such as the nasal cavity and paranasal sinuses is a rare pathology. Their evolution is often insidious and patients consult most often because of sinonasal manifestations localized on the same side as the ectopic tooth. This pathology was most often found in the age group ranging from 36 to 60 years old (69,4%), followed by the age group from 16 to 36 (21,1%) and the group over 60 (9,5%). Knowing that tooth formation starts at a very early stage, it could be computed that at a younger age the patients more or less suffered from sinonasal symptoms but supposed that they were related to common cold and managed them by self- medicated painkillers. Only when the symptoms persisted over years and the patients came to an age when they started to worry about the risk of cancer, did they seek more thorough examination [7]. The prevalence of ectopic teeth was higher in male (72,1%) than in female (27,9%). According to Sudhoff H. [3], the occurrence of dystrophic enamel formation could be related to male endocrinal influence. The sinonasal symptoms such as unilateral headache and facial pain (96,8%), stuffy nose on one side (54,8%), runny nose on one side (51,6%) and facial swelling on one side (6,4%) usually responded to conventional sinusitis treatment. However, they quickly recurred a few days after the ending of the treatment. This was often the main reason for practitioners to request CT scan that detected the presence of ectopic teeth [4]. In this study, ectopic teeth in frontal sinus accounted for 61,3% cases, in maxillary sinus for 19,4%, nasal cavity for 12,9% and ethmoid sinus for 6,4%. Other studies showed that ectopic teeth are mostly found in the maxillary sinus [5], [6], [7], and very rarely in the ethmoid sinus. None mentioned about the presence of ectopic teeth in the pterygoid sinus, though there was one case in the literature that reported about a patient suffering from intense headache pain and cured after surgical removal of an ectopic tooth located at the ostium between the pterygoid and ethmoid sinus [5]. Confronting craniofacial pain severity with the location of ectopic teeth, it was shown that intense pain was related to 100% cases with ectopic teeth in the ethmoid sinus and 64,7% cases in the frontal sinus. In the maxillary sinus, pain was moderate in 83,3% cases and mild in 75% cases. Büyükkurt MC et al. also reported that ectopic teeth in the maxillary sinus caused moderate pain [6]. In this study sample, ectopic teeth were single in 77,4% cases and multiple in 6,4% cases. Upon histological examination, the toothlike structure did not display all dental tissues but only a core surrounded by a few layers of enamel. The absence of dental pulp tissue proved that the tooth was displaced into an ectopic place at a very early stage of tooth formation [6]. The low percentage of missing tooth in the dental arch (6,4%), which was also reported by several authors, suggested that most ectopic teeth are supernumerary ones [3]. Due to the ectopic location outside the oral cavity, and lack of normal nutrition source from the maxillary bone, most of the toothlike structures were different in size as compared to normal teeth; in the ethmoid sinus they were smaller and in other sinuses, they were bigger or developed into multiple teeth or odontomas.

V. CONCLUSION

This case series on ectopic teeth located in nasal and paranasal sinuses showed that unilateral headache and facial pain occurred in 96,8% cases, stuffy nose, runny nose and purulent sanious discharge in 54,8% cases. Pain was always severe with ectopic teeth located in the ethmoid sinus (100%) and in other sinuses when they blocked the sinus ostium. CT scan imaging disclosed the presence of only one tooth in 77,4% cases. Most of the ectopic teeth were supernumerary ones. As compared to normal tooth size, the ectopic teeth in nasal cavity, maxillary and frontal sinuses were bigger and in the ethmoid sinus, smaller. Surgical removal was indicated in case of ectopic teeth located at the sinus ostium and blocking sinus drainage.

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RÉSUMÉ:

CARACTÉRISTIQUES CLINIQUES ET IMAGERIE TOMOGRAPHIQUE DES DENTS ECTOPIQUES DANS LES SINUS NASAUX ET PARANASAUX

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Le but de cette étude est de décrire les caractéristiques cliniques et l'imagerie sur CT scan des dents ectopiques faisant éruption dans les cavités nasales et les sinus paranasaux en vue de définir les indications pour leur ablation chirurgicale et contribuer des preuves au diagnostic et traitement de cette pathologie rare. Les symptômes souvent rapportés par les patients étaient: algie craniofaciale unilatérale (96.8%), nez bouché sur un côté (54,8%), rhinorhée sur un côté (51,6%), saignement nasal et oedème facial unilatéral (6.45). Les dents ectopiques ont été retrouvées dans la cavité nasale dans 12.9% des cas, dans le sinus frontal dans 61.3% des cas, dans le sinus maxillaire dans 19.4% des cas et dans le sinus ethmoidal dans 6.4% des cas. L'imagerie tomographique a détecté la presence d'une dent unique dans 83.9% des cas, d'un odontome dans 12.9% des cas et de dents multiples dans 3.2% des cas. L'examen clinique a révélé une dent manquante au maxillaire dans 6.4% des cas. Dans la cavité nasale, le sinus

frontal et maxillaire, la taille moyenne de la dent ectopique étaitent supérieur à la normale tandis que dans le sinus ethmoidal elle était inférieure à la normale.

Mots clés: *Dent ectopique, sinus, odontome, épistaxis, dent absente*

THE ROLE OF MAGNETIC RESONACE IMAGING FOR THE RELATIVE BETWEEN ANNULUS FIBROSUS TEAR AND LUMBAR DISC HERNIATION IN THE ELDERLY PATIENT

Le Duc Nam*, Nguyen Quoc Dung*

ABSTRACT

Purpose: The aim of the studied magnetic resonance imaging of lumbar intervertebral disc to detect the number of annulus fibrosus tear with and without herniation disc, frequency of three types annulus fibrosus tear, and answer the question about the correclation between annulus fibrosus tear and nuclear moving (bulging disc and disc herniation).

Materials and methods: The retrospective cross - section study for 81 patients over 60 year of age with low back pain and lumbar spine, in whom we studied a total 405 lumbar intervertebral discs levels to findings and classifying by two group of nuclear moving that included bulging and herniation disc. In each group, we tried to finding the annular tear on T2W and we tried to classify the annulus fibrosus tear by three types that included concentric (Type I), radial (Type II), and transverse (Type III). We studies the relative of the disc moving (bulging and herniation) with the AFt.

Results: in 81 subjects (32 men and 49 women), with mean age of 74,15 ± 6,43 years (range, 60-90 years). Annular tears were seen in 287 of 405 (70,8%) discs and the radial tears were most common (52,2%). Compared and contrast with dics moving with annular tear and without disruptions demonstrated significantly higher relative between annular tear and nuclear moving and annular tear can lead to rapid for disc herniation.

Conclusions: In the elderly patient, the annulus fibrosus tears is high frequence. High signal intensive of MRI suggest a "gold standard" for diagnostic of annular tears and high MRI valuation for demonstrated the relative between annular tears and disc moving.

Keywords: annular tear, annulus fibrosus tear, bulging disc, disc herniation, MRI…

I. INTRODUCTION:

The disc has a strong outer ring of fibers, called the annulus fibrosus (AF), and a soft, called the nucleus pulposus, jelly - like center. When the disc is injured, AF can tear or rupture anywhere (***Fig 1***).

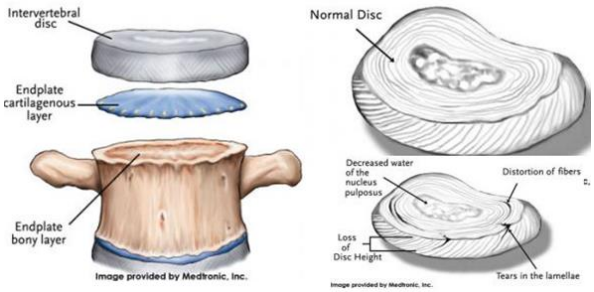

Fig 1. *The normal annulus fibrosus and the mechanism of annular tear*

The AF tear (AFt) was classified by three types that included concentric AFt (type - I), radial AFt (Type - II), and transverser AFt (Type - III) - ***Fig 2*** [**1**].

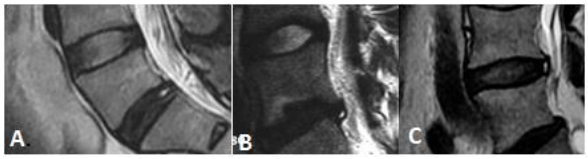

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Fig 2. *Three types of annular tear: concentric (A), radial (B), and transverse (C) - Sagital T2W MRI*

AFt is associated with disc movement (DM) or not but the AFt and DM is the common reason of chronic low back pain in orthopedic spine medicine today. In initial history, the discography was only imaging can be diagnostic. Computer tomography (CT) - Discography used and it is still known as the most specific imaging modality and remains the only pain-provocative test or neuro foramina infitration, but simultaneously shows high false-positive rates [**2**]. Today, Magnetic Resonace Imaging (MRI) is the most commonly performed diagnostic imaging modality in early diagnostic management of back pain because of the demonstration of high soft tissue contrast, the absence of radiation dose, and its noninvasive nature. A hyperintense signal intensity zone within the annular fibrosis on T2 signal is considered diagnostic of AFt on MRI [**3**]. Long - term follow - up studies to answer the main question that AFt precedes the appearance of nuclear movement and AFt can lead to rapid disc herniation, but it is not clear. Therefore, the aim of the studied MRI of lumbar intervertebral disc to detect the number of AFt, frequency of three types AFt, and answer the question about the relationship between AFt and DM.

II. MATERIALS AND METHODS:

1. Patients and methods:

Study design comprise as a retrospective cross - section study. Subjects who had low back pain and lumbar spine MRI performed at Huu Nghi Hospital, Ha Noi, Viet Nam, from January 2015 through December 2015. There were 81 patients, in whom we studied a total of 405 lumbar intervertebral discs that met the criteria choice.

2. Imaging analysis:

We chose patients aged over 60 with chronic low back pain. The ages and gender of the subjects are given in Table 1.

For MRI we use a 1.5 Tesla MRI system of GE Health care, USA. Protocols of 1.5 Tesla MRI system is summarized in table 1. All images were reviewed by two radiologists (with over 4 years and 20 years of radiology training) on PACS workstation (INFINITT Healthcare, Korea). We evaluated 405 disc levels to findings and classifying by two group that included bulging and herniation disc. In each group, we tried to find AFt on T2w and we tried to classify the AFt by three types that included concentric (Type 1), radial (Type 2), and transverse (Type3). We studies the relationship of the disc moving (bulging and herniation) with the AFt.

3. Statistical analysis:

Statistical analysis was performed using the software Statistical Package for the Social Sciences SPSS) (Version 20.0, IBM, Chicago, USA). A p value of < 0.05 was considered statistically significant.

III. RESULTS:

A total of 81 patients aged over 60 with low back pain at Huu Nghi Hospital, Ha Noi, Viet Nam, from January 2015 through December 2015. There were 81 patients, in whom we studied with retrospective cross - section a total of 405 lumbar intervertebral discs met the criteria choice.

1. Patient characteristics:

A total 405 discs from L1-L2 to L5-S1 on lumbar spine MRI examinations of 81 subjects (32 men and 49 women) with mean age of 74,15 ± 6,43 years (range, 60-90 years), age common at 71-80 (55,56%) (Table 1).

Table 1: Ages and gender of subjects (n=81):

Age \ Gender	Male	Female	Total	(%)
60-70	9	16	25	30,86
71-80	18	27	45	55,56
81-90	5	6	11	13,58
Total	32	49	81	
%	39,5	60,5		100
$\overline{X}$ ± SD	74,15 ± 6,43			

Time onset of disease was more than 3 years which were in 79% (Table 2) and only in 12,3% of the patients with less than 1 year. The first hospitalized was in 31/81= 38,3% of total patients, and the rehospitalized was in 50/80= 61,7%. First hospitalized versus rehospitalized had a *p* value < 0,05.

Table 2: Duration of disease

Time \ Duration	Firsthospitalized	Rehospitalized	Total	%
< 1 year	5	5	10	12,3
1-3 years	2	5	7	8,7
3-5 years	16	15	31	38,3
>5 years	8	25	33	40,7
Total	31	50	81	100
%	38,3	61,7		

2. MRI of the relationship between AFt and disc change:

Sum - results: During the retrospective cross - section study, a total of 405 discs from L1-L2 to L5-S1 on lumbar spine MRI were randomized by two radiologists (Table 4). The moving of the total of 405 discs, 162 (40%) were bulging discs, 243 (60%) disc herniations. MRI evaluation of included 405 discs resulted in 287 (70,8%) discs with annular tears, 118 (29,2%) without annular tears. Of the 287 annular tears on T2W MRI, 150 (52,2%) were radial tears, 96 (33,1%) were concentric tears, 41 (14,7%) were transverse tears. Of the reviewed 287 discs with annular tears, 90 (31,4%) were bulging disc (42 were concentric AFt, 30 radial AFt, 18 transverse AFt), 157 (52,9%) were disc herniations (44 were concentric AFt, 120 were AFt, 23 were transverse AFt).

Table 2: MRI protocols of the 1.5 T system

	Sagital T1W FSE	Sagital T2W FSE	Axial T2W FSE
TR	460	3200	3200
TE	15	102	116
FOV	320	320	200
Matrix	512x256	512x288	256x224
Slice thickness	4.0	4.0	4.0
FA	90	90	90

T tesla, FSE fast spin echo, TR repetition time, TE echo time, FOV field of view, FA *Fractional anisotropy*

The relationship between annular tears and disc moving: in both subjects with annular tears and those without disruption, 162 bulging discs were low, significant differences < 0,05 in both groups (90 (55,56%) with annular tears versus 72 (44,44%) without annular rupture), 243 disc herniations with high significant differences with p < 0,05 in both groups (157 (64,6%) with disruption, 46 (35,4%) without disruption), the comparison between bulging disc without annular tears (61,01%) versus disc herniations without annular tears (38,99%) had high significant differences with p < 0,05. Of the observed 287 annular tears on T2W MRI, radial tears were more than others type with 150 discs (52,2%). Comparison of the disc moving in the three types of annular tears, the concentric or transverse AFt with bulging disc versus disc herniations had low significant differences with p < 0,05, the radial AFt with bulging disc were lower than these with disc herniations that had high significant differences with p < 0,05 (20% vesus 80%).

Table 4: MRI of the relationship between AFt and disc change

AF tear \ Disc moving		Bulging disc	Herniation disc	Total	
Present	**Concentric**	42	44	96	287
	Radial	30	120	150	
	Transverse	18	23	41	
Absent		72	46	118	
Total		162	243	**405**	
%		40	60	**100**	

IV. DISCUSSION:

The annular tear is one of the more common causes of chronic low back pain in orthopedic spine medicine today. It was first described in 1952 by Cloward who was diagnostic of AFt with discography [**4**]. Unfortunately, long - term follow - up studies to answer the main question that AFt precedes the appearance of nuclear movement and AFt can lead to rapid disc herniation, but it is not clear. Our results was finding the high relationship between AFt and DM.

In our study, the mean age of 74,15 ± 6,43 years (range, 60 to 90 years), age common at 71-80 (55,56%), and 70,8% was annular tears. Osti et al (1992) reported for 33 patients with the mean age was 35 years (range, 24 to 64), and 50% was annular tears [**3**]. In addition, Yu S et al (1998) who has reported for 20 patients, the mean age was 40 (range, 10 to 86 years), 21-35% of radial annular tears over age 40 year [**6**]. The high differences could have been the critical choice of our subjects being older than 60 years. Our and their study confirmed that the ages were high related with the annulus fibrosus tears.

In olderly patents, frequencies of annular tears was common in females that would be in relation with estrogen hormon. Our results were reported 60,5% in females

vesus 39,5 % in males. Yu S et al (1998) who has reported for 11 females and 9 males [**6**]. Sharma (2009) like us with 13 men and 33 women [**10**].

The degeneration disc were a chronic disease with long time period, 79% of total patients were more than 3 years for time onset, 61,7% patients were rehospitalized.

The disc has a strong outer ring of fibers, it consists of many strong and elastic cartilage fibrers. Disruption can occur in all the side of the annulus fissure, and it often occurs in posterior and lateral - posterior side inasmuch as the weak part of the annulus fibrosus what had fewer fibrers, leading to bulging disc and herniation disc. When the disc moved outside of AF, it often causes an autoimmune reaction and inflammation to the surrounding tissues, specifically around the nerve roots, sensitizing them and causing pain [**7**]. The diagnosis of the annular fissure is done both clinically and by combining sophisticated imaging techniques for confirmation. Annular tears are easily detected by discography, when injected contrast from the nucleus to the annular boundary. Unfortunately, discography is an invasive procedure. Almost doctors not understand this condition of the lumbar spine, but some radiologists reading the MRI studies may not realize the importance of the annular fissure. Today, MRI is the most commonly performed diagnostic imaging modality in early diagnostic management of back pain because of the demonstration of high soft tissue contrast, the absence of radiation dose, and its noninvasive nature. A hyperintense signal intensity zone within the annular fibrosis on T2 signal is considered diagnostic of AFt on MRI [**3**]. The finding of AFt on MRI has been found by some research, Yu et al (1988) first discussed the diagnostic value of MRI and identified 3 types of annulus fibrosus tears [**5**]. A hyperintense signal intensity zone that call a “white spots” within the annular fibrosis on T2 signal MRI is still being evaluated and considered diagnostic of AFt [**3**]. In our knowledge, when the annulus fissure tears there is an attempt from the body to try to repair this by a small vascular bud that begins to grow into the area in an attempt to try to heal this lesion, but the healing is usually incomplete. The MRI is sensitive to water concentrations and thus it will pick up these little vascular changes as a “high intensity zone” or HIZ (meaning a fissure is present). Unfortunately, the HIZ has a significant correlation between abnormal disc morphologynature, but it not clear, and it may represent an area of secondary inflammation as a result of an annular tear, so the lumbar disc HIZ observed on MRI in patients with low back pain is likely to represent painful internal disc disruption [**8,9**]. The AFt observed on MRI shows high concordance. Secondary to AFt was disc movement outside of outer fibers that includes bulging disc and disc herniation that shows on MRI. The AF tear (AFt) was classified by three types that included concentric AFt (type - I), radial AFt (Type - II), and transverse AFt (Type - III) [**1**]. Our results demonstrated 287 annular tears, radial tears were common with 150 (52,2%) , 96 (33,1%) were concentric tears, 41 (14,7%) were transverse tears. In our knowledge, Shamar (2009) like us observed 46 patients with 276 discs, 73,55% were AFt (34,3% with type I, 56, 9 % with type - II, 6,1% with type - III) [**10**]. Yu (1988) from that, type III tears were the most common, type I were common and type II were slightly less common. The clinical significance of these

tears had high difference. Type-I tears have no clinical significance because no nerve endings penetrate the disk. Type-II tears have been thought to be clinically significant that could be detected diskographically and some time needed surgical treatment. Cloward described "discogenic pain" secondary to radial tears and developed the interbody fusion procedure for treating these patients [**4**].

A disc derangement occurs when a portion of nuclear material moves into a weakened area or tear in the disc and the nuclear material becomes entrapped, causing severe back pain [**9**]. We showed HIZ and movement disc (bulging disc and disc herniation), our results demonstrate a strong association between MR imaging demonstrable annular tears and nuclear movement, as has been previously noted. The relative distribution of signal intensity and movement in disks without and with annular tears in our study had high differences. We found a relatively common occurrence of annular tears in the absence of imaging changes usually associated with disc herniation. In 243 disc herniations, 81,07% with AFt, 18,94% without disruption. In addition, in 287 discs with annular tears, disc herniation were most common with 68,64% (197/287) versus 31,36% (90/287) of bulging discs. The significance of the association of annular tear areas with disc moving is not clear. However, we found that the radial AFt with bulging disc were lower than those with disc herniations that had high significant differences. Yue (2012) showed that patients with central annular tears or without tears have significantly lower disability scores than those with paracentral tears, whose outcome scores were significantly worse . In particular, patients with central tears improve more with less postoperative leg pain than patients with paracentral annular tears [**11**]. Histologic studies and our knowledge, the appearance of annular tears is a signaling of disc herniation remains unclear. However, our results indicate that annular tears are probably one of the earlier imaging manifestations of the disc moving, and their presence is associated with a more rapid appearance of nuclear movement.

Limitations of the Study:

Association of annular tears with clinical symptoms were not studied and demonstrated. We think the data of this study was limited to elderly patients. In the future, we spread this study wih detecting of the relation between the AFt and disc degeneration, correclation with clinical symptoms.

V. CONCLUSIONS:

In the elderly patient, the annulus fibrosus tears had a high frequency. The intense MRI suggest a “gold standard” for the diagnosis of annular tears. Our results demonstred that the annular tears appear to moving in the nucleus pulposus and AFt can lead to rapid disc herniation.

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RÉSUMÉ:

RÔLE DE L'IMAGERIE DE LA RMN DANS LA DETERMINATION DE LA RELATION ENTRE LE DÉCHIREMENT DE L'ANNEAU FIBREUX ET DE L'HERNIE DISCALE DE LA VERTÈBRE LOMBAIRE CHEZ LE PATIENT ÂGÉ

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Objectif: Le but de l'étude est de détecter le nombre d'anneaux fibreux déchirés avec ou sans hernie discale, la fréquence rencontrée de chacun des trois types de déchirement de l'anneau fibreux, et de donner la réponse à l'hypothèse d'une correlation entre le déchirement de l'anneau fibreux et le déplacement du nucleus (le disque qui fait saillie et l'hernie discale).

Matériel et méthode: L'étude rétrospective en cross-section de 81 patients avec douleur lombaire basse avec MRI, âgés de plus de 60 ans, chez lesquels un total de 405 de disques intervertebraux ont été mis en examen pour classification en deux groupes de déplacement du nucleus, provoquant la saillie, et l'hernie discale. Pour chaque groupe, nous avons tenté de retrouver le déchirement en T2W et classifier le déchirement de l'anneau fibreux qui comporte trois types: concentrique (Type I), radial (Type II), et transverse (Type III). L'étude du déplacement du disque résultant ou non en hernie discale, en Aft.

Résultats: Chez 81 individus (32 hommes et 49 femmes), l'âge moyen étant de 74±6.43 ans (60-90 ans). Le déchirement de l'anneau fibreux a été retrouvé dans 287 / 405 disques (70.8%) et le déchirement radial est le plus fréquent (52.2%). Ce qui est en contraste avec les disques se déplacant avec déchirement de l'anneau fibreux mais sans hernie, et démontrant ainsi une grande relation entre le déchirement de l'anneau fibreux et le déplacement du nucleus, résultant rapidement en hernie discale.

Conclusion: Chez le patient âgé, les déchirements de l'anneau fibreux sont fréquents. Le signal intense du MRI suggère "un standard d'or" de diagnostic de déchirement de l'anneau

fibreux, un facteur important de la relation entre les dechirements de l'anneau fibreux et le deplacement du disque.

Mots clés: *Déchirement de l'anneau fibreux, disques faisant saillie, hernie discale, MRI.*

THE IDEAL TIME TO BEGIN ORTHODONTIC TREATMENT OF CROWDED TEETH

Nguyen The Dung*

ABSTRACT

The two basic strategies are often applied to treat crowded teeth: (1) Treated through two stages: one in mixed dentition stage (early treatment) and one in permanent tooth stage; (2) Tenaciously treated only during adolescene years (late treatment).

From 2008 to 2017, a prospective cohort study was conducted to evaluate the outcome of early and late treatments of crowded teeth patients resulting from under developed of arch dimensions (tooth size arch length discrepancy, TSALD).

The results show that early treatment of patients with crowded teeth due to the under development arch dimension can beneficially adjust the crowded teeth condition; which allows for monitoring of the growth of both teeth and arch dimension and especially without the necessity of tooth extractions. The outcomes increase the patient's confidence in communication and parental satisfaction. The outcomes resulting from early treatment is more effective in restoring normal, more stable and less relapsed occlusion. It also will reduce the level of tenacity in treatment at permanent tooth stage; which will not damage the periodontal tissue and tooth enamel.

Keywords: *Crowded teeth, Early orthodontic treatment.*

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I. INTRODUCTION:

Late or early orthodontic treatment for crowded teeth has been a controversial topic among orthodontists since the 1980s. Early orthodontic treatment is performed on mixed dentition, while late orthodontic treatment involves extractions of first premolars in permanent dentition. According to 189 scientific studies reviewed by Lopes Filho H. [6] and his associates, there is limited evidence to demonstrate which route of treatment is best. Lopes Filho H. and his associates have observed, "Early orthodontic treatment has the advantages of reducing the duration of active treatment (treatment with fixed instruments) and reducing relapse after the treatment, but the level of evidence is not convincing enough to confirm that this is the best approach".

However, recent studies [1,2,3,4,5,7] have provided evidence that orthodontic treatment should be performed during mixed dentition period to prevent the progression of malocclusion and occlusal trauma as well as the severity of overjet. Early intervention allows monitoring and controlling the growth of permanent teeth and jaws without extractions, increasing patients' social confidence as well as parents' satisfaction towards their children's orthodontic treatment. The early treatment has shown

better and more stable outcomes with less relapse, reduced the number of active treatments on permanent dentition and caused less damage to periodontal attachment apparatus and enamel.

According to O'Shaughnessy KW. et. al [8], many authors have expressed a positive trend in early treatment that it will lead to effective results, reduce occlusal trauma and increase the stability of treatment outcomes. Yet, these authors' claims are based on their professional experience and reported clinical cases. Therefore, the objective of this study is to answer the question:

For patients with crowded teeth caused by underdevelopment of the jaws' arch length, should they be treated with early treatment during mixed dentition period or with late treatment, which requires extractions of first premolars?

Objective: To find the most favorable time to start the treatment for patients with crowded teeth caused by underdevelopment of the jaws' arch length.

II. SUBJECTS AND STUDY METHODS

2.1. Subjects:

**** Group 1:*** Patients who had early orthodontic intervention for their malocclusion due to crowding teeth at the age of mixed dentition, 7.5-9 years old.

**** Group 2:*** Patients who had late orthodontic treatment for their malocclusion due to crowding teeth at the age of permanent dentition, ≥ 12 years old.

2.1.1. Selection criteria:

**** Group 1:*** Patients from 7.5-9 years of age, fully erupted anteriors and first permanent molars (6 years-old molars), malocclusion with anterior crowding, and agreed to participate in the orthodontic treatment.

**** Group 2:*** Patients who were 12 years old or older, fully erupted anteriors and first permanent molars, malocclusion with anterior crowding, and agreed to participate in the orthodontic treatment.

2.1.2. Exclusion criteria: Patients with malocclusion but their anteriors were not crowded, had crossbites, or didn't agree to participate in the orthodontic treatment.

2.2. Study Methods: Prospective cohort study, selected patients starting orthodontic treatments from 02/2008-02/2017.

2.3. Data Collection: For all patients participating in the study, the following data was recorded into the study medical records:

- Clinical occlusion evaluation, Cephalometric xray, Panorex, and xrays analysis, front profile and side profile photoshoot, alginate impressions for study models/casts, facial and skeletal measurements.

- Treatment planned and made sure patients fully understand their treatment plans.

- Starting the treatment plans for:

**** Group 1***:

- Starting the early treatment with fixed 2x4 appliance.

- Then in phase 1, using 0.014 Ni-Ti round wire to start tooth movement, uprighting and aligning, following by using 0.016 x 0.025 SS archwire to maintain the anterior vertical.

- In phase 2, continued the treatment with the straight-wire appliance.

**** Group 2:***

- Late treatment, if the amount of dental crowding is within 5-7mm and patient < 15 years old, performed interproximal enamel reduction of first premolars.

- If the amount of dental crowding > 9mm and patient ≥ 15 years old, extractions of first premolars.

- Follow-up examination: Monthly follow-ups until patients' occlusion and facial appearance were stable. Cephalometric and Panorex Xrays taken to compare pre-op and post-op treatment outcomes.

2.4. Data Analysis: Data was analyzed by using SPSS software for Windows 22.0.

2.5. Result Evaluation:

- The differences in outcomes of pretreatment and post-treatment were analyzed independent t-test and chi-square test, with P value < 0.05 was considered statistically significant.

- Cephalometric analysis: FACAD® software (Ilexis AB, Swedish) was used to evaluate the changes in the pre-op and post-op outcomes.

III. STUDY RESULTS:

Numbers of participating patients:

* ***Group 1:*** 36 patients: 14 males and 22 females; average age: 8.2917±0.59010 years old. Average duration of treatment duration: 3.6806±0.57511 years.

* ***Group 2:*** 45 patients: 27 males, 18 females; average age: 18.2444±4.09632 years old. Average duration of treatment duration: 2.3378±0.29794.45 years.

Table 3.1. **Average value (mm) of preop and post-op overjet and overbite**

Occlusion Correlation		Pre-treatment		Post-treatment		P
		Average value	Standard deviation	Average value	Standard deviation	
Group 1	Overjet	4.7242	0.19150	2.0689	0.1036	< 0.001
	Overbite	3.4167	0.7653	2.0089	0.0066	< 0.001
Group 2	Overjet	4.6067	0.17665	2.5060	0.1462	< 0.001
	Overbite	3.4778	0.07351	1.3935	0.0473	< 0.001

**** Group 1:*** The average overjet reduced from 4.7242mm to 2.0689mm (p< 0.001), and the average oberbite reduced from 3.4167mm to 2.0089mm (p< 0.001).

**** Group 2:*** The average overjet reduced from 4.6067mm to 2.5060mm (p< 0.001), and the overbite reduced from 3.4778mm to 1.3936mm (p< 0.001).

Table 3.2. **The crowding condition of anterior teeth before and after the treatment.**

	Maxillary	Pre-treatment	Post-treatment	P
		Number of patients	Number of patients	
Group 1	Proper	9	36	< 0.05
	Anterior crowding	27	0	
Group 2	Proper	9	45	< 0.05
	Anterior crowding	36	0	
	Mandible			
Group 1	Proper	11	16	< 0.05
	Anterior crowding	25	20	
Group 2	Proper	16	33	< 0.05

	Anterior crowding	29	8	

**** Group 1:*** All the patients with maxillary and mandibular anterior crowding had their anteriors corrected to be normal after the treatment, ($p< 0.05$).

**** Group 2:*** All the patients with maxillary and mandibular anterior crowding had their anteriors corrected to be normal after the treatment, ($p< 0.05$). In this group, 8 patients had their midline shifted (17.77%).

Table 3.3. **Average values of Cephalometric variables before and after the treatment.**

	Cephalometric variables	**Pre-treatment**		**Post-treatment**		**P**
		Average value	Standard deviation	Average value	Standard deviation	
Group 1	SNA	84.8778	0.37880	83.7131	0.13253	< 0.001
	SNB	79.6431	0.11411	80.0725	0.03008	< 0.001
	ANB	4.3508	0.12489	2.1569	0.06112	< 0.001
	I - Pal	110.28	0.32545	109.12	0.3988	< 0.001
	I - MP	1.1592	0.3055	1.6186	0.1748	< 0.001
	Inter incisal	126.63	0.40994	124.04	0.8634	< 0.001
Group 2	SNA	85.1044	0.29365	83.6478	0.03661	< 0.001
	SNB	79.6500	0.06571	80.0738	0.01072	< 0.001
	ANB	4.3389	0.17993	2.1160	0.03172	< 0.001
	I - Pal	110.05	0.35967	109.13	0.03513	< 0.001
	I - MP	1.5616	0.01127	1.6071	0.00843	< 0.001
	Inter incisal	126.59	0.14842	124.07	0.15268	< 0.001

* Comparison of the average values of Cephalometric variables in pre-op and post-op treatment outcomes: decreased SNA, increased SNB, decreased ANB, reduced inter-incisal, decreased I-Pal, and increased I-MP with $p<0.01$.

Table 3.4. **Comparison between two groups**

Average values of variables		**Post-treatment result**	**P**
Average duration of treatment	Group 1	3.6806 years ±0.57511	**P < 0.001**
	Group 2	2.3378 years ±0.29794	
Overjet	Group 1	2.0689 ± 0.1036	**P < 0.05**
	Group 2	2.5060± 0.1462	
Overbite	Group 1	2.0089 ± 0.0066	**P < 0.001**
	Group 2	1.3935 ± 0.0473	
SNA	Group 1	83.7131 ± 0.13253	**P < 0.05**
	Group 2	83.6478 ± 0.03661	
SNB	Group 1	80.0725 ± 0.03008	**P < 0.001**
	Group 2	80.0738 ± 0.01072	
ANB	Group 1	2.1569 ± 0.06112	**P < 0.001**
	Group 2	2.1160 ± 0.03172	
	Group 1	109.12 ± 0.3988	

I - Pal	Group 2	109.13 ± 0.03513	**P > 0.05**
I - MP	Group 1	1.6186± 0.1748	**P < 0.001**
	Group 2	1.6071 ± 0.00843	
Inter incisal	Group 1	124.04 ± 0.8634	**P > 0.05**
	Group 2	124.07 ± 0.15268	

IV. DISCUSSION:

4.1. Early treatment for teeth crowding:

Crowded teeth caused by underdeveloped arch length and arch circumreference can be early treated by extractions of some deciduous teeth in mixed dentition or late treated with extractions of first premolars in permanent dentition. The traditional early treatment on mixed dentition involves with extractions of primary canines, then extractions of first premolars. The purpose of the extractions of these teeth is to provide the appropriate primate space and leeway space for permanent teeth to come in at proper position.

Nowadays, the ideal time for starting orthodontic treatments is a controversial topic. According to Lopes Filho H. and et. al (2015) [6], there are 159 orthodontists in the United States agreed that " When compared to the late treatment, the advantages of eartly orthodontic treatment are simpler, more affordable, shorter duration of treatment, and more stable outcomes."

From 2008 to 2017, we conducted a prospective cohort study to evaluate the outcomes of early and late orthodontic treatments on patients with anterior crowding, which was caused by underdeveloped arch length and circumreference. 36 patients (14 males and 22 females) with anterior crowding malocclusion were early treated with fixed 2x4 appliance to correct the improper overbite and overjet and to properly align the crowding anteriors. The results were good: the anteriors were repositioned correctly; the arch length and positions of permanent molars could be controlled. All of these 36 patients' social confidence has been improved and their parents have been very happy about their children's quality of life.

4.2. Late treatment for teeth crowding:

Crowded teeth caused by underdeveloped arch length and arch circumreference can be late treated on permanent dentition. If the crowding is within 5-7mm, the arch length and circumreference must be increased and interproximal enamel reduction of first premolars must be performed. If the crowding is > 9mm, first premolars must be extracted.

45 patients (27males, 18 females) were late treated with 9 patients had interproximal enamel reduction of first premolars and 36 patients had their first premolars extracted. After the treatment, these patients had their anterior crowding corrected and achieved stable occlusion; but there were 8 patients had their midline shifted (17.77%). Before the treatment, all 45 patients had low social confidence and their parents were not happy about their children's crowded teeth. Also, 7 patients who were older than 18 years old had periodontal disease and halitosis because their crowding malocclusion had caused difficulty to keep up good oral. And during the treatment, all 36 patients (80%) regretted that they had their first premolars extracted to create spaces for moving and uprighting their crowded teeth.

4.3. Advantages of early treatment compared to late treatment.

Table 3.4 showed significant differences in duration of treatment and post-treatment results of overjet, overbite, SNA, SNB, ANB and I-MP between the two groups who received early and late treatments. Also, table 3.2 presented a significant difference in the post-treatment anterior crowding between the two groups. Some patients in the late treatment group had their post-treatment midline shifted, accounting for 17.77%. For the duration of treatment, the study also indicated that the duration of active treatment (with fixed appliances) on the early treatment group was significantly shorter than the late treatment group who required extractions of their first premolars. However, the total duration of treatment for the early treatment group was considerably longer than that for the late treatment group.

Thus, the total time of starting the orthodontic treatment early and following up lasted twice as long as the total time of late treatment; and the cost of early treatment could be greater. Nonetheless, the patients who started early treatment wore their fixed appliances for a shorter period of time and got their smiles aesthetically corrected early; and they gained more social confidence while their parents felt more satisfied about the treatment outcomes.

V. CONCLUSION

Early treatment of patients with teeth crowding due to underdeveloped arch length and circumreference can fix the crowding condition and allow for monitoring of the development of arch length and erupting positions of permanent teeth. Especially, early orthodontic treatment do not require extractions of permanent teeth and increase patients' confidence in communication early as well as satisfaction of patients' parents. Moreover, the early treatment is also an effective way to restore normal occlusion with a more stable and less relapsed outcome; thus it will reduce the level of active treatment of permanent dentition and cause less damage to periodontal health and enamel.

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RÉSUMÉ:

LE MOMENT IDÉAL POUR COMMENCER LE TRAITEMENT ORTHODONTIQUE DE DENTS SURNUMÉRAIRES

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Deux stratégies fondamentales ont été appliquées dans le traitement des dents surnumeraires: (1) Traitement en deux étapes: une chez les individus à dentition mixte (traitement précoce) et chez les individus à dentition permanente; (2) Traitement appliqué seulement a l'adolescence (traitement tardif).

De 2008 a 2017, une étude prospective a été menée pour evaluer le devenir de ces traitements, précoce ou tardif, résultat du sous-développement des dimensions de l'arche (non-concordance des dimensions dentaires et de l'arche, TSALD).

Les résultats ont montré que le traitement précoce des patients avec dents surnuméraires dues au sous-développement des dimensions de l'arche, est en mesure d'ajuster la maladie sans avoir recours à l'extraction dentaire, ce qui est bénéfique à la confiance du patient et la satisfaction de ses parents. Ce traitement est efficace dans une meilleure prévention de l'occlusion, et la restauration stable a l'état normal. Il pourra réduire le traitement prolongé au moment où les dents sont a l'etat adulte, ce qui evite les dégâts survenus au tissu périodontal et l'émail dentaire.

Mots clés: *Dents surnuméraires, traitement orthodontique précoce.*

PRE AND POST TREATMENT PHOTOS OF SOME PATIENTS

Fig.1 *PHAM VAN P. 9 years old male with anterior crowding malocclusion, early treatment with fixed 2x4 appliance and MTB straight wire.*

Fig.2 *TRAN D. Q. 9 years old female with anterior crowding malocclusion, early treatment with fixed 2x4 appliance.*

Fig.3 *TRAN A. T. 19 years old male with anterior crowding malocclusion, late treatment with extractions of first permanent premolars and MTB straight wire.*

THE EFFECT OF SPERM DNA DAMAGE ON ASSISTED REPRODUCTION OUTCOMES

Luong Thi Lan Anh*, Nguyen Thi Trang*, Hoang Thu Lan*

ABSTRACT

The sperm deoxyribonucleic acid (DNA) integrity is important for success of natural or assisted fertilization as well as normal development of the embryo, fetus and child. The aim of this research is to evaluate DNA fragment index (DFI) in male with failure of assisted reproduction technique (ART). Subjects: 80 men who are failure in intrauterine insemination (IUI) or in vitro fertilization (IVF). Methods: evaluation DNA fragment index (DFI) by Halosperm kit. Results: The DFI average is 34.0%. The percentage of men in the two groups of IUI failure and IVF failure was not statistically significant. DFI in men with a failure ≥ 2 times higher than that of men with one-time in both IUI and IVF groups. Conclusion: Infertile men who are planning to undergo ART procedures with their partner should have their sperm evaluated for DNA damage. The results of this evaluation may be used to counsel the couple about their chances for live birth and for genomic abnormalities in their offspring.

Keywords: *DNA fragment index (DFI), Sperm Chromatin Dispersion (SCD), assisted reproduction technique (ART).*

I. INTRODUCTION

Assisted reproduction techniques such as Intrauterine insemination (IUI), In vitro fertilization (IVF), Intra-cytoplasmic Sperm Injection (ICSI) have brought great happiness to many couples giving birth that they cannot imagine before. However, not all cases using assisted reproduction techniques are successful. Spermatozoa's ability to fertilize not only depends on the perfection of morphology, structure, but also on the integrity of sperm DNA [1], [2]. This integrity was assessed through the sperm DNA index (DFI). DFI <15% may conceive naturally. If DFI 15 -> 30%, it is difficult to get pregnant naturally. DFI> 50%: difficult to conceive even with IVF, DFI> 60%, can only use ICSI, but very limited success, the only chance is to use donor sperm. Failure of sperm DNA leads to poor fertilization or poor growth, congenital deformities, and miscarriage. About 25% of infertile men have high DFI, 10% of infertile patients have normal semen, but DFI is high. High level of DNA fragmentation also affects fertilization and embryo quality [2], [3]. This results in poorly assisted reproductive measures and miscarriages [4], while the cost to patients for reproductive measures is not cheap.

In Vietnam, sperm DNA damage analysis is not yet common. At reproductive clinics center, most cases of male reproductive health have not been assigned to this test before the procedure. Therefore, this study was conducted with the aim of determining the DFI in men failing to assisted reproduction techniques (ART).

II. MATERIALS AND METHODS

80 couples in reproductive age, men with sperm concentration of ≥ 5 million /ml, but infertility and failure of IUI / IVF, testing for sperm DNA damage, performed at the Genetic Counseling Center, Hanoi Medical

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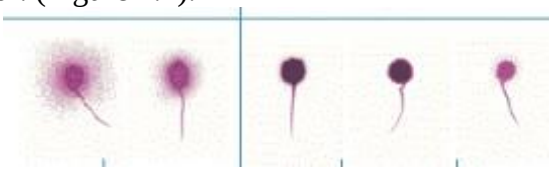
University Hospital, from June, 2016 to December, 2017.

Research process

Semen is taken by men, checking semen and sperm concentration. Using a Halosperm Kit (IVD Certified) to check spermatozoa with chromatin dispersion. Follow the manufacturer's instructions; Samples of spermatozoa with chromatin dispersion were made and fixed on a glass slide. Under the optical microscope, counting at least 500 spermatozoa in the semen to determine the level of DFI. The sperm DNA damage was determined by the sperm halo of Fernandez et al. (Figure 2.1).



(1) (2) (3) (4) (5)

Figure 1. Spermatozoa without fragmentation and with fragmentation

Notes:

(1) Spermatozoa with big halo: those whose halo width is similar or higher than the diameter of the core.

(2) Spermatozoa with medium-sized halo: their halo size is between those with large and with very small halo

(3) Spermatozoa with small halo: the halo width is similar or smaller than 1/3 of the diameter of the core.

(4) Spermatozoa without halo.

(5) Spermatozoa without halo and degraded: those that show no halo and present a core irregularly or weakly stained.

$$\text{DFI (\%)} = \frac{(3)+(4)+(5)}{\text{Sperm couting}} \text{ x } 100$$

DFI is determined, classified by high levels (> 30%), average (15-30%), normal (<15%).

III. RESULTS

DFI in men failed to ART

DFI average = 34.0 ± 24.9 (%). The DFI <15% group with 17 cases, DFI with 15% -30% with 31 cases, DFI > 30% with 32 cases.

Table 1. *DFI average*

DFI group \ DFI average	DFI ± SD (%)
< 15%	11.4 ± 1.7
15 - 30%	18.8 ± 4.0
> 30%	55.7 ± 21.3

Men with DFI> 30% had an average DFI of 55.7%. Men with DFI <15% and DFI 15-30% had an average DFI of 11.4% and 18.8%, respectively.

Rate of ART failure according to DFI level

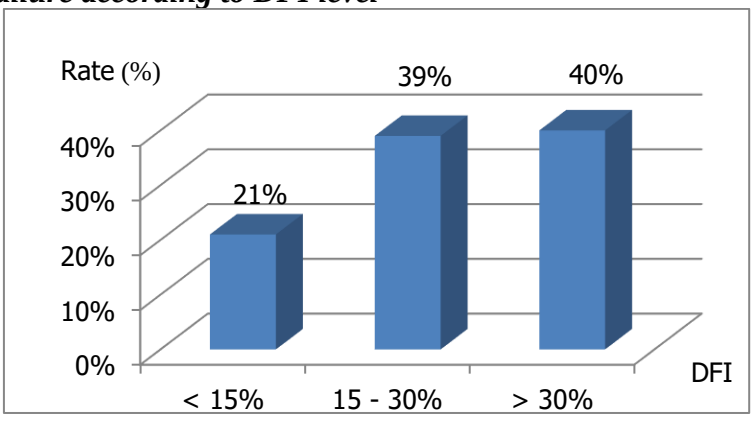


Figure 2. *The rate of sperm DNA damage in men with ART failure*

The percentage of men with DFI failure with DFI> 30% and DFI 15-30% had the highest rate of 40% and 39%, respectively, with DFI < 15% accounted for the lowest rate of 21%.

DFI and IUI/ IVF

There are 57 IUI failure and 51 IVF failures cases. The IUI failure group had an average DFI of 34.8 ± 2.6 (%). The IVF's had an average DFI of 30.6 ± 2.3 (%).

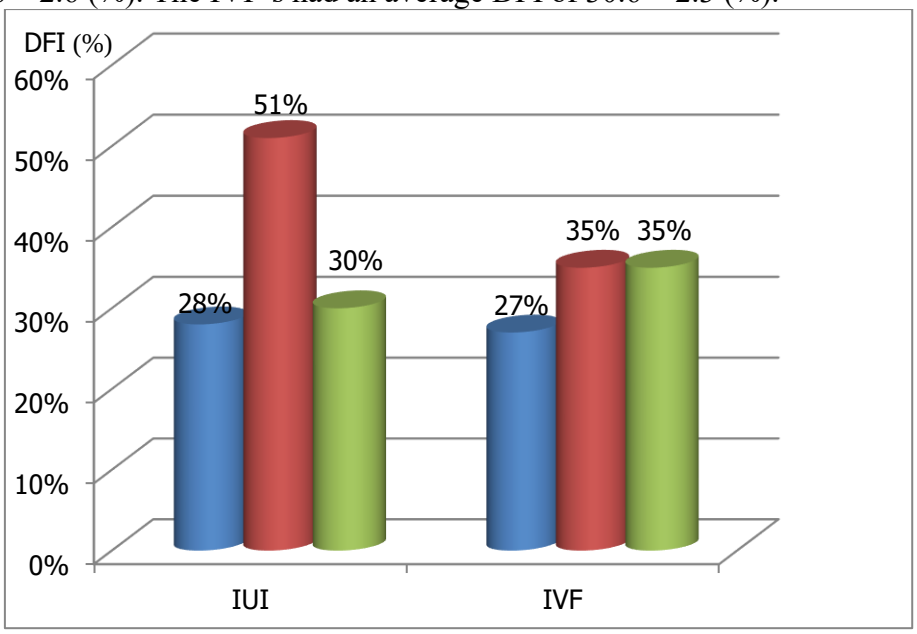


Figure 3. *DFI in men with ART failure one time and more than one*

DFI in the IUI failure group with once, twice, ≥ 3 times respectively, 28%, 51%, 30%. IVF failure group with once, twice, ≥ 3 times respectively 27%, 35%, 35%. The difference between IUI and IVF was not statistically significant (p> 0.05).

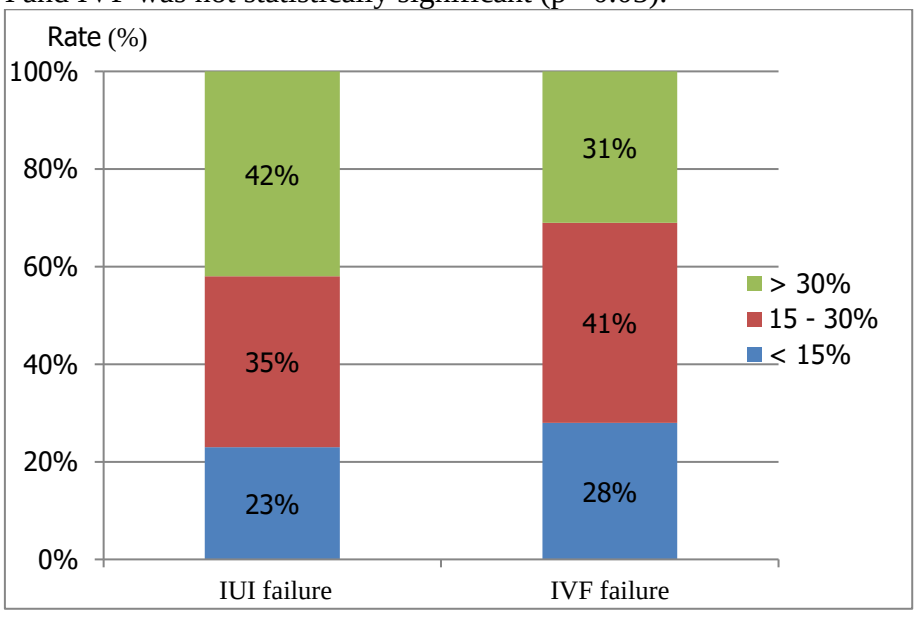


Figure 4. *Percentage of men with sperm DNA damage in ART failure*

The proportion of men with DFI levels in the two groups of IUI failure and IVF failure was not statistically significant. The percentage of men with DFI level <15% was <23% and 28% (p> 0.05). The percentage of men with DFI level 15 to 30% is 35% and 41% (p> 0.05). The percentage of men with DFI level > 30% was 42% and 31% (p> 0.05).

IV. DISCUSSION

Rate of sperm DNA damage

In our study, mean DFI in men who failed to ART was 34.0 ± 24.9 (%). It was estimated highly, similar to research of Bungum M. (2007) with DFI averaging 30.8%. Clearly, the degree of sperm DNA damage negatively affects reproductive outcomes. The percentage of men with DFI> 30% was highest (40%) and DFI 15-30% in 39%, DFI <15% the lowest is 21%. A study by Bungum M. et al. (2007) on 998 ART cases (387 IUI, 388 IVF and 223 ICSI), 333 failure cases, in which men with DFI> 30% accounts for 29% [5]. According to Simon L. et al. (2013) on 253 IVF failure cycles, ICSI had 89% of men with DFI> 25% and 61% of men had a DFI >50% [6].

The effect of sperm DNA damage on ART outcomes

Ours research showed high levels of sperm DNA damage in men with ART failure, DFI> 30%. Saleh R.A. (2003) found a negative correlation between DFI and the success of ART (r = -0.7; p <0.01) [7]. It is said that, a significantly lower chance of pregnancy in IUI with DFI > 27% (Bungum M. et al.). The study of Henkel R. (2003) showed a significantly lower chance of pregnancy in IUI with DF> 27%, in IVF with DFI > 36.5% [8].

Meseguer M. (2011) also showed that DFI as an independent indicator for predicting the ART success, for each DFI increased by 10%, the probability of not pregnant in IVF or ICSI increase to 1.31 times [9]. Corresponding study of Bungum M. et al. (2007) in 998 IUI, IVF and ICSI cycles showed that success rates for men with DFI> 30% were 3%, 34%, 58%, respectively. The authors point out that when DFI> 30%, ICSI should be a more selective than IUI, IVF. The DFI level of 30 to 40% is a statistical threshold for IUI failure. Therefore, if having DFI> 30%, please do not indicate ART for infertile males. According to Erenpreiss J. (2006), there is a variation in the incidence of DNA damage in individuals, so it is important to test DFI before ART. Men who have high DFI do not take part in ART but need antioxidants, which play an important role in reducing DFI [10].

DFI and IUI/ IVF

In the study, 28 men with IUI, IVF failure together. We did not find a statistically significant difference between the rates of sperm DNA damage in the two groups of IUI and IVF failure (p>0.05). The percentage of men with DFI of 15-30% and DFI > 30% are high in both groups, suggesting that men fail to ART with high rates of sperm DNA damage.

Therefore, the analysis of sperm DNA analysis should be done routinely in reproductive health centers and ART centers.

V. CONCLUSIONS

Men who failed in ART had a high DFI of 34.0%. Similar DFI in the two groups of IUI and IVF. DFI in men with a failure to deliver a birth defect ≥ 2 times higher than that of men with one-time spousal support failure in

both IUI and IVF groups. Thus, it is prudent to check for DNA damage in infertile patients undergoing ARTs.

VI. ACKNOWLEDGEMENTS:

The authors wish to thank the Northern ARTs center, all colleagues in Genetic Counseling Center in HMU Hospital for support.

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RÉSUMÉ:

LES EFFETS DES DÉGÂTS SUR LA REPRODUCTION ASSISTÉE DE L'ACIDE DÉSOXYRIBONUCLÉIQUE DU SPERME

Luong Thi Lan Anh*, Nguyen Thi Trang*, Hoang Thu Lan*
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L'intégrité de l'acide désoxyribonucléique (DNA) du sperme est importante pour la fertilization naturelle ou assistée, aussi bien que le développement normal de l'embryon, du foetus et de l'enfant. Le but de cette étude est d'évaluer l'index du fragment DNA (DFI) chez le mâle avec échec de la reproduction assistée (ART). Les sujets pour étude: 80 hommes, avec échec de l'insémination intrautérine (IUI) ou de la fertilization in vitro (IVF). Méthode: Evaluation de l'Index du fragment (DFI), au moyen du kit Halosperm. Résultats: La moyenne du DFI est de 34.0%. Le pourcentage d'hommes avec échec tant avec IUI qu'avec IVF n'a pas de signification statistique. Le DFI chez l'homme avec ≥ deux fois est plus élevé que chez l'homme dont l'échec est seulement une fois dans les deux essais (IUI et IVF).

Conclusion: Les hommes infertiles qui désirent les procédures ART avec leur partenaire devraient évaluer les dégâts survenus au DNA de leur sperme. Les résultats de l'examen pourraient être utilisés pour les conseils au couple sur les chances de survie du nouveau- né, et sur les anomalies du génome de leur progéniture.

Mots clés: *Index du fragment DNA (DFI), Sperm chromatin dispersion (ACD), technique de reproduction assistée (ART)*

PRELIMINARY TREATMENT RESULTS OF THE LATERAL ANKLE INSTABILITY USING MODIFIED BROSTROM TECHNIQUE

Do Duc Trung*, Nguyen Quoc Dung*

ABSTRACT

Lateral ligaments injuries are common in ankle trauma and will be likely to lead to ankle instability. If left untreated, it will lead to ankle degeneration. There are many classic procedures available to treat chronic lateral ankle instability; however, the postoperative results are poor. **Purpose:** To evaluate the preliminary treatment results of the lateral ankle instability using modified Brostrom technique. **Materials and methods:** 6 patients with chronic lateral ankle instability, aged from 24 to 38 years (mean age of 34) were treated with modified Brostrom technique. The median follow-up time was 32 months (from 4 to 36 months). The results were evaluated according to AOFAS. **Results:** The mean AOFAS score was 89,2 (from 85 to 95). The last results were assessed in 6 patients: Excellent in 4/6 patients and good in 2/4 patients. **Conclusion:** Preliminary treatment results of modified Brostrom technique in patients with chronic lateral ankle instability demonstrated satisfactory results. It is necessary to have more time to follow up and assess.

Key words: *Chronic instablility - lateral ankle - modified Brostrom.*

I. INTRODUCTION

The ankle is the most commonly injured articulation and ankle sprain is one of the most common sport-related injuries accounting for 40% of all athletic injuries. The ATFL and CFL are most commonly torn. Initial recommended treatment for acute lateral ligament injuries is a conservative management which includes immediate use of RICE (rest, ice, compression, elevation), a short period of immobilization and protection with bandage, and early range of motion, weight-bearing and neuromuscular training exercises. Although most incidences are successfully treated by the conservation measure but 30-40% have persistent pain, oedema, stiffness and recurrent ankle instability. Recurrent ankle sprains may alter the biomechanics at the ankle joint which can potentially lead to cartilage degeneration over time. Surgery is indicated if conservative treatment fails and the goals of surgery are to re-establish ankle stability and function without compromising motion and without complications. There is a variety of surgical techniques available for ligamentoplasty, which can be divided into 2 groups: the anatomic and non-anatomic reconstructions. Non-anatomy techniques use tissue grafts harvested at distance such as Watson - Jones, Evans, Chrisman-Snook and Pisani procedures; however, the results in the literature are still restricted. Lately, anatomy repair of the lateral complex with the Brostrom modification has had high success rate and the risk of complications is low.

We have been performing the modified Brostrom procedure since July 2014 at Department of Joint Surgery, 108 Military Central Hospital. The aim of our study was evaluate prelimitary results from patients who underwent modified Brostrom surgery for treatment of lateral ankle instability.

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II. MATERIALS AND METHODS

A prospective**,** descriptive cross-sectional study was conducted in 06 patients who had lateral ankle instability and underwent modified Brostrom procedure, performed by one single surgeon. Included were patients who had symptoms of chronic lateral ankle instability such as persistent pain, a feeling of giving way, swelling, stiffness. Patients with synovitis, osteochondral lesions, bony avulsions, or fractures were excluded from our study.

1. Clinical preoperative evaluation: Each patient had a thorough history and physical examination. Range of motion in both dorsiflexion and plantar flexion was performed subjectively by the operating surgeon on the injured ankle and compared with the contralateral ankle. Any decrease in range of motion of greater than 5° from normal or more than 5° of difference from the contralateral ankle was documented. Provocative tests were also performed on the injured ankle that included the anterior drawer test, and talar tilt test. In addition, the injured ankle was also stressed under a minifluoroscopy machine in the clinic to confirm lateral ankle instability.

Figure 1: Anterior Drawer Test Talar Tilt Test

Radiography: Assessment of ankle bones.

MRI: MRI scan was obtained on all study patients before surgery to determine if there were any associated injuries or conditions such as synovitis or OCD lesions.

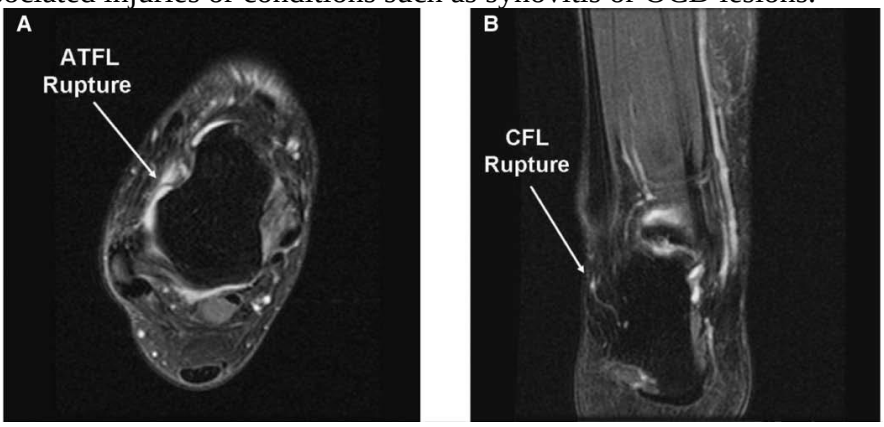

Figure 2: Complete tear of ATFL and CFL are seen as ligament defect on T2 - weighted image. Tone ends of discontinuous ligament are surrounded by fruid signal (arrow).

2. Surgical methods:

Each patient received general anesthesia with a peroneal nerve block. The patient was placed in a supine position with a towel bump under the ipsilateral buttock. A thigh

tourniquet was utilized during the operation to control bleeding (250 mmHG).

Step 1: Expose the lateral ankle ligaments and capsule:

A 5 cm J incision was made anteriorly over the lateral malleoli. Care was taken to identify and avoid the sural nerve. The proximal edge of the inferior extensor retinaculum was then identified, carefully dissected and mobilized. The lateral ankle capsule was then identified along with the remnants of the anterior talofibular ligament. The calcaneofibular ligament (CFL) can be identified at the tip of the distal fibula with inferior retraction of the peroneal tendons. We also inspected the peroneal tendons for tears at this time.

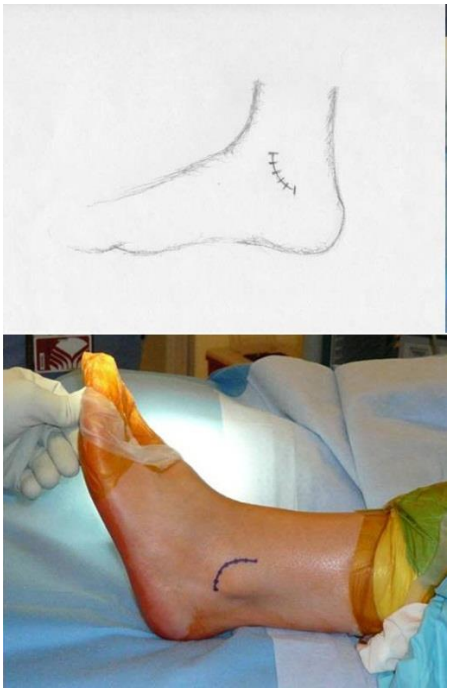

Figure 3: *J incision*

Step 2: Drill holes, place suture anchor, mattress ligaments and capsule:

The distal tip if the fibula at the ATFL and CFL footprint was debrided with a curette and surgical blade. Drill holes were then made at the ATFL and CFL insertion site. A suture anchor was placed at the anatomic foot print of each, the ATFL and CFL, respectively in the distal fibula. A third suture anchor was inserted approximately 1 cm above the ATFL insertion with the same drill hole technique. Care was taken to make sure that the drill hole tunnels did not intersect with each other. The suture from anchor #1 was placed into the CFL in a horizontal mattress fashion. The inferior limb of anchor #2 was placed into the capsule just inferior to the ATFL, the superior limb (Anchor #2) and the inferior limb of anchor #3 was placed into the ATFL ligament using a horizontal mattress. Lastly, the superior limb of suture #3 was place above the ATFL into the capsule. Next, the remnants of the ATFL and CFL along with a capsular-periosteal flap were tied down to the three suture anchors with the foot at neutral dorsiflexion and slight eversion. The extensor retinaculum was then advanced and repaired to the periosteum of the distal fibula to reinforce our repair with interrupted 1-0 vicryl sutures (this is also done with the foot in neutral dorsiflexion and slight eversion).

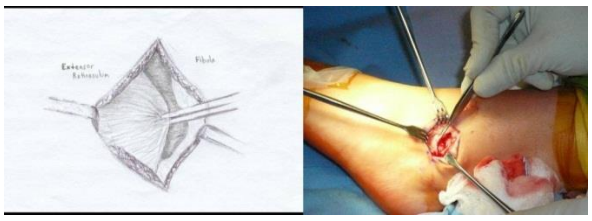

Figure 4: *The proximal edge of the inferior extensor retinaculum is identified and carefully dissected then mobilized for advancement later in the procedure.*

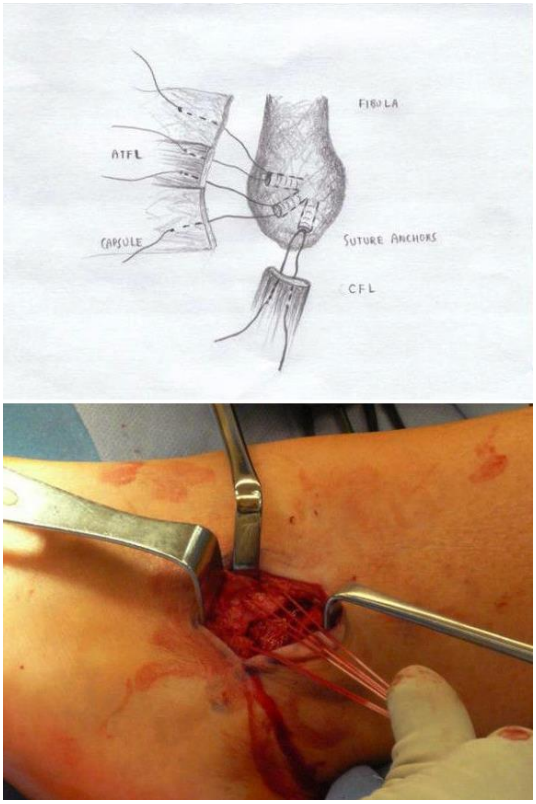

Figure 5: *Two suture anchors placed at the footprint of the ATFL and CFL insertion site. A third suture anchor is placed approximately 1 cm above the ATFL insertion site to reinforce the repair. The orientation of the sutures from each anchor is also illustrated*

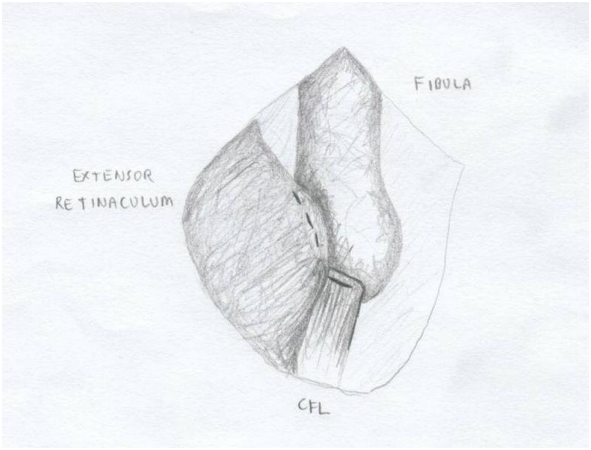

Figure 6: *The extensor retinaculum was then advanced and repaired to the periosteum of the distal fibula*

Step 3: The skin was closed subcutaneously using 2-0 vicryl sutures, followed by 4-0 nylon interrupted stitches.

Figure 7: *The incision was closed*

3. Postoperative rehabilitation methods:

- Post - operative: All patients were placed in a well-padded posterior and sugar-tong splint with the foot in neutral and slight eversion with non-weight bearing instructions until their follow-up visit in 10 to 14 days. Toe range of motion was encouraged in order to diminish venous stasis. Aspirin of 325 mg PO daily for 14 days was also prescribed for each patient. At the first postoperative follow-up visit, ankle incision was inspected and the stitches were removed.

- Week 2 to 4: The patient were placed in a short leg walking cast for 2 weeks. Protect and progressive weight bearing was allowed over the following 2 weeks.

- Week 4 to 6: The patients were placed in a protective ASO (ankle support orthosis) brace and started on gentle active assisted range of motion of the ankle.

- Week 6 to 12: Proprioception and strength training were also started during the 6 to 8 weeks interval with plyometrics starting at 8 to 12 weeks.

- 12th post operative week: Patients were allowed to return to sports or normal activities without any limitations shortly after week 12.

4. Outcome assessment:

At 3 months after surgery, patients underwent follow-up. The function of the patients' ankles was assessed using the American Orthopaedic Foot and Ankle Society (AOFAS) scale, which gives a maximum score of 100 and evaluates pain (40 points), functional status (50 points) considering functional limitation, use of supports, distance covered, ground characteristics, step alterations, sagittal movements, etc., and alignment of the foot with the ground (10 points).

III. RESULTS

There were 06 patients (04 males, 02 females), the age of the patients ranged from 24 to 38 years, with a mean age of 32 years. Among the 6 ankles, 05 were on the right side, 01 on the left side. The event causing the lateral ankle instability was sports-related injury in 6 patients. 3/6 patients were treated with ice theraphy after injuries and 6/6 patient didn't immobilize ankles with brace. All patients complained about persistent pain with activity, recurrent sprains and a sense of instability of the ankle.

Clinical assessment: All patients had positive anterior drawer test and varus talar tilt test when compared to the normal contralateral ankle.

There were no degenerative signs on preoperative radiographs.

Both ATFL and CFL were injured on MRI of 6 patients.

The mean follow-up time was 32 months (from 4 to 36 months). 06 patients believed that their ankle was more stable after the surgery. 01 patient complained about the persistant hypoesthesia in the territory of the superficial peroneal nerve and had a persistant oedema after exercise. 01 patient had ankle pain after exercise . No patient had limping. 05 patient had normal inversion/eversion and flexion/extension range of motion, only 01 patient had flexion limited to 5°. Clinical examination: Both anterior drawer test and talar tilt test were negative in 6/6 patients. Stress radiography tests were negative on the injured side when compared to the uninjured side. There were no degenerative signs on ankle radiography of 6 patients.

The function of patients' ankles was assessed using AOFAS, we had 5 poor results (<69 point), 1 moderate result(<79 point). The mean AOFAS score was 63.5 before surgery (from 57 to 76). The AOFAS score rose from a mean of 63.5 before surgery to a mean of 89.2 (from 85 to 95) at the final follow-up, corresponding to a mean increase of 25.7 points. The last results were excellent in 4 cases and good in 2 cases.

The average time to return to work was 6.5 weeks (6-7 weeks). Patients returned to their previous sports activities at an average of 14 weeks (12-16 weeks) after surgery. 04 patients returned to pre-injury work activities and 02 patients returned to lower extremity sports and normal leisure activities.

IV. DISCUSSION

Based on the literature, we believe that a modified Brostrom lateral-ligament repair provides increased stability by reinforcing local host tissue, offering a quicker functional recovery and reduce the risk of osteoarthritis. Undoubtedly, some of these procedures show excellent results in the initial period but in long run they are shown

to develop persistent instability, abnormal kinematics, stiffness, loss of movement and weak eversion. Also the extensive incision required for the procedure [1-2] heightens the risk of wound infection, dehiscence, and sural nerve damage, etc.

In 1985, Chrisman-Snook et al. [16] published their results of 48 patients operated with the non-anatomic technique using half of the tendon of the peroneus brevis. The results showed 38 (79%) with excellent results, 7 (15%) had good result with some symptoms and 2 patients (4%) were estimated sufficient as they had no regain of total functionality. Of the 36 patients reexamined, inversion was identical with the uninjured side, but limited in 50% of patients in the range of 5-20°. 39% of patients had numbness of the ankle, which persisted in 11% of the cases associated with troubles of the sensibility, also neuroma and recurrent instability has been observed.

In 1988, Karlsson et al. [8] analyzed the long term outcome of the original technique and found only 50% of satisfaction among the patients. Kitaoka et al. [9] published results of Evans technique in 18 patients and found instability walking on uneven ground, frequent and sporadic pains, limitation of physical activities with recurrent strains as common problems. 94% of these patients were satisfied with the operation. Modified Evans procedure and its outcome have been studied by few researchers [10-11] in a series of 25-85 patients and follow up period from 7 to 20 years. The studies have shown 35-55% of excellent results but showed limited inversion and flexion/extension movements with some revision because of a loosening of the graft and degenerative changes in long run.

The Castaing ligamentoplasty, a technique very popular in France, uses the distal part of the peroneus brevis. Jarde et al. [7] published a series of 46 patients operated with this technique with a 5.5 year follow up. With the Kitaoka score they had 43% of very good results, 39% of good, 11% of sufficient and 7% of bad results. Early complications included delayed scar healing, abscesses, neuromas, algoneurodystrophia. Also light pain after long physical exercise, relapse of ankle sprain, oedema, unaesthetic scar and limited leisure activities was observed. Some major physical hindrance that has been observed includes diminution of the inversion amplitude between 50 and 70% compared to the healthy side, no tiptoeing, derangement, could not squat, could not stand on one leg. It is not that these complications are completely missing with the anatomic procedures, but they are fewer in number with the faster recovery.

Another important element was the residual mobility of the ankle and hindfoot. We found a normal sagittal motion in 04 patients and a moderate limitation of 15-29° in 02 patients according to the AOFAS score. The hindfoot mobility was normal in all patients. 02 patients that returned to work late and they had to change playing volleyball to table tennis. The recovery time of patients was slightly longer in the current study compare to the series by Jarde et al. who had a Castaing procedure . The technique used in the current study was little invasive so nobody complained about discomfort of their scar wearing high shoes.

Other studies analyzing Brostrom surgeries showed good results in equal measure. In 2010 a prospective study using bioabsorbable anchors in modified Brostrom-Gould surgery showed excellent results for 28 out of 30 ankles [13]. A recent case series

on athletes, employing similar technique as in the present study showed efficient return to high-demand sports similar as their pre-injury functional level . A study has shown combination of open Brostrom-Gould technique and debridement by arthroscopy for chronic ankle instability and anterior impingement, patients had mechanically and functionally stable ankles after 12 months with no recurrences of impingement [12]. In 2009 a series of 31 patients was published after 27.5 months of arthroscopic repair of the lateral ligament and showed good clinical results with an AOFAS score of 85.3 [15]. In 1996, Keller et al. [5] followed 44 patients for 2.5 years with 85% of excellent, 13% of good results. The complications observed in few cases were slight wound dehiscences, edemas for more than 6 months, pain with recurring sprain and rigidity. In 1996, Hennrikus et al. [6] compared the Chrisman-Snook operation with the Brostrom- Gould surgery and both groups showed 80% excellent or good result. However more complications were found in the patient treated by the Chrisman-Snook procedure. In 2006, Fujii et al. [4] compared the Brostrom and Gould procedure to the Evans tenodesis on 6 cadavers, and reported that the later procedure gave a better stability at the expense of mobility, which is, better preserved with the former. Nevertheless, one has to keep in mind that none of the single techniques is able to restore completely contact and motion patterns.

Based on research studies, we believe that a modified Brostrom lateral ligament repair should be considered the first choice for persistent ankle instability, this approach provides increased stability by reinforcing local host tissue, preserving subtalar and talocrural motion, eliminating the comorbidity associated with tendon-graft harvest, offering a quicker functional recovery and reduce the risk of osteoarthritis. The preliminary results were promising. Compared to mentioned studies, our indications were similar and our results had negligible differences. Because our median follow-up time was shorter and the number of patients was smaller, the objectivity and accuracy of the treatments results were not perfect. Therefore, we need to conduct our study with a longer follow-up time and a larger number of patients in order to enhance the objectivity of the study.

For postoperative care, immobilization of the ankle and exercises are extremely important. Since it is a very large field, we will discuss this in a separate study.

V. CONCLUSION

There were 6 patients (04 male, 02 female), the age of the patients ranged form 24 to 38 years, with a mean age of 32 years. The function of patients' ankles was assessed using AOFAS, we had 5 of poor results (<69 point), 1 of moderate result(<79 point). The mean AOFAS score was 63.5 before surgery (from 57 to 76). The AOFAS score rose from a mean of 63.5 before surgery to a mean of 89.2 (from 85 to 95) at the final follow-up, corresponding to a mean increase of 25.7 points. The last results were excellent in 4 cases and good in 2 cases. The average time to return to work was 6.5 weeks (6-7 weeks). Patients returned to their previous sports activities at an average of 14 weeks (12-16 weeks) after surgery. 04 patients returned to pre-injury work activities and 02 patients returned to lower extremity sports and normal leisure activities.

We believe that a modified Brostrom lateral ligament repair should be considered

the first choice for persistent ankle instability, this approach provides increased stability by reinforcing local host tissue, preserving subtalar and talocrural motion, eliminating the comorbidity associated with tendon-graft harvest, offering a quicker functional recovery and reduce the risk of osteoarthritis. For postoperative care, immobilization of the ankle and exercises are extremely important, which greatly affects the outcome of treatment.

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RÉSUMÉ:

RÉSULTATS PRÉLÉMINAIRES DU TRAITEMENT DE L'INSTABILITÉ LATÉRALE DU COUP DU PIED UTILISANT LA TECHNIQUE MODIFIÉE DE BROSTROM

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Le traumatisme des ligaments latéraux sont fréquents dans les blessures du coup du pied et souvent conduit à son instabilité. Laissé sans traitement, il peut causer sa dégénérescence. Il existe plusieurs procédures classiques du traitement de cette instabilité chronique, cependant, les résultats post-opératoires ne sont pas satisfaisants.

Objectif: Evaluer les résultats préléminaires du traitement de l'instabilité du coup du pied utilisant la technique modifiée de Brostrom.

Matériel et méthode: 6 patients avec instabilité chronique du coup du pied, âgés de 24 à 38 ans (âge moyen 34) ont été traités avec la technique modifiée de Brostrom. La durée moyenne du suivi étant 32 mois (de 4 a 36 mois). Les résultats évalués selon AOFAS.

Résultats: Le score AOFAS moyen étant 89.2 (de 85 à 95). Les derniers résultats ont été obtinus chez les 6 patients, excellents chez 4/6 patients et bons chez 2/4 patients.

Conclusion: Les résultats préléminaires de la technique modifiée de Brostrom chez les patients avec instabilité chronique latérale du coup du pied ont été prouvés satisfaisants. Un suivi de plus longue durée est indispensable pour son évaluation.

STUDY OF CLINICAL AND ELECTROMYGRAPHY CHANGES IN PATIENTS WITH CERVICAL SPONDYLOSIS TREATED BY THE ELECTRO-ACUPUNCTURE

Pham Hong Van*, Le Van Quan**

ABSTRACT

Objective: To assess effects of the electro-acupuncture on patients with cervical spondylosis. ***Subjects and methods:*** 50 healthy people (control group) and 50 patients with cervical spondylosis (treatment group) were treated by electro-acupuncture. ***Results:*** In the treatment group, after 7 days of treatment, there was a reduction on averaged points in VAS and an increase of the cervical spine stretch. Assessment the effects of treatments by surface-electromyography (sEMG), we found there was a decrease of neck muscle spasm, these were: increases of mean maximum intensity of muscle contraction and muscle contraction energy while there was a decrease of time to reach peak of intensity of muscle contraction. These changes were similar to control group. ***Conclusion:*** In the present study, we provided new evidence of effects of the electro-acupuncture that reduced pain and lumbar stiffness.

Keywords: *Cervical spondylosis, electro-acupuncture, surface- electromyography.*

I. INTRODUCTION

The cervical spine, the best flexibility part of the spine, has a wide range of motion and bear the weight of upper body and is subjected to constant muscle contraction in the neck area. Over time, aging and pressures from the contraction of neck muscles will lead to degeneration of the spine. Cervical spondylosis does not cause death but the protracted disease gives uncomfortable feelings such as pain, numbness, fatigue. This problem severely affects individual's activities, reducing work productivity, decreasing quality of life.

On the other hand, if not properly diagnosed and treated, the disease can lead to spinal cord compression and disability. It makes the patient become a burden for family and society. Therefore, research into the treatment and prevention of this disease is an urgent need for social life and is an important issue in public health care. Both modern medicine and traditional medicine have many methods of treatment for degenerative diseases such as acupuncture, massage, acupressure, spinal stretch, etc in which acupuncture has confirmed the treatment effects to the symptoms of cervical spondylosis. For the purpose of clarifying the effect of electro- acupuncture in the treatment of cervical spondylosis by providing scientific basis to prove the effect of this treatment method, we used surface-electromyography method with the objective of studying the clinical and electromyography variability in patients before and after treatment.

II. MATERIALS AND METHODS

2.1. Subjects

60 people over 35 year olds, regardless of sex, weredivided into two groups:

- The treatment group consists of 50 patients with degenerative spondylitis. They

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were diagnosed with neck syndrome due to degeneration of the neck, examined and treated at the Central Acupuncture Hospital.

- The normal group that includes 50 people selected from healthy people without degenerative spondylitis

* Criteria for selecting subjects: patients were diagnosed with degeneration of the spine with the following expression:

- acute and subacute pain in neck area, with signs of neck spine syndrome (pain, limited motion of cervical spine); nerve root syndrome (pain spread from neck to hand, with the pain increases when moving cervical spine or cough, sneezing, etc).

- Xray: There is an image of degeneration of the neck spine on x-ray film

* Criteria for exclusion:

- Patients with neck- shoulder syndrome, but on X-ray film without spinal degeneration, or causes due to disk herniation, TB, cancer, spinal injury.

- Patients with other diseases such as heart failure, mental illness, hyperthyroidism.

- Patients receiving other treatment methods or non-compliance with treatment procedures.

2.2. Experimental procedures

* Research design: randomized clinical trials, comparisons before and after treatment.

* Study Procedure: Patientsselected for the study were treated with electro-acupuncutre for 30 minutes per day x 7 days according to the regimen: The acu-points: Feng Chi (GB20), EX C3-C7, Jian Jing (GB21), Jian Zhen (SI9), Jian Yu (LI14), He Gu (LI4). And tonifiation of the acu-point: Shen Shu (UB23).

2.3. Research indexes

- Changes in the pain levels according to the VAS score: assess the subjective pain sensation of the patient daily using the Visual Analogue Scale (VAS by Astra - Zeneca). Patients were instructed to evaluate the pain sensation with images showing pain, and then self-assessing their pain level: no pain, mild pain, moderate pain, severe pain and a lot of pain.

- Changes in the levels of limitation of movement of the cervical spine: the levels of limitation of movement of the cervical spine were determined and assessed according to Ho Huu Luong: unrestricted, light level, severe, very severe.

- Changes of surface- electromyography: Electromyography in the neck was determined at pre-treatment, after 1 treatment and after 7 days with Powerlab (A/D Instrument, Australia). Using FE132 electromechanical module Bio Amp, analyzed using the Peak Analysis module of the LabChart 7 Pro software. Data was selected and exported into excel files.

Data fromElectromyography analysis included:

+ Baseline: The average electrical strength of the rest of the muscle.

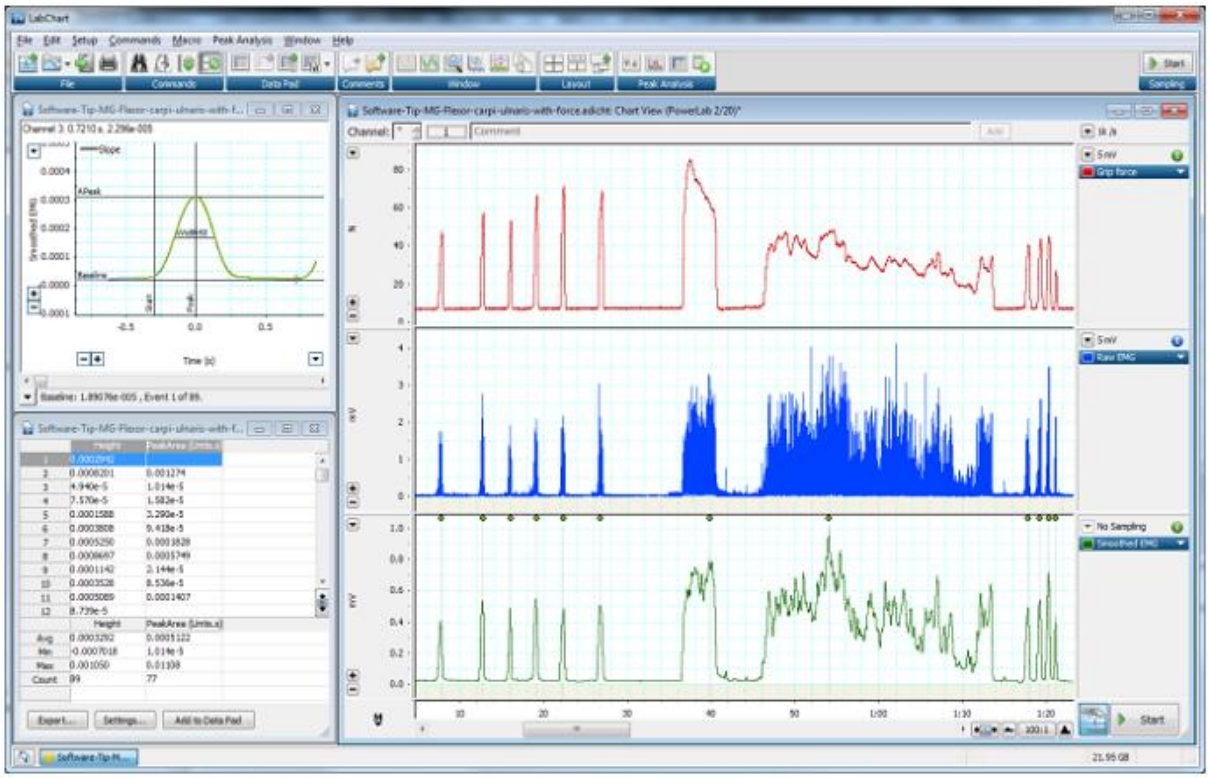
+ Peak: The maximum intensity when muscle contraction occurs

+ PeakArea:The area at the bottom of the curve created by the contraction of the muscle. This is the index representing the total energy generated during muscle contraction.

+ Time to Peak: The time from the muscle beginning to shrink until the the muscle stretch out maximum.

Surface - electromyography procedure: Patients were require to lye on stomach. Electrodes were applied to the cervical region of the neck, horizontal to vertebrae C3-C7 (the electrodes are 2cm from the line between the spinal column and separated by 2 cm). The

reference electrode is located in the line between the vertebral column C5.Electromyography was conducted when the patient lies still and relaxed during about 1 minute. After then, electromyography was done when the patient lies still and the muscles of the neck shrinking at their maximum for 10 seconds. Data from the electromyography was analyzed using the Peak Analysis module of LabChart 7 Pro (figure 1).



2.4. Data analysis: Data was analyzed by SPSS 19.0. Differences in pain scales, movements and electromyography between two groups were analyzed by two way ANOVA. Significant difference was determined at $p<0,05$. All data was expressed as, mean ±SD

III. RESULTS AND DISCUSSION

3.1. Changes in the pain levels by VAS scales

According to the standpoint of physiology, pain is a protective mechanism of the body, which is common to all animals. Pain is considered to be an important factor affecting human behavior [2]. At present, it is thought that pain is the integrated function of the body to encourage different functional systems to protect the body from harmful elements. One of the difficulties of studying pain is the pain assessment because pain tolerance and the response to pain of each person is very different. For patients with cervical spondylosis, pain is a symptom, that obliges the patient to see a physician with the desire to be free from pain. In this study, we assessed pain based on subjective perceptions of patients on the VAS scale, it is used widely in research and assessment of pain through improvement of spinal movement according to Ho Huu Luong.

Table 3.1. Improvement of pain score on VAS (n = 50)

Pain level	Before treatment (1)		After treatment (2)		p
	n	%	n	%	
No pain	0	0	28	56	$p_{2-1} < 0.001$
Mild pain	0	0	19	38	
Average pain	27	54	3	6	
Severe pain	23	46	0	0	
X ± SD	6.12 ± 1.10		1.70 ± 0.76		

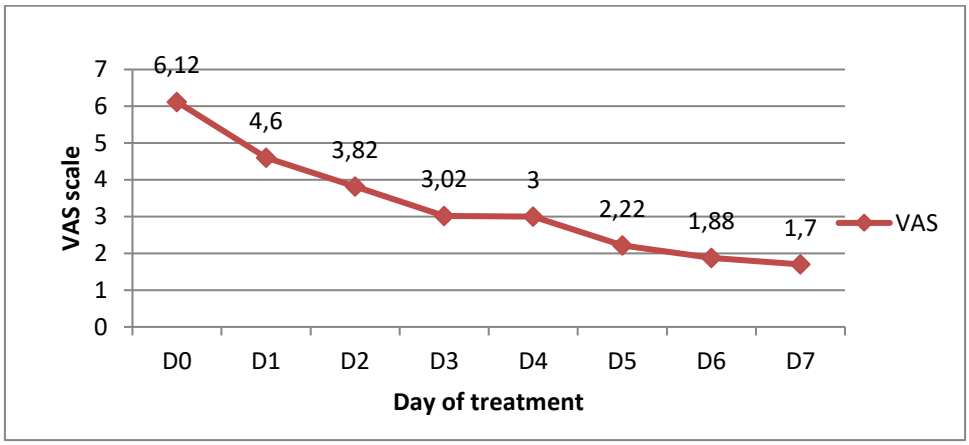


Table 3.1 showed that after 7 days of treatment, no patient had severe pain, 56% of patients had no pain, 38% of patients had mild pain, only 6% of patients had average pain level. The difference in pain level before and after treatment was statistically significant at p <0.001.

Results of pain intensity changes according to the VAS scale have reflected the analgesic effect of the electro-acupuncture method. The electrical impulses of the acupuncture stimulate have stimulated the body to increase its pain tolerance and maintain stability throughout the course of treatment.

Table 3.2. Improve the movement of cervical vertebra

Movement of cervical vertebra	Before treatment (1)		After treatment (2)		p
	n	%	n	%	
No limit or restriction	0	0	30	60	$p_{2-1} < 0.01$
Mild limit	10	20	18	36	
Average limit	36	72	2	4	
Severe limit	4	8	0	0	
Total	50	100	50	100	

Pain and movement limitations are common symptoms of degenerative disease, and these are also problems that cause the patient to go to the doctor for treatment. The contraction of the muscles along the spine, the contraction of the binding organs including muscles, ligaments, articulation, etc have reduced the activity of the cervical vertebra.

The results in table 3.2 show that: before treatment,100% of patients had limited mobilities of the cervical vertebra at average and severe level.

After the treatment by electro-acupuncture, 30/50 (60%) patients had no limited mobilities of the cervical vertebra, 18/50 (36%) patients had limited mobility of the cervical vertebra at **mild level,** 2/50 (4%) patients were limited mobility of the cervical vertebra at average **level and no patient** has limited mobility of the cervical vertebra at severe level.

The results of the study indicated electro-acupuncture have good effects to improvement in ranges of movement of the spine.

According to traditional medicine, pain is called "Thong". In the "To Van" book wrote "when Qi and Xue circulation well, there is no pain; when the meridians was deadlocked, the circulation of Qi and Xue is not very well, then there will be painful"

Pain causes muscle contraction, when the muscle contraction will prevent blood to nourish the muscle, which makes the pain increasing, creating a pathological twist.Acupuncture has the effect of regulating the functioning of the meridian system. A ccording to traditional medicine, acupuncture is to regulate the Qi, when the Qi and Xue circulation well, the muscles are fully nourished, from which will escape muscle contraction. When the condition of muscle contraction is liberated, the nourishment locally in the neck will be improved and the pain will cease

Studies of some authors show that the electrodes have a vasodilating effect, increasing blood flow to organs, enhancing cellular nutrition. The electro- Acupuncture therapy used electric impulses acted on the acupuncture points of the body, to creating the biological stimulation, enhancing respiration in the cell, improving microcirculation, etc. Therefore, electro-acupuncture also have effects to regulates the Qi, Xue, rebalance the yin and yang, that is also the ultimate goal of the acupuncture to healing.

3.2. Electromyography changes under the influence of electro- acupuncture

Electromyography method using surface electrodes (sEMG) is a safe and non-invasive technique. This method allows to measure the energy levels of the muscles at rest and during transport by placing an electrode on the skin surface, without inserting electrodes deeply inside muscles.

Table 3.3. *Changes in baseline voltages of sEMG recordings*

Subjects / Time	Treatment group (n=50) (b)	Control group (n=50) (a)	p
Before treatments (1)	1.14 ± 0.21	0.22 ± 0.04	$p_{1-2}>0.05$
	$p_{a-b}<0.01$		
1 day after treatments (2)	1.07 ± 0.19	0.22 ± 0.04	$P_{2-3}<0.05$
	$p_{a-b}<0.01$		
7 days after treatments (3)	0.96 ± 0.18	0.22 ± 0.04	**$p_{1-3}<0.01$**
	$p_{a-b}<0.01$		

Table 3.3. showed thatmean baseline voltagesof sEMG recordings in the treatment group were significantly higher than this in the control group in both before and after treatments ($p<0.01$). After treatments, mean baseline voltages of sEMG recordings decreased as compared to these before treatmentsin treatment group only. However, significant differences were only expressed in 7 days after treatments ($p<0.01$).

Table 3.4. *Changes in peaks of voltages of sEMG recordings (mV)*

Subjects / Time	Treatment group (n=50) (b)	Control group (n=50) (a)	p
Before treatments (1)	2.62 ± 0.37	3.18 ± 0.46	$p_{1-2}>0.05$
	$p_{a-b}<0.01$		
1 day after treatments (2)	2.71 ± 0.40	3.18 ± 0.46	$P_{2-3}>0.05$
	$p_{a-b}<0,01$		
7 days after treatments (3)	2.94 ± 0.48	3.18 ± 0.46	**$p_{1-3}<0.01$**
	$p_{a-b}<0.05$		

Table 3.4. showed thatpeaks of voltages of sEMG recordings in the treatment group were significantly higher than this in the control group in both before and after treatments ($p<0.01$ and $p<0.05$). After treatments, peaks of voltages of sEMG recordngs decreased in the treatment group only, as compared to these before treatments. However, significant differences were only expressed in 7 days after treatments ($p<0.01$).

Table 3.5. *Changes in time to peaks of muscle contractions (ms)*

Subjects / Time	Treatment group (n=50) (b)	Control group (n=50) (a)	p
Before treatments (1)	174.35 ± 32.48	152.67 ± 21.52	$p_{1-2}>0.05$
	$p_{a-b}<0,01$		
1 day after treatments (2)	170.18 ±28.82	152.67 ± 21.52	**$P_{2-3}<0.05$**
	$p_{a-b}<0,01$		
7 days after treatments (3)	159.26 ±35.49	152.67 ± 21.52	**$p_{1-3}<0.05$**
	$p_{a-b}>0.05$		

Time to peaks of muscle contractions in the treatment group were significantly higher than these in the control group, in both before and after treatments ($p<0.01$). Furthermore, within groups, time to peaks of muscle contractions were significantly lower at 7 days after treatments, in compared to these before treatments, in the treatment group only ($p<0.05$).

From the analysis of the change of surface electromyogram of patients with hand neck syndrome due to cervical spondylosis show that the electroacupuncture have reduced spasm of the neck muscles including the adjacent muscles of the spine, increasing the maximum muscle contraction in the patient. On the other hand, when the muscle contraction, the blood to the muscle reduction cause of muscle anemia is also causing pain.

Based on practical experience and results of treatment achieved in the study of a number of authors at home and abroad with acupoint selection method based on the traditional medicine theory combined with symptoms according to the physiological - anatomy - neurology of modern medicine (cervical spondylosis affects the movement of the cervical spine), so in this study we have chosen the treatment acupoint protocol, toniacupuncture BL 23 to tonic kidney, disperacupuncture SI 9, LI 15, LI 4 in order to muscle decontraction, Jiaji point C2-C7 is located close to the spine, close to the disc and capsula articularis, longitudinal ligament, yellow ligaments, ligaments - ligaments so

electricacupunctuer these points have effect to reduce stiffness of the neck muscles, muscles in the neck and the shoulders decontraction, blood to nourish the muscles better, increased mobility and flexibility of the spine, thereby enhancing the kidney qi, meridians qi and blood circulation thereby relieving pain expession in the clinical level of pain in the patient to be improved, increasing the range of movement thereby increasing the activity of the cervical spine.

Thus, by using surface electrodes EMG methods as the least invasive technique of modern biomedicine, objective evaluation of the effect of electroacupuncture on the improvement of the lumbar muscle contraction, thereby evaluating objectively the effect of electroacupuncture in the treatment of pain due to spondylosis [8], [9]. Electroacupuncture is one of the methods of treatment that combines physiotherapy and traditional medicine using acupoint stimulate by pulse power. Acupuncture has the effect of regulating qi, pain relieving, electrical stimulation stimulates the receptors in the skin, muscles and organs where the current passes through, causing more reflexes such as increasease local circulation and nutrition. Increased metabolism, enhanced redox reactions should have resolved the pain and muscle contraction, improve the movement of the spine. The results of pain treatment due to cervical spondylosis of the electroacupuncture has been demonstrated objectively through the change of surface electromyogram.

IV. CONCLUSION

Results in the present study indicated that electro-acupuncture had effects to treatments for patients with cervical spondylosis. These were:

- In the treatment group, after 7 days of treatment, there was a reduction on averaged points in VAS and an increase of the cervical spine stretch.

- In sEMG recordings, in the treatment group, there were decreases in baseline voltages of sEMG recordings and time to peaks of muscle contractions at 7 days after treatments in compared to these before treatments.

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RÉSUMÉ:

ÉTUDE SUR LES CHANGEMENTS CLINIQUES ÉLECTROMYOGRAPHIQUES, CHEZ LES PATIENTS AVEC SPONDYLOSE CERVICALE TRAITÉS PAR ÉLECTRO-ACUPUNCTURE

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Objectif: Evaluer les effects de l'électro-acupuncture sur les patients avec spondylose cervicale.

Sujets d'étude et méthode: 50 subject en bonne santé (groupe contrôle), et 50 patients avec spondylose cervicale (groupe traitement) traités par electro-acupuncture.

Résultats: Dans le groupe traitement, après 7 jours de traitement, il y a réduction de la moyenne des points VAS et une augmentation de l'extension des vertèbres cervicales. Dans l'évaluation des effets du traitement par l'électromyographique de surface (sEMG), nous avons trouvé une diminution du spasme musculaire du cou, une augmentation de l'intensité moyenne maxima de la contraction musculaire et de l'énergie de contraction musculaire. Ces changements sont similaires chez le groupe contrôle.

Conclusion: Dans notre étude, nous avons fourni une nouvelle évidence des effets bénéfiques de l'électro-acupuncture sur la réduction de la douleur et de la rigidité lombaire.

Mots clés: *Cervical spondylosis, electro-acupuncture, surface-electromyography.*

PHYTATE REMOVED SOYBEAN MILK IMPROVED LOCOMOTOR AND EXPLORATORY ACTIVITIES IN RATS

Le Van Quan*, Pham Hong Van**
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ABSTRACT

The present study was conducted to investigate effects of phytate removed soybean milk to locomotor and exploration abilities of experimental animals. In the present study, 30 rats were randomly seperated into 3 experimental groups: Group 1 (control group) contained 10 saline-treated rats; group 2 (normal soybean milk group) included 10 normal soybean milk treated rats and group 3 (phytate removed soybean milk group) contained 10 phytate removed soybean milk treated rats. Rats were administered 5ml saline or milk 1 time/day for 4 weeks. At the 4th week after treatments, rats were required to perform the open field test. Results showed that average speeds and travel distances in the open field as well as durations in the center area of open fields of rats in the group 3 were higher than these in group 1 and group 2. These results indicated that phytate removed soybean milk might increase locomotor and exploration abilities in experimental animals.

Keywords: *Rats, Open field test, phytic acid removed soy milk, locomotor and exploratory activities*

I. INTRODUCTION

Soybean milk is one of general liquids for drinking in Vietnam. Soybean milk contains many nessecary components for us, such as many kinds of protein which contain necessary acid amins, and a lot of ions [1]. However, it has been demonstrated that these proteins and ions have forms to connect to phytic acid which reduced absorption rates of proteins and ions in soybean milk [2].

Recently, it has been proved that phytase enzyme might be used to remove phosphate components, including phytic acid, in the food [3]. Thus, adding enzyme phytase to soybean milk might proteins and ions from acid phytic. Therefrom, absorption rates of components including proteins and ions increase. Based on these principles, we producted a soybean milk which were removed acid phytic by enzym phytase. And we also certified that there are increases of ions, consisting of Calci, Fe and Zn of the this soybean milk in experimental animals.

From our above study, next studies should be conducted to investigate effects of phytic acid removed soybean milk to physiological functions of living organisms. Locomotor and exploration functions, of physiological functions relating to roles of proteins and ions, especially calcium should be investigated firstly. Thus, we conducted the present study with the aim: ***Assessing the effects of phytic acid removed soybean milk to locomotor and exploration abilities of experimental animals.***

II. MATERIALS AND METHODS

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2.1. Subjects

30 Wistar rats (150-250g) from the animal center of Vietnam Military Medical University were used in the present study. Animals were housed in individual cages, maintained controlled temperatures and 12 hours light/dark cycles. During experimental time, rats were fed the similar food and water. The experiment was conducted in the department of Physiology, Vietnam Military Medical University. All procedures in the present study were treated in strict compliance with the Guidelines for the Care and Use of Laboratory Animals of Vietnam Military Medical University.

2.2. Materials

Phytic acid non-removed Soybean milk and phytic acid removed milk were supplied from Hanoi National University of Education.

2.3. Animal grouping and treatments

Rats were separated randomly into 3 groups: group 1 (control group) contained 10 saline-treated rats; group 2 (control milk group) contained 10 phytic acid non-removed soybean milk treated rats and group 3 (phytic acid removed milk group) contained 10 phytic acid removed soybean milk treated rats. All rats were administrated 5 ml saline or milk 1time/day for 4 weeks.

2.4. Open field test

60 minutes after drug treatments, mice were placed in the center of a open field box. Open field box was a square box (40 × 40 × 60 cm), covered with polypropylene sheets inside the wooden box (figure 1). Animals were allowed to free explore inside open field box for 5 minnutes. Behaviors of animals were recorded using a digital video system. Data was analyzed offline by ANY-maze software (Stoelting Co., Wood Dale, IL, USA).

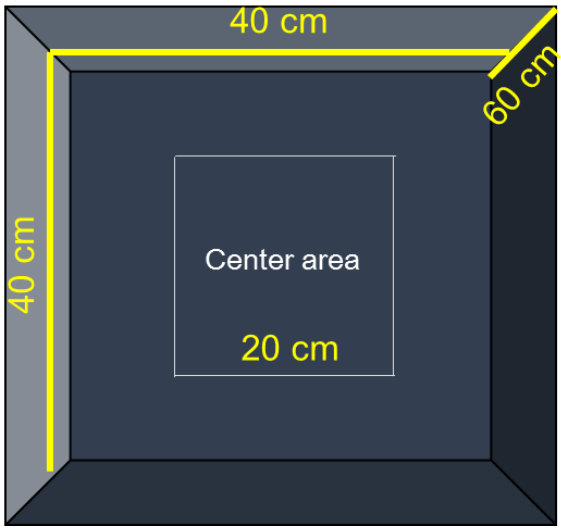

Figure 1. *Open field*

2.5. Research indicators

In the present study, we analyzed locomotor abilities of animals by two research indicators which were travel distances (m) and average speeds (m/s) in the open field. After then, to evaluating exploration abilities of animals, distances and durations of animals in the center areas of open field (fig. 1) were analyzed.

2.6. Data analysis

Travel distances and average speed in the open field as well as distances and durations in the center area were analyzed by one way ANOVA following by Tukey tests for multiple comparisons. A significant difference were determined at $p < 0,05$. All results in the present study were expressed as mean±SEM.

III. RESULTS

3.1. Changes in travel distances of rats in the open field area

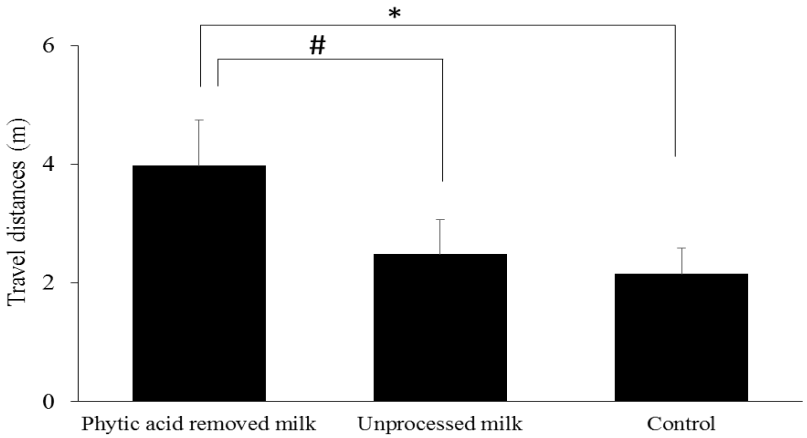

Figure 2. *Travel distances in the open field*

Figure 2 showed travel comparison of distances of animals in the open field area between experimental groups. One way ANOVA indicated that there was a tendency to be significant difference between experimental groups [F(2, 27) = 2.532, p <0,099]. Post hoc showed that mean travel distance of rats in phytic acid removed milk treated group was significantly longer than this in saline treated group [Tukey test, p <0,05] and tended to be significant longer than this in unprocessed milk treated group [Tukey test, p <0,1].

3.2. Changes in average speeds of rats in the open field area

Figure 3 showed comparison of average speeds of rats in the open field area between experimental groups. Although one way ANOVA didn't show a significant difference in average speeds between experimental groups, it seems that average speeds of rats' travels in phytic acid removed milk treated group was higher than these in unprocessed milk treated group as well as saline treated group. This result along with an increase in travel distances of phytic acid removed milk treated rats indicated that phytic acid removed milk might increase locomotor abilities of experimental animals.

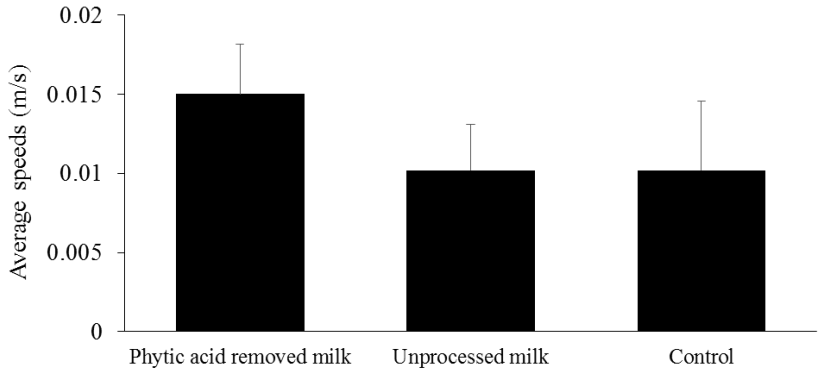

Figure 3. *Average speeds in the open field*

3.3. Changes in travel time in the center area of open field

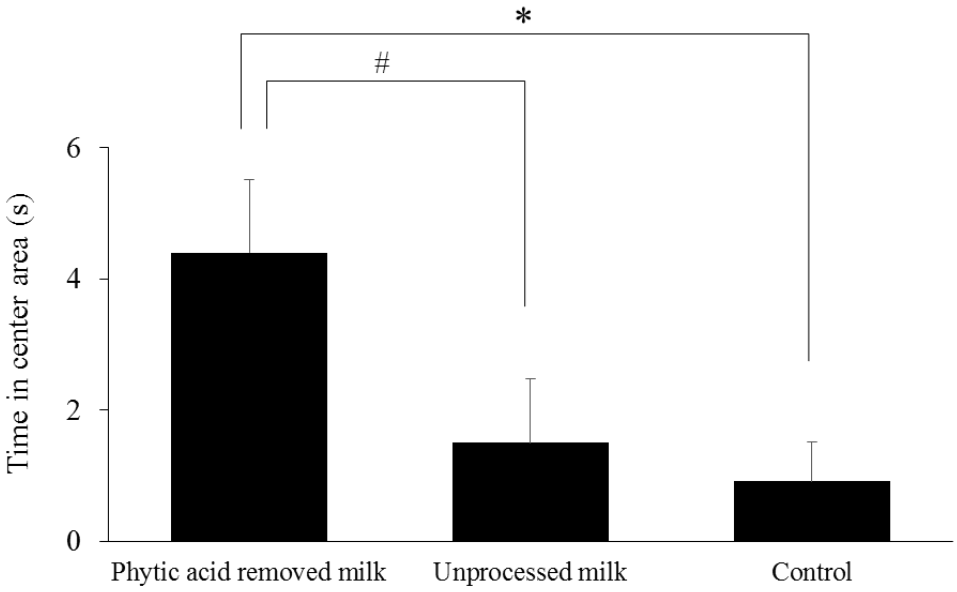

Figure 4. *Travel time in the center area of open field*

Figure 4 showed changes in travel time of rats in the center of open field. Results indicated that travel time of rats in the center areas in phytic acid removed milk treated group was significantly longer than this in saline treated group [Tukey test, $p<0,05$] and tended to be significantly longer than this in unprocessed milk treated group [Tukey test, $p<0,1$]. This results indicated that phytic acid removed soybean milk might improve exploration abilities of experimental animals.

IV. DISCUSSION

In the animal experiments, there are some behavioral tests to evaluate locomotor function and exploration ability. One of them is open field test which allows to assess locomotor functions by analyzing travel distances and average speeds in the open field area and to study exploration ability by comparing differences in travel time in the center area of open field [4,5]. In the present study, we concentrated to investigate effects of phytic acid removed soybean milk to

locomotor and exploration abilities of experimental animals. Thus, open field test was suitable for the aim of our present study. In the present study, we found that travel distances and average speeds of phytic acid removed milk treated rats were higher than these of saline and unprocessed milk treated rats. These results indicated that phytic acid removed soybean milk might improve locomotor function of experimental animals. An interpretation for these results might relate to roles of ions, such as calci, Zn as well as protein. A recent study has demonstrated that aging rats fed with the soluble milk protein supplementation improve their locomotion function [6].

Furthermore, exploration abilities of animals were also improved after administrations phytic acid removed milk for 4 weeks. That is, travel time of this milk treated animals was longer than these of saline or unprocessed milk treated rats. An improvement in exploration abilities of animals might involve in effects of calci. Godinho et al (2002) provided evidence of effects of calci to motor and exploratory acitivities of animals. Rats were maintained in on high calcium drinking water expressed higher exploratory activities [7]

In conclusion, in the present study, we found that phytic acid removed milk helps to improve motor and exploratory activities of animals. These are: phytic acid removed milk treated rats exhibited longer travel distances and higher average speeds in the open field area and longer durations in the center area of open field.

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RÉSUMÉ:

LE LAIT SOJA DÉBARRASSÉ DU PHYTATE A MONTRÉ L'AMÉLIORATION DE LA LOCOMOTION ET DE FACULTÉS EXPLORATRICES DU RAT

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Ce travail vise à l'investigation sur le lait soja débarrassé du phytate sur la locomotion et les facultés exploratrices des animaux d'expérimentation. Dans cette étude, 30 rats ont été répartis au hasard en trois groupes d'expérimentation. Groupe 1 (groupe contrôle) comprend 10 rats recevant de solution salée, groupe 2 (groupe de 10 rats recevant du lait soja normal), et groupe 3 comprenant 10 rats recevant du lait soja débarrassé du phytate. Tous les rats on recu 5ml de soluté sale ou de lait 1 fois/jour pour 4 semaines. Au bout de la 4eme semaine, après traitement, les rats doivent executer le test appele "champ ouvert" (open field). Les résultats ont montré que la vitesse moyenne, et la distance parcourue aussi bien que la vitesse à partir du centre du champ dans le groupe 3 étaient supérieures aux groupe 1 et 2. Ces résultats ont indiqué que le lait soja débarrassé du phytate pourrait améliorer la locomotion et les facultés exploratrices du rat.

Mots clés: *Rats, open field test, phytic acid removed soya milk, locomotor and exploratory activities.*

SURVEYING ORAL HEALTH STATUS OF CHILDREN WITH AUTISM DISODER PEACE KINDERGARTEN - BINH DUONG 2017

Vo Truong Nhu Ngoc*, Do Hoang Viet*, Hoang Bao Duy*,
Nguyen Tuan Anh**, Phan Nguyen Hong An** , Dao Thi Tam**

ABSTRACT

Objectives: Studying in 174 children aged 3 to 8 years with autism in Peace kindergarten to describe the oral health status in children with autism. ***Methods:*** cross-sectional analysis. ***ResulTotal:*** The autism group had a male-to-female ratio of 5,2:1 The rate of decay at medium level density is 64.37%. Mean dmft and DMFT were 2.60 and 0.85. SiC is at high level dentistry 5.2. 26.43% children had gingivitis. PLI = 2.35. ***Conclusions:*** The rate of decay in children with autism in Peace kindergarden was at medium level. Mean dmft and DMFT scores were low. However, the SiC was in high level deposit. Older children (6 - 8 years) had more tooth cavities and gingivitis than the younger (3 - 5 years).

Key words: *Caries, gingivitis, autism, austistic.*

I.INTRODUCTION

In Viet Nam, within 10 years due to the economic and social development the increase of consuming sugar, milk... in diets leads to the increase of tooth decay. Furthermore, the lack of specialists in dentistry caused many drawbacks in controlling dental caries and gum disease. According to the survey of the National Institute of Odonto - Stomatology VietNam in 2001, 84.9% of children (6 to 8 years) had cavities [1].

Besides, the number of autistic children tends to increase as a consequence of the socio-economic's changing. As compared with normal children, autistic's ones lack the ability to communicate causing many disadvantages in oral hygiene instruction and dental treatment. To contribute to work out a dental plan for autistic children, we conducted initial research topics to the following objectives: (1) A description of the caries status in children with autism in Peace kindergarten and (2) Determine gingivitis in children with autism at Peace kindergarten.

1. Background

Dental caries is an infectious disease of calcification organization which is characterized by the destruction of the mineral composition of inorganic and organic destruction of bone tissue [2]. Cavity is a complex process including chemical reactions relating to the movement of ions between the tooth surface and oral environment and the biological processes between bacterial plaque with defense mechanisms of the host. According to the National oral health 1st report in Viet Nam, 1990, the caries rate and mean DMFT score by age group were as follow: 12 years: 55.69%, DMFT = 1.82; 15 years: 60.33%, DMFT = 2.16. According to the National oral health 2nd report, 2001 [1] 12 years:

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decay rate: 56.60%, DMFT =1.174; 15years: decay rate: 67.60%, DMFT = 2.16. Thereby showing caries increases with age in both decay rate and DMFT index. The percentage of dental caries in children 6-8 years is quite high: 84.9% (*primary* teeth), 56.3% (permanent teeth). Moreover, gingivitis or gum disease is acquired in childhood. Gingivitis is caused by varied reasons, such as short of specific vitamins, occlusal trauma, bacteria and poor oral hygiene. In overall, the main cause is bacteria and poor oral hygiene. These factors will create plaque which is the main cause of gingivitis. Children rarely have periodontal diseases except gum's. In Vietnam, as the National oral health 1st report 1st, 1990, the percentage of gingivitis in 12 years old children is 95% [3]. As Tran Van Truong and colleagues (Viet Nam, 2001) found the percent of gum bleeding in children [1]: 6-8 years: 42.7%, 9 -11 years: 69.2%.

2. Autism

Autism is a developmental disorder that affects many aspects of the development, especially in the influential communication skills and social relationships [4]. Child autism is characterized by three main specific characteristics [5]: (1) Defects in quality of social relationships: children do not respond when called, do not have eye contact, like playing alone... (2) Defects in quality communication: children do not speak or say very little, meaningless word pronunciation, difficulties in initiating and maintaining conversation. (3) Restricted concern, repetitive and abnormal behavior: Children like to line up objects as toys, repetitive behavior such as clapping, hands on, shake. There is no formal investigation of the prevalence of children with autism in Vietnam. Nguyen Thi Huong Giang and colleagues studied in 506 children with autism at the National Pediatric Hospital, the rate of male / female is 8/1, percentage of patients in Binh Duong is 56.13% [5]. Dinh Thi Hoa studied 65 subjects aged 3 to 18 years in treatment at Bach Mai Hospital showed signs of speech delay children [6].

Parents usually notice signs of autism in the first two years of their child's life .These signs are the adaptation disorders of thinking, language and social relationships, almost autistic children have lower IQ level than normal. On account of autistic characteristics, it is hard to instruct oral hygiene and dental care for children with autism. Furthermore, oral diseases are easy to expand in these children [7]. According to a survey in Saudi Arabia, DMFT of children aged 6 -16 years old with autism was 1.6 ± 0.64 compared with children without autism was 0.6 ± 0.29 [8].

At present, Vietnam does not have any report on the oral health of children with autism, while the figure of children with autism is increasing.

II. MATERIALS AND METHODS

The study was carried out in Peace Kindergarten- Binh Duong - Viet Nam in 2017. A total of 174 children were included.

Subject's selection: children with autism in preschool Peace, Ages: 3-5 and 6-8 years old. Consent for examining the children was obtained from the parents and respective head master.

Exclusion criteria: can't cooperate during examine, Incomplete information gathering votes.

Examine caries, gingivitis by eye in ligh, examine and drying tools.
Time and place of study: from 05/2017 to 10/2017 at Peace Kindergarten (Binh Duong

City) and School of Odonto Stomatology - Hanoi Medical University.

Examinations:

All subjects were examined by one examiner for oral hygiene status and dental caries: The dmft/DMFT [9], significant caries index (SiC), gingival index(GI) with codes and criteria established by Loe and Silness in 1964 [10], DI.S (simplified debris Index). Met Need Index (MNI), an indication of treatment received by an individual is determined using the ratio of the mean missing (M) plus filled (F) teeth to mean decayed, missing and filled teeth (DMF) that is M+F/DMF (Jackson).

Using diagnostic criteria for caries in ICDAS.

Table 1.1. *ICDAS codes and criteria*

Code	Description
0	Sound tooth surface: no evidence of caries after 5 sec air drying
1	First visual change in enamel: opacity and discoloration (white or brown) is visible at the entrance to the pit or fissure seen after prolonged air drying
2	Distinct visual change in enamel visible when wet, lesion must be visible when drying
3	Local enamel breakdown (without clinical visual signs of dentinal involvement) see when wet and after prolonged drying
4	Underlying dark shadow from dentine
5	Distinct cavity with visible dentine
6	Extension (more than half the surface) distinct cavity with visible dentine

Data Analysis:

Data were collected and analyzed by the method of biostatistics, using SPSS 18.0 software and statistical algorithms.

2.6. Research ethics

All subjects and their parents will be explained about the purpose and content of the prior studies. The examinations were conducted only with the consent of subjects and their parents. Any personal information and research subjects, data from surveys, interviews will be kept confidentially.

The data and information collected will only be used for the purpose of study and research, not for any other purpose. The results of this survey will be used to plan a medical strategy for autistic children's oral health.

III.RESULT AND DISCUSSION

The study was conducted on 174 children in Peace kindergarten. The group aged 3 - 5 accounted for the largest percentage (62.07%, including 90 boys and 18 girls), and the group aged 6 - 8 accounted of 37.09%(56 boys, 10 girls). The autism group had a male-to-female ratio for 5.2:1 (83.91% against 16.09%). It might reflect the higher prevalence of autism in males as it was reported in other studies [5]. In the examination, there are 28 objects (25.93%) that can't cooperate to dry teeth and define PLI by GC Plaque indicator.

3.1.Dental caries

According to the WHO, there are two criteria to evaluate caries status in the community: prevalence of caries in a community; dmft/DMFT index to evaluate the risk of cavities and tooth decay in a community. High scores show the risk existing in high level.

3.1.1. Caries prevalence

The decay rate was 64.37% with no significant difference across gender **(Chi sq,** p = 0.567). While 78.78% older group had caries, the rate of caries in 3 -5 year old group is smaller 55.55%. The caries prevalence varied significantly by age group (Chi-sq, p=0.03).

According to the classification of the level of caries of the world health organization (WHO), the caries rate in our study is determined as average level, though Peace kindergarten located in Cau Giay District, center of Binh Duong-VietNam's Capital. This rate is higher than the study of Necmi in autistic children 7-16 years old (58.1%) (2007)[12]. Rate of milk tooth decay tends to raise with age, in the 3-5 year old group decay rate is 55.55% while the 6-8 year old group is 78.78%. This difference is due to the time that milk exists in the mouth longer, more exposure risk factors that cause tooth decay; moreover, the eruption of 1st molar and the restricted communication skills of children with autism increase the risk of caries with age. Therefore, the role of education on oral health and dental caries prevention at early stage is very important to reduce the risk of tooth decay and other complications in older ages.

The results of our study show that 30.30% children in 6 -8 year old group had permanent teeth decay. Rate of permanent teeth decay are treated is 0.00%. This suggests that children hadn't received essential dental care and parent's attention.

Table 3.1. *Rate the level of dental caries lesions milk by age (number 1 and number 2, corresponding to the 1st and 2nd ICDAS code, code 3 code corresponding ICDAS III or higher)*

Age	Code 1		Code 2		Code 3		T - Test
	n	%	n	%	n	%	
3 - 5	28	14.00	50	25.00	122	61.00	**p = 0.001**
6 - 8	0	0.00	22	9,09	220	90.91	
TOTAL	28	6.34	72	16.29	342	77.37	

In our study the rate milk teeth decay in early stage (code 1 and code 2, matched ICDAS code I and code II) was 22.63%. The rate of established decay and severe decay (code 3, matched ICDAS code III, IV, V, VI) was 77.37%. The level of caries tends to worse with age, early stage decay in 3-5 age group was 39%, in 5-8 age group was 9.09%. So the education of oral hygiene and prevention of caries will have better effect in the younger children.

The rate of early stage decay in permanent teeth accounted for 27.58% (16/56 permanent teeth decay). The proportion of established decay and severe decay in permanent teeth accounted for the highest percentage 72.42% (40/56 permanent teeth decay). If we only diagnosed established decay, we have omitted

many early stage caries requiring treatment. In addition, ***fluoridation and remineralization efficiency*** have the great effects on early stage decay, especially code 1.

3.1.2 dmft/DMFT and SiC

Table 1.1 *dmft by age group*

Age	dt		mt+ft			dmft	T-Test
	dt	dt/dmft (%)	mt	ft	(mt+ft)/dmft (%)		
3 - 5	1.85	100.00	0.00	0.00	0.00	1.85	p = 0.004
6 - 8	3.67	96.07	0.03	0.12	3.93	3.82	
TOTAL	2.54	97.69	0.01	0.04	2.31	2.60	

Dmft by gender group

	dt		mt+ft			dmft	T-Test
	dt	dt/dmft (%)	mt	ft	(mt+ft)/dmft (%)		
Nam	2.52	97.67	0.01	0.05	2.32	2.58	p = 0.881
Nữ	2.69	100.00	0.00	0.00	0.00	2.69	
TOTAL	2.54	98.07	0.01	0.04	4.66	2.60	

The overall mean dmft was 2.60. 6 - 8 year old group had the highest dmft index values (3.82) and the 3-5 age group's score was 1.85. In contrast to other research inn autistic children in the world, dmft index in our study is higher than Ceyhan Altun's (Turkey, 2010) 2.04 [13]. The difference is due to the interventions and prevention of tooth decay in Turkey. In our study, objects were children in capital Binh Duong, been educated about oral hygieneand examined by dentists. But as a consequence of autistic characteristic, the autism's ability to manage their own oral health is lower than other children . Children with autism have multiple medical and behavioral problems, which make their dental treatment extremely difficult so that MNI is very low (2.31%).

dmft index in autistic male is higher than in female (2.69 compared to 2.58). However, this difference is not statistically significant (T-test, p> 0.05). It can be explained that there's no different autistic characteristic between male and female.

DMFT score was 0.85, lower than dmft (2.60). This suggests that the longer the duration of teeth's exposure to risk factors, the higher chance of dental caries.

SiC

In 2000, the World Health Organization (WHO) has introduced SiC (Signification caries index) in order to bring attention to the individuals with the highest caries values in each population under investigation [14]. By using SiC, we can predict treatment needs of patienTotal in the future. The overall SiC is generally high 5.2. SiC of 6 - 8 years age group is higher than 3-5 years age group (3.17 compared to 6.1). It is recommended that regular contact be made with parents and caregivers and educated on the need for diet modification, improvement in oral hygiene and regular dental visiTotal for their wards. To achieve the target introduced by WHO that SiC Index for countries should be less than 3 DMFT in the 12-year-olds by the year 2018 requires us to strengthen prevention

activities such as oral hygiene instruction, diet, fluoridation...

3.2.Periodontal status

In the present study, we evaluated the GI (gingival index) of Loe and Silness introduced in 1963 [10]. Overall percent of gingivitis is 26.42%. The rate of gingivitis in male group and female group were 28.8% and 14.28%, respectively. Our result is lower than the Vishnu's (India, 2012) which was 50% children with mixed dentition [15]. However, our objects were the children with the milk or early stage of mixed dentition, so their ability of oral hygiene is better.

There are 20 children among 3 - 5 years age group had gingivitis, 26 in 6-8 years age group (39.4%). The overall Di.S index was 2.35. Mean Di.S of 6 - 8 years age group is higher than 3-5 years old group (2.80 compared to 2.08). This difference is statistically significant with $p < 0.05$. This difference can be explained by the growth of first molars and the changing of occlusion with mixed dentition in older children that cause difficulties in controlling oral hygiene.

IV. CONCLUSION

The caries prevalence of autistic children in Peace kindergarten stayed at average level. The overall dmft/DMFT scores were low. However, SiC was showing high number of 5.2. The overall percentage of gingivitis is 26.43%. Mean Di.S index was 2.35.

As a consequence of autistic characteristic it is important for the dentist to concentrate on a preventive approach and provide proper dental education to autistic children and their parents.

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RÉSUMÉ:

INSPECTION DE L'ETAT D'HYGIENE BUCCALE CHEZ LES ENFANTS ATTEINTS D'AUTISME AU PEACE KINDERGARTEN - BINH DUONG 2017

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Objectif: L'étude est menée sur des enfants de 3 à 8 ans, au jardin Peace Kindergarten, pour l'inspection de l'état d'hygiene buccale chez les sujets atteints d'autisme.

Méthode: L'analyse est cross-sectionnelle.

Résultats: La proportion M/F: 5.2/1. Le taux de caries dentaires est en moyenne 64.37%. La moyenne en dmft et en DMFT sont 2.60 et 0.85. SiC est élevé: 5.2. 26.43% ont une gingivite, le PLI = 2.35.

Conclusion: Les caries dentaires sont en nombre moyen. Les dmft et DMFT sont bas. Pourtant, le SiC est élevé, les plus âgés (6 à 8 ans) ont plus de cavites et plus de gingivite que les plus jeunes (3 à 5 ans).

Mots clés: *Caries, gingivite, autisme, autistic.*

RISK FACTORS OF ISCHEMIC CEREBROVASCULAR ACCIDENT: AN ACTUAL STATE IN PHU THO GENERAL HOSPITAL

Nguyen Quang An*, Nguyen Huy Ngoc*

ABSTRACT

Introduction: High rate of ischemic stroke recently due to many uncontrolled risk factors. ***Aims:*** Investigating most important risk factors in ischemic stroke patients presented in Phu Tho Provical General hospital. ***Methods:*** A prospectively observational study. ***Results:*** TIA was seen at 13.0% of all cases and risk of progressing to severe or death with OR = 5.2; 63.5% of all patients appeared with hypertension had the risk of being severe or death with OR 3.2. Pre-exist of heart diseases was available in 28.1% cases with OR = 2.6 in the risk of getting worse or death. Hyperlipidemia rate was high, risk of deterioration with OR = 2.6. Alcohol and tobacco addiction was found in 72.6% patients and risk of becoming death or worse 2.4 times higher than alcohol and smoke - free patients. ***Conclusion:*** Some risk factors had good predictive prognosis value in ischemic stroke.

Key words: *Risk factors, Ischemic stroke, ischemic cerebrovascular accident*

I. INTRODUCTION

In Europe, it is estimated that about 1 million cases of cerebrovascular accident presented annually while in United State of Amedica, rate of stroke is 794/100.000 of population and only 400.000 patients are to be discharged. [6] In Asia region, the incidence of stroke is different between different countries: in Japan, rate of stroke is 303/100.000 of population, in China this is 115,6/100.000, in which 370/100.000 of Bejing population only[6].

More and more people are taking notice about stroke nowadays and knowledge of stroke was also significantly improved especially in fast and accurate diagnostic imaging techniques, pathology-based treatments and the widespread establishment of stroke centers. Many acchievements were reached in both stroke prevention and treatment. Nonetheless, mortality of stroke is still high, and stays third after cardiovascular diseases and cancer, and most common in neurologic diseases which contributed 20% of all internal medicine conditions [3].

Stroke, which includes acute ischemia stroke (AIS) and acute haemorrhagic stroke (AHS) in which AIS was most common with the incidence of 80 - 85%. In EU, US and developed countries, AHS was seen in 10-15%. In Asia region, AHS could be increased but never higher than AIS. In Vietnam, Le Van Thanh et al (1990) investigated 2962 stroke patients: 40.42% was AHS and 59.58% AIS. In another study of Hoang Khanh in Hue city, AHS accounted for 39.42% and AIS was about 60.58%[3].

In Vietnam, average life expectancy is currently increased due to developed social-economic conditions and more and more stroke were seen. Many studies were conduted focussing on AIS but most of those were done in the national - level hospitals. Phu Tho is a midland and mountain province

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with 5.528 km^2 square, population of 1.4 million; 36 nations with different condition and life standard. Poor people contributed a large part (31.8% in 2005 and 20.34% in 2010). Alcohol was overused due to traditional habits and smoke in popular environment is common. Risk factors of AIS weren't noticed appropriately. In another hand, stroke patients are cared for in different facilities: ICU, emergency room, Internal medicine wards, cardiology wards, neurology wards…There for, a study in AIS in Phu Tho which was never conducted before is highly recommended to be done to investigate the actual state of AIS to prepare resources in diagnosis and treatment of AIS. **AIMS:** To evaluate important risk factors of AIS in Phu Tho Provincial general hospital

II. OBJECTIVES AND METHODS

Objectives:

190 AIS patients who received medical care in Phu Tho provincial general hospital between October 2014 and October 2016.

Including patients criteria:

Clinical criteria: WHO diagnostic criteria of AIS in 1990 [10]: sudden symptoms (minutes to hours, days) which prolong more than 24 hours, with focal symptoms (belonging to impair arteies) without correlation to trauma.

Work up: Brain MRI showing at least one of 2 signs [4]: Homogeneous intensity on T1W, hyperintensity on T2W in subcortical area and loss of differences between parenchyma and cortex. Hypodense signal on T1W and hyperintense signal on T2W.

Excluding criteria: *Transient ischemic attack (TIA), ischemic stroke in a patient with pre-history of head trauma or blunt trauma. Co-morbidity of encephalitis, menigitis or brain tumour; ischemic stroke converted to haemorrhage; relapsed ischemic stroke or normal finding on MRI.*

Methods: Prospective observation study

Statistic Analysis: Software SPSS 18.0 and STATA 10.0.

III. RESULTS

Pre-history of addiction

Table 1: *Tobacco and alcohol abuse*

History	Group II (n = 64)		Group I (n = 128)		n (%) n = 192
	N	%	n	%	
Alcohol abuse	22	34.4	27	21.1	49 (25.8%)
Tobacco addiction	27	42.2	26	20,3	52 (27.4%)
Alcohol and tobacco addiction	17	25.5	21	16.4	37 (19.4%)

Other pre-medical history

Table 2: *Pre-medical histoty playing role of risk factors*

History	Group II (n = 64)		Group I (n = 128)		n (%) (n = 192)
	N	%	n	%	
Hypertension (HTN)	52	80,2	70	54.7	122 (63.5%)
Diabetes	12	19,8	18	14.1	30 (15.6%)
Heart diseases (Heart failure,	21	33.3	33	25.8	54 (28.1%)

AF, mitral valve stenosis)					
TIA	18	28.6	07	5.4	25 (13.0%)

Table 3: *Blood pressure measurement in HTN group*

Blood pressure	Minimum	Maximum	Mean	SD
Systolic BP (mmHg)	140	180	152	10.2
Diastolic BP (mmHg)	70	120	94	8.9
Years of HTN	1	20	7	4.7

Table 4: *Patients Classification based on risk factors number*

		Number of risk factors						Total
		0	1	2	3	4	5	
Group II	n	4	14	12	9	15	10	64
	%	6.2	21.8	18.7	14.1	23.4	15.8	100
P		**< 0.05**						
Group I	n	11	45	38	12	15	5	128
	%	8.5	35.2	29.7	9.4	11.7	5.5	100

Predictive value of some risk factors

Table 5: *Patient distribution based on severity*

	n	%
Group I (mild and medium)	128	66.7
Group II (severe -death)	64	33.3
Tổng số	192	100%

Table 6. *Predictive value of pre-medical historical risk factors*

Diseases	Yes	No	Total
Hypertension			
Group II	52 (81,0%)	12 (19,0%)	64
Group I	71 (55,4%)	57 (44,6%)	128
OR = 3,2	95% CI = 1,3 - 7,8		p = 0,009
Heart diseases (Heart failure, AF, mitral valve stenosis)			
Group II	22 (34.3%)	42 (65.6%)	64 (100%)
Group I	34 (26.5%)	94 (73.5%)	128 (100%)
OR = 26	95% CI = 1.1 - 6.1		p = 0.034
Diabetes			
Group II	13 (20.3%)	51 (79.7%)	64 (100%)
Group I	19 (14.8%)	109(85.2%)	128 (100%)
OR = 2.2	95% CI = 0.9 - 5.1		p = 0.073
TIA			
Group II	19 (29.7%)	45 (70.3%)	64 (100%)
Group I	08 (6.2%)	120 (93.8%)	128 (100%)
OR = 5.2	95% CI = 1.7 - 15.8		p = 0.004
Tobacco addiction			
Group II	28 (43,7%)	36 (56.3%)	64 (100%)
Group I	24 (18,8%)	104 (81,2%)	128 (100%)

Diseases	Yes	No	Total
OR = 2,4	95% CI = 1,0 - 5,6		p = 0,044
Alcohol abuse			
Group II	23 (35,9%)	41 (64,1%)	64 (100%)
Group I	28 (21.9%)	100 (78.1%)	128 (100%)
OR = 2,5	95% CI = 1,1 - 6,0		p = 0,038
Hyperlipidemia			
Group II	42 (65.6%)	22 (34.4%)	64 (100%)
Group I	53 (41.4%)	75 (58.9%)	128 (100%)
OR = 2.6	95% CI = 1.2 - 5.9		P = 0.02

Table 7. *Predictive valuse of MRI finding*

Severity	Size of ischemic area		n (%)
	< 3cm	≥ 3cm	
Group II	27 (42.2%)	37 (57.8%)	64 (100%)
Group I	81 (63.2%)	47 (36.8%)	128 (100%)
OR = 3.4	95% CI = 1.5 - 7.4		p = 0.002
Severity	**Number of ischemis area**		**n (%)**
	1	>1	
Group II	48 (75.0%)	16 (25.0%)	64 (100%)
Group I	94 (73.5%)	34 (26.5%)	128 (100%)
OR = 0.7	95% CI = 0.3 - 1.7		p = 0.536

IV. DISSCUSSION

Tobacco addiction

Smoking has become a crucial issue in modern societies. Vietnam is one of the countries in which smoking rate is highest in all over the world: 50% of adult males have smoking habit which counts about 17 million smoking people. Many studies before show the strong corelation between smoking and stroke. In this study, 27.4% patient smoked (table 3.29) which was higher than results of Phan Thi Huong (16.0%[8]), Dinh Van Thang 17.9%). This results from the smoking rate of Vietnamese that increased significantly recently.

Patients with pre-social habit of smoking has an increased risk of converting to severe condition or death in AIS with OR = 2.4 (p = 0.044; CI: 1.02 - 5.6). Our result is considered simirlarly to other Vietnamese and international authors. In Le Quang Cuong study, smoking increased the risk of AIS 1.9 times in female and 2.5 times in male while Wolf P.A et al concluded that smoking rose up the risk of stroke about 40% in male and 60% in female. The study named Framingham of Wolf P.A et al conducted within 26 years showed that heavy addiction (more than 40 cigarrettes a day) had a risk of stroke 2 times higher than light addiction (less than 10 cigarrettes a day) and this risk reduced greatly 5 years after smoke quitting. Therefore, smoking is seriously considered a risk of AIS.

Alcohol abuse

25.8% of our study population is alcoholic which was similar to Le Ngoc Trong (26.9%) and Dang Quang Tam (31%)[2]; and higher than Pham Thi Thu Ha (6.62%) and Phan Thi Huong (7.06%)[8].

The Odd ratio of alcohol abuse on severity and death was 2.5 (p = 0.038, CI = 1.1 - 6.0) comparing to non-alcohol use. Many others studies impressed the role of alcoholic in the deterioration of stroke. Zhang's study in China found that heavy alcoholic people had a risk of stroke 1.9 times higher than other. Mukamal K.J observed alcohol addicts during 14 years expressed that the habbit of drinking 10-29 gram ethanol a day, 3 - 4 days a week induced the lowest risk of stroke whereas people consumped more than 2 glasses of whiskey a day had the highes risk. Le Quang Cuong reported that, ethanol consumption increased 10% in the population would rise the stroke morbidity up to 29% and mortility up to 16%.

Because alcoholism significantly induced hypertension, increased platelet cell adherence, fulminant atrial fibrilation which all contributed to AIS. Hence, ethanol abuse, especially in such a long duration had a bad affect on the severity of stroke, especially AIS.

Hypertension (HTN) history

From our results, HTN was seen in 63.5% of population that was higher than Dao Thi Bich Hoa (40%) [1]. This resulted from HTN became more and more popular, especially in developed countries. In a report of WHO in 2000, in all over the world, it is estimated that 972 million people had HTN and this number was predicted to be 1.5 trillion people in 2025. In United State of America where medical system is considered the best in the world, only 77.6% people recognized of HTN. Because our result collected by asking the patients directly or their family member so that the actual number of HTN in our population should be much higher than 63.7% that we had.

Other studies shew that both systolic and diastolic blood pressure independently induced different types of stroke. Recent studies found that systolic BP higher than 160mmHg and diastolic BP higher than 95mmHg could increase the risk of AIS 3.1 times in men and 2.9 times in women. If systolic BP stayed in the range of 140 and 159 mmHg and diastolic Bp stayed in the range of 90 and 94mmHg would rise the risk of stroke up to 50% [1].

The longer duration with HTN, the more severe symptoms of stroke patient could suffered. In our study, mean duration of HTN is 7 years. Consequently, chronic HTN patients ought to pay a highly - warned attention to AIS.

From our finding, HTN put the AIS patient in the risk of getting worse of even death 3.2 times higher than non-HTN with CI: 1.3 - 7.8 and p = 0.009). Other author estimated that 10mmHg reduction of systolic BP in adult would decrease 30% in the risk of death due to heart diseases and also drop 40% risk of mortality due to stroke. Because of this, early recognition and regular treatment of HTN and comunity education for this issue are extremely necessary. However, even in United State of America, only 67.9% in 73 millions and only 44.1% of those were tightly controlled. So the difficulty in HTN management is not just belong to developing countries but also of developed ones.

Diabetes mellitus

There has been a huge amount of trials worldwide affirmed that diabetes mellitus or diabetes is a crucial risk of atherosclerosis which played an important role in embolism

appearence and AIS. In United State in 1976-1980 diabetes patient had a risk of AIS 2.5 to 4 times higher than people who hadn't diabetes. In Honolulu CardioVascular Programe, the Japanese Haiwaiee with diabetes had a 2 times risk of DVT comparing to others without diabetes, independently. In another investigation Framingham, although the most influence of diabetes was on micro-vascular diseases but that still had a bad effect on coronary and cerebral vascular[11].

In our study, the Odd ratio of diabetes on AIS is 2.2 but with p > 0.05; this suggested that diabetes could increase the risk of getting AIS or being worse with AIS however the p value suggested that we could try with a larger population to confirm this number. Within our AIS population, diabetes took 15.6% which was higher than previous studies such as Phan Thi Huong 6.2%[8], Pham Thi Thu Ha l.62%. One of the reasons was diabetes rate in our country increased in the last few years. The recent report found that diabetes morbidity rose 8% to 20% annualy putting Vietnam in the list of countries which had a fastest increased number of diabetes worldwide.

Explaining the sharply elevation of diabetes rate recently, we considered the higher standard of living, imbalance between nutrition and phycical activities. These should be considerable factors to be strictly justified to reduce diabetes and AIS morbility.

Previous Heart Diseases

In our study, 28.1% patient had previous heart diseases similar to results from Dawng Quang Tam 21.2% [2], Dinh Van Thang 6.5%, and Nguyen Xuan Than 6.1%. Those patients had an increased risk of severe and death with OR = 2.6 (CI = 1.1 - 6.1; p = 0.034). This factor had a highly predictive value with p < 0,05. In a patient with pre-exist cardiovascular diseases, the risk of AIS was higher and when the suffered from AIS, the possibility of deterioration was higher because exist cardiovascular conditions could appeared embolism from the heart and reduced peripheral and also cerebral perfusion. Atrial fibrilation (AF) was a common impairment and was a strong risk of AIS, a well-care of AF therefore would prevent AIS's appearence effectively.

Framingham study shew that there was an clear elevation of AIS in AF patients: 1.5% at the age of 50- 59 and 23.5% at the age of 80-89. The author also impressed that 8% of men and 11% of women could had AIS within 6 years after an acute myocardial infarction (MI). Besides AF, other cardiovascular conditions such as dilated myocardiopathy (DMC), mitral valve prolapse (MVP), mitral valve stenosis (MVS), heart failure (HF), artificial heart valve, acute endocarditis and other congenital heart defects could induce AIS with different risk level.

Our study didn't focus on the detail diagnosis of heart diseases due to the small number of this group. Furthermore, heart diseases was just a limited part between other important factors needed to be investigated. However from our limited data, the actual information from the patients who had previous heart diseases did improve our belief and effecacy in the treatment of AIS patients.

Previous Transient Ischemic Attack

TIA, if avalable was an important factor influenced on the risk of AIS but also the severity of AIS, especially the death risk in the first few days after the AIS on set. TIA was combined with neurological deficits existed only within 24 hours and recovered

completely but tended to relapse multiple times later. However, TIA highly warned about a widepread atherosclerosis and easy to become worse which could result in AIS and multifocal ischemic stroke. In Flemming KD's study, 8% of TIA patient suffered from actual AIS in the first month, 20% of these patients had risk of acute MI, stroke or sudden death in the first 12 months.

In our study, TIA was found in 13.0%, similar to Le Thi Hoa Binh 12.8%, Le Van Thinh 11% [5], and Dinh Van Thang 8.9%. When patient had TIA, risk of severe AIS was highest with OR =5.2, p = 0.004). So then, if the patient has previous TIA, patients would had the risk of becoming severe or death 5.2 times higher than patients without TIA before. TIA was a clear sign of "nearly" obstruction in cerebral vascular system which raised up an important alarm of further poor-prognosis complications after.

In the studies of Flemming, Brown and Petty, TIA had the highest risk of severe AIS comparing to all other risk factors such as HTN, diabetes and heart diseases. Because of this, TIA treament could help to prevent further AIS in the future and was considered more crucial than reperfusion therapies after AIS happened already. From those results we strongly recommend to investigate and closely observe TIA signs to acchive adequate diagnosis and treatment. Therefore we could prevent poor-outcome complications and reduce severe AIS or death.

Total Number of Risk factors in a patient

In the mild and medium group, patients had only one or maximum two risk factors while in the severe or death group most patients had at least 3 risk factors, the difference was significantly. Therefore, the more risk factors patient had previously, the more severe symptoms patients could suffered. In the study of Nguyen Thi Hoa Binh and Le Tu Phuong Thao, most of patients had 2 risk factors, rarely one, especially many patients brought 3 and more risk factors. This rang an alarming notice because uncontrolled hyperlipidemia, HTN, diabetes would contributed directly in the severity of AIS. Every each factor had a special effect on each other. For example, patient with hyperlipidemia tent to had atherosclerosis and HTN whereas incontrolled diabetes surely increased atherosclerosis and therefore increased the risk of ischemic stroke.

V. CONCLUSSION

TIA was found in 13.2% patient which could progress to severe group with OR = 5.2. Hypertension was seen at 63.7% patient and had a risk of being severe 3.2 times higher than normotensive cases. Patient with heart diseases contributed 28.4% of population and risk of getting worse with OR = 2.6. High rate of hyperlipidemia was caught with risk of deterioration with OR = 2.6). Cigarretes and alcohol abuse was 72.6%; smoke adiction had a risk of being worse with OR = 2.4 while the risk of alcohol abuse was with OR = 2.5.

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RÉSUMÉ:

LES FACTEURS DE RISQUE DE L'ACCIDENT ISCHÉMIQUE CÉRÉBROVASCULAIRE: LEUR ÉTAT ACTUEL A L'HÔPITAL GÉNÉRAL DE PHU THO

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Introduction: Un grand nombre d'accidents ischémiques cérébrovasculaires est du à plusieurs facteurs de risque incontrôllés.

But: Investigation sur les facteurs de risque les plus importants d'accidents ischémiques cérébrovasculaires chez les patients se présentant à l'hôpital général de la province de Phu Tho.

Méthode: C'est une étude propective, et d'observation.

Résultats: Le TIA a été observé dans 13.0% de tous les cas et risque d'évoluer vers l'état grave ou le décès avec OR=5.2; 63.5% des patients se présentent avec hypertension artérielle, évoluant vers l'état grave ou la mort avec OR=3.2. Une cardiopathie pré-existante: 28.1%, avec OR=2.6% pour l'évolution vers l'aggravation ou la mort. L'hyperlipidémie comportait un risque élevé de détérioration, avec OR=2.6. L'addiction à l'alcool et le tabac a été retrouvé chez 72.6% de patients, et le risque d'évoluer vers un état plus grave ou la mort est de 2.4 fois plus grand que chez la personne qui en est indemne.

Conclusion: Il existe quelque facteurs de risque ayant un bon prognostic dans l'ictus ischémique.

Mots clés: *Risk factors, Ischemic stroke, ischemic cerebrovascular accident.*

EFFECTS OF DIPEPTIDYL PEPTIDASE INHIBITORS AS ADD-ON TO ORAL DIABETIC DRUG(S) IN PATIENTS WITH TYPE 2 DIABETES IN NATIONAL HOSPITAL OF ENDOCRINOLOGY

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ABSTRACT

Objectives: To evaluate effects of Dipeptidyl Peptidase (DPP)-4 Inbibitors as add-on in patients with type 2 diabetes inadequately controlled with oral antidiabetic drug (OAD) monotherapy or combination. ***Subjects and methods:*** An intervention study was conducted in 101 patients with adult type 2 diabetes inadequately controlled with OAD monotherapy or combination other than DPP-4 inhibitors with HbA1c > 7 to 10%. The outcome measures were fasting plasma glucose (FPG), 2 hour postprandial glucose (2hPPG) and HbA1c that were assessed at the baseline, after 12 and 24 weeks. A DDP-4 inhibitor was started with a half or full dose for the first 12 weeks and could increased to full dose for the last 12 weeks if started as half dose. The other OAD and their doses were kept unchainged during the whole study. ***Results:*** The mean age and diabetes duration was 54.1 ± 10.1 and 2.4 ± 3.4 years, respectively. Before the study start, metformin monotherapy was used by 60.4% of patients, and the most used combination was metformin plus sulfonylurea (34.6% amng all the patients). Sitagliptin was the only used DPP-4 inhibitor with mean dose of 88.1mg/day and 86.6mg/day for the first and second 12 weeks. After 24 weeks, compared the baseline, the mean FPG, 2hPPG and HbA1c significantly further decreased by 1.91 mmol/L, 3.42 mmol/L and 1.45%, respectively (p < 0,001 for all), and the proportions of patients achieving MoH 2017 FPG, 2hPPG and HbA1c targets significantly increased from 18.8%, 11.9% and 0%, respectively (p < 0,001). ***Conclusions:*** The add-on of the DPP-4 inhibitor Sitagliptin in patients with type 2 diabetes inadequately control with metformin alone or OAD combinations resulted in substantial improvements of glycemic control for a period of 24 weeks.

Key words: *Type 2 diabetes, Dipeptidyl Peptidase Inhibitor.*

I. INTRODUCTION

Number of type 2 diabetes is increasing all over the world, especially in developing countries. It causes numerous severe complications in almost all body organs and systems, in particular eyes, kidneys, nerves, heart and blood vessels.

Type 2 diabetes has multiple pathophysiologic defects. Beside the long well known defects such as insulin resistance, beta cell failure and increased hepatic glucose production, relatively new defects have been discovered some of which are incretin defects and inappropriately increased glucagon secretion. Multiple

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pathophysiologic defects and progressive beta cell failure results in failure of even multiple old OAD combinations in long run. It is necessary to develop new antidiabetic drug classes that aim at these new defects and complement the old OADs effects. One of the new OAD classes is Dipeptidyl peptidase (DPP-4) inhibitors that prolong endogenous incretins that are rapidely inactivated by that enzyme. Incretins are gut hormones secreted in response to nutrients (mainly carohydrates). There are two incretins: glucagon like peptide (GLP) - 1 and glucose-dependent insulinotropic peptide (GIP). They simulate insulin release and supress glucagon release in response to a meal in a glucose-dependent manner, slow gastric emptying and enhance satiety. Add-on of DPP-4 inhibitors to ongoing different OAD monotherapy or combinations have been shown to improve blood glucose control in numerous studies abroad, but has not been studied in Vietnam. The present study aims at evaluating effects of DPP-4 inhibitors as add-on therapy in patients with type 2 diabetes inadequately controlled with oral antidiabetic drug (OAD) monotherapy or combination in National Hospital of Endocrinology.

II. SUBJECTS AND METHODS

2.1. Subjects are patients with type 2 diabetes diagnosed by the WHO 1998 criteria and inadequately controlled with OAD(s).

2.1.1. Inclusion criteria

Patients with type 2 diabetes were recruited into the study if they met the all following criteria:

- age of 30 years or above
- HbA1c level ranging from 7,0% to 10,0%
- current use of oral antidiabetic drug monotherapy or combination other than DPP4 inhibitors with stable doses for at least 3 months before the recruitment
- giving consent to participate in the study

2.1.2. Exclusion criteria

Patients were excluded if they had any of the following:

- severe or acute illness such as coma or precoma, unstable angina pectoris, acute stroke, acute myocardial infarction, cachexia.
- stage 3a or more advanced chronic kidney disease
- liver enzyme levels ≥ 3 times of the upper normal limits.
- current use of any of DPP4 inhibitors, GLP-1 angonists or insulin
- declining consent to participate in the study

2.2. Methods

2.2.1.Study design: This was an uncontrolled trial evaluating effects on blood glucose of DDP4 inhibitors added to other oral antidiabetic drug monotherapy or combination in patients with type 2 diabetes who had not reach HbA1c target of below 7,0%.

The baseline oral antidiabetic drug(s) and their doses remained unchanged during the follow-up. Sitagliptin, a DPP-4 inhibitor, was added with a starting dose of 50 or 100mg once daily. In the former case, the dose increased to 100 mg daily at week 12 if HbA1c was still above 7,0%. The duration of the intervention was 24 weeks.

2.2.2. Sample collection: All the patients who met the inclusion and exclusion criteria were recruited into the study.

2.2.3. Outcomes measures

The patients' baseline characteristics that were assessed included age, sex, BMI, diabetes duration, use of oral diabetic drugs, and blood glucose control indices (FPG, 2hPPG and HbA1c). The three last measurements were reassessed at weeks 12 and 24.

- The Ministry of Health (MoH) 2017 targets of blood glucose control were as follow: FPG: 4,4 - 7,2 mmol/L; 2hPPG: < 10 mmol/L; HbA1c < 7,0%.

2.4. Statistical analysis: SPSS version 20.0 was used for data analyzing. The effects of adding DPP-4 inhibitors on blood glucose were evaluated by comparing the blood glucose control indices in weeks 12 and 24 to those at baseline, and the rates of achieving blood glucose control targets at those points of time.

III. RESULTS

3.1. Patients baseline characteristics

3.1.1. Sex, age and BMI

Table 3.1. *Distribution of patients by sex*

Sex	Number	Percents
Male	48	47,5
Female	53	52,5
Total	101	100,0

Comments: A total of 101 eligible patients with type 2 diabetes participated in the study, including 48 men (47,5%) and 53 women (52,5%).

Table 3.2. *Patients' Distribution by age groups and mean age*

Age	Number	Percents
30-39	9	8.9
40-49	26	25.7
50 - 59	**41**	**40.6**
60 -69	17	16.8
70 - 79	8	7.9
Total (%)	101	100.0
Mean ± SD	54.1 ± 10.1	

Comments: The mean age was 54.1 ± 10.1 years. Most patients were in age range from 40 to 69 years, making up 83.1% of the study populations.

Table 3.3. *Distribution of patients by BMI*

BMI (kg/m^2)	Number	Percents
Lean (< 18,5)	0	0
Normal (18,5 - 22,9)	39	38.6
Overweight/Obese (≥ 23,0)	**62**	**61.4**
Mean ± SD	23.5 **±** 2.1	

Comments: The mean BMI was 23,5 ± 2,1 kg/m^2. 61.4% of patients were overweight or obese.

3.1.2. Diabetes duration

Table 3.4. *Distribution of patients by diabetes duration*

Diabetes duration (years)	Number	Percent's
< 5	85	84.1
5 - 10	11	10.9
> 10	5	5.0
Mean ± SD	2.4± 3.4	

Comments: The mean diabetes duration (defined as time period elapsed since diabetes was diagnosed) was 2.4 ± 3.4 years. Most patients had diabetes for less than 5 years (84.1%).

3.2. Antidiabetic drug use before the study

Table 3.5. *Antidiabetic drug use before the study*

Antidiabetic drug		n	Percents in all patients	Percents in separate mono- or combination
Monotherapy	***Metformin***	**61**	60.4%	100.0%
Combination	***Sulfonylurea + Metformin***	**35**	34.6%	87.5%
	Sulfonylurea + Acarbose	1	1.0%	2.5%
	Metformin + Acarbose	2	2.0%	5.0%
	Sulfonylurea + Metformin + Acarbose	2	2.0%	5.0%

Comments: Before the intervention at baseline, all the patients were on oral antidiabetic drug(s) only (no patient was on insulin). Metformin was the only oral antidiabetic drug monotherapy and was used by the majority of all the patients (60.4%). 39.6% patients were on oral antidiabetic drug combinations among which the dominating combination was sulfonylurea and metformin one that made up 34.6% among all the patients and 87.5% among the combinations.

3.3.Baseline blood glucose indices

Table 3.6. *Mean of blood glucose indices*

Blood glucose indices (n = 101)	Mean ± SD
FPG (mmol/L)	8.62 ± 1.67
2hPPG (mmol/L)	12.36 ± 2.36
A1C (%)	7.93 ± 0.83

***Comments*:** The mean FPG, 2hPPG and HbA1c was 8.62 ± 1.67 mmol/L, 12.36 ± 2.36 mmol/L and 7.93 ± 0.83%, respectively.

Table 3.7. *Rate of patients achieving and not achieving blood glucose targets at baseline*

Targets by MOH 2017	Not achieving targets		Achieving targets	
	Number	Percents	Number	Percents
FPG (4.4 - 7.2 mmol/l)	82	81.2	19	18.8
2hPPG (< 10.0 mmol/l)	89	88.1	12	11.9
HbA1C (< 7.0 %)	101	100.0	0	0.0

Comments: At baseline only minority of the patients achieved FPG and 2hPPG targets that made up 18.8% and 11.9%, respectively. All the patients did not achieved HbA1c target at baseline.

3.3. Add-on of DPP-4 inhibitors

All the patients received sitagliptin at a daily dose of 50mg or 100mg that was unchanged until week 12. At week 12 the daily sitagliptin dose increased from 50mg daily to 100mg daily in 5 of patients.

Table 3.8. *Use of Sitagliptin during the study*

Sitagliptin use	Week 1 - 12	Week 12 - 24	p
Sitagliptin 50mg/day [n(%)]	24 (23.8%)	27 (26.7%)	> 0.05
Sitagliptin 100mg/day [n(%)]	77 (76.4%)	74 (73.3%)	> 0.05
Mean ± SD (mg per day)	88.1 ± 21.4	86.6 ± 22.2	> 0.05

Comments: All the antidiabetic drug(s) used before the study start and their doses remained unchanged during the whole study. All the patients received sitagliptin at a daily dose of 50mg or 100mg that was unchanged until week 12. For weeks 1 to 12, 23.8% and 76.4% patients used daily 50mg and 100 mg of sitagliptin, respectively. After week 12, 6 patients decreased sitagliptin from 100mg to 50mg and 3 patients increased sitagliptin from 50mg daily to 100mg so that 26.7% and 73.3% of the patients took daily sitagliptin dose of 50mg and 100 mg, respectively. That resulted in a decrease of the mean daily dose from 88,1mg to 86.6mg, but all the dose changes were not statistically significant.

3.4. Effects of adding DPP-4 inhibitors on blood glucose

Table 3.9. *Changes of blood glucose indices at week 12 compared with baseline*

Blood glucose indices	Baseline	Week 12	Changes	*p*
FPG (mmol/L) (n=101)	8.62 ± 1.67	6.92 ± 1.67	-1.70 ± 2.06	< 0.001
2hPPG (mmol/L) (n=101)	12.36 ± 2.36	9.56 ± 1.19	-2.80 ± 2.26	< 0.001
HbA1C (%) (n=101)	7.93 ± 0.83	6.72 ± 0.86	-1.21 ± 0.86	< 0.001

Note: Values are mean ± SD

***Comments*:** Compared with the baseline values, the mean FPG, 2hPPG and HbA1c at week 24 decreased by 1.70 ± 2.06mmol/L, 2.80 ± 2.26mmol/L and 1.21 ± 0.86%, respectively, all reductions were statistically significant with p < 0.001.

Table 3.10. *Changes of blood glucose indices at week 24 compared with baseline*

Blood glucose indices	Baseline	Week 12	Changes	p
FPG (mmol/L) (n=101)	8.62 ± 1.67	6.59 ± 0.95	-1.91 ± 1.90	< 0.001
2hPPG (mmol/L) (n=101)	12.36 ± 2.36	8.90 ± 0.94	-3.42 ± 2.26	< 0.001
HbA1C (%) (n=101)	7.93 ± 0.83	6.41 ± 0.74	-1.45 ± 1.00	< 0.001

Note: Values are mean ± SD

***Comments*:** Compared with the baseline values, the mean FPG, 2hPPG and HbA1c at week 24 decreased by 1.91 ± 1.90mmol/L, 3.42 ± 2.26mmol/L and 1.45 ± 1.00%, respectively, all reductions were statistically significant with p < 0.001.

Table 3.11.*Changes of blood glucose indices at week 24 compared with week 12*

Blood glucose indices	Week 12	Week 24	Changes	p
FPG (mmol/L) (n=87)	6.85 ± 1.62	6.59 ± 0.95	-0.26 ± 1.70	0.151
2hPPG (mmol/L) (n=87)	9.56 ± 1.22	8.92 ± 0.94	-0.64 ± 1.26	< 0.001
HbA1C (%) (n=87)	6.72 ± 0.85	6.41 ± 0.74	-0.31 ± 0.82	0.001

Note: Values are mean ± SD

***Comments*:** Compared with week 12, the mean FPG, 2hPPG and HbA1c at week 24 decreased by 0.26 ± 1.70mmol/L, 0.64 ± 1.26mmol/L and 0.31 ± 0.82%, respectively. The reduction was not significant for FPG (p = 0.151) but those for 2hPPG and HbA1c were statistically significant (p < 0.001 and 0.01, respectively).

Table 3.10. *Changes of rates of achieved blood glucose targets at weeks 12 and 24 compared with baseline*

MOH 2017 targets	Baseline (N=101) (1)		Week 12 (N=101) (2)		Week 24 (N=87) (3)		p
	n	%	n	%	n	%	
FPG (4.4 - 7.2 mmol/l)	19	18.8	70	69.3	70	69.3	$p_{12} < 0,001$ $p_{13} < 0,001$
2hPPG (< 10.0 mmol/l)	12	11.9	71	70.3	79	78.2	$p_{12} < 0,001$ $p_{13} < 0,001$
HbA1C (< 7.0 %)	0	0.0	62	61.4	70	69.3	-

Comments: The rates of patients achieving MOH 2017 blood glucose targets increased at weeks 12 and 14 compared with the baseline: for FPG target 69.3% and 69.3%, respectively,

compared with 18.8% at baseline (p < 0,001 for both); for 2hPPG 70.3% and 78.2%, respectively, compared with 11.9% at baseline (p < 0.001 for both), and for HbA1c 61.4% and 69.3%, respectively, compared with 0% at baseline.

IV. DISCUSSIONS

1.Baseline patients' characteristics

In our study the female and the male mad up 52.5% and 47.5%, respectively, similar to a study of Nguyễn Thị Thu Thao (2014) in which the female made up 52.0% and the male 48%. That was consistent with absence of sex differences in diabetes rate in general [4].

The patients' mean age was 54.1 years, which showed tendency of type 2 diabetes development in younger age. Other domestic studies by Nguyen Thi Phi Nga (2009) and Nguyen Thi Thu Thao (2014) also reported this tendency [3],[4]. The patients, mean BMI was 23.49 kg/m^2, nearly two thirds were overweight or obese (61.4%) that was the same equivalent the study by Nguyen Thi Thu Thao (2014) [4]. That increased overweight or obese prevalence in patients with type 2 diabetes may reflect the tendency in our general population over time.

Most patients had short duration of diabetes with 84.1% having diabetes less than 5 years. Only small proportion of patients had diabetes for more than 10% (5%).

The baseline mean FPG, 2hPPG and HbA1c was 8.62 mmol/L, 12.36 mmol/L and 7.93%, respectively. Most patients did not achieved MOH 2017 PFG and 2hPPG targets that were 81.2% and 88.1%, respectively. All the patients had baseline HbA1c > 7%.

Most patients in our study were outpatients so their blood glucose control was better than in the hospitalized patients participating in other studies in Vietnam. In a study by Nguyen Thi Ho Lan in the hospitalized type 2 diabetes patients at National Hospital of Endocrinology (NHoE) the baseline mean FPG and HbA1c was 12.1 mmol/L and 9.8%; in a study by Nguyen Thi Duyen in hospitalized patients with type diabetes the mean FPG and HbA1c was 10.32 mmol/L and 9.29%, respectively [1],[2].

2. Use of OAD during the study

All the patients were on OAD only before the study start. About two third (60.4%) of the patients were on metformin therapy that was the only used monotherapy. 39.6% of the patients were on different OAD combinations of which the metformin and sulfonylurea combination was the dominating one with a proportion of 87.5% among all the combinations and 34.6% among all the patients.

All the patients received sitagliptin at a daily dose of 50mg or 100mg that was unchanged until week 12. About one quarter of the patients used daily 50mg of sitagliptin that is half of its full dose for the whole study and the other three quarters of the patients used the full daily dose of 100mg. The mean daily dose of sitagliptin was 88.1mg and 86.6mg for the first 12 and second 12 weeks, respectively.

2.Effects of add-on of DPP-4 inhibitors on blood glucose

In our study the add-on of sitagliptin to the patients who were already on other OAD monotherapy or combinations their blood glucose control substantially improved with significant reductions of the mean FPG, 2hPPG and HbA1c, and high proportion of the patients achieved blood glucose indices targets. After 12 weeks, compared with the

baseline, FPG, 2hPPG and HbA1c significantly decreased by 1.7 ± 2.06 mmol/L, 2.8 ± 2.26 mmol/L and 1.21 ± 0.86%, respectively, compared with the baseline values. After 24 weeks, blood glucose further improved so that compared with the baseline FPG, 2hPPG and HbA1c significantly decreased by 1.91 ± 1.90 mmol/L, 3.42 ± 2.26 mmol/L and 1.45 ± 1.0%, respectively.

Concerning the blood glucose targets achievement, at week 12 and 24, about two thirds of the patients achieved MoH 2017 targets of FPG (4.4 - 7.2 mmol/L), 2hPPG (< 10 mmol/L) and HbA1c (< 7%). At week 12, 69.3%, 70.3% and 61.4% of the patients achieved the targets of FPG, 2hPPG and HbA1c, respectively, and after 24 weeks, the proportions were 69.3%, 78.2% and 69.3%, respectively. Those were substantial increases compared with the baseline when the proportions of the patients achieving the targets were only 18.8%, 11.9% and 0%, respectively.

Numerous randomized control trials have proved that sitagliptin add-on to other OAD monotherapy (mainly metformin) or combinations improved glycemic control compared with placebo in type 2 diabetes patients not achieving blood glucose targets.

A double-blind, randomized, placebo-controlled, two-period crossover study of Brazg et al [8], patients with type 2 diabetes (n = 28) with inadequate glycemic control on metformin monotherapy (on a stable dose of 1500 mg/day) evaluated effects of adding sitagliptin 50mg b.i.d. The sitagliptin add-on resulted in significant least-squares (LS) mean reductions in 24-h weighted mean glucose of 32.8 mg/dl, significant LS mean reduction from baseline in mean daily glucose of 28 mg/dl, FPG of 20.3 mg/dl and fructosamine of 33.7 mmol/l in patients treated with sitagliptin relative to placebo ($p < 0.05$) [8].

Charbonnel et al studied effects of sitagliptin add-on (100 mg/day) to ongoing metformin monotherapy (≥ 1500mg/day) in type 2 diabetes patients with mean HbA1c of 8% compared with continued metformin monotherapy alone [5]. After 24 weeks FPG and HbA1c in the sitagliptin add on group significantly decreased by 1.4 mmol/L and 0.65% (both p values < 0.001), respectively, compared with those indices in the metformin monotherapy group. A significantly greater proportion of patients achieved an A1C < 7% with sitagliptin (47.0%) than with placebo (18.3%).

Hermansen at al [7] conducted a randomized placebo controlled trial on 441 type 2 diabetes patients (of ages 18-75 years) with baseline HbA1c of 8.34% who were on glimepirid (≥ mg/day) alone or in combination with metformin (≥ 1500mg/day) to compared effects of the addition of sitagliptin 100 mg once daily or placebo for 24 weeks. At the end of study mean baseline HbA1c was 8.34% in the sitagliptin and placebo groups. After 24 weeks, sitagliptin reduced HbA1c by 0.74% ($p < 0.001$) relative to placebo. In the subset of patients on glimepiride plus metformin, sitagliptin reduced HbA1c by 0.89% relative to placebo, compared with a reduction of 0.57% in the subset of patients on glimepiride alone. The addition of sitagliptin reduced FPG by 20.1 mg/dl ($p < 0.001$) and 2hPPG (in a meal tolerance test) by 36.1 mg/dl ($p < 0.001$) relative to placebo.

In a study by Chien et al [9], Taiwanese type 2 diabetes patients (n = 97) were randomized to receive the existing OAD combinations or add-on with sitagliptin (100 mg daily) for 24 weeks. Compared with the

change of 0.0% (95% confidence interval: -0.6% to 0.5%) from a baseline of 10.0% in the controlled arm, HbA1c change from a mean baseline of 9.5% was -1.14% ± 1.18 after add-on sitagliptin (p< 0.0001).

In randomized controlled trials that compared combination of sitagliptin and metformin with metformin or sitagliptin monotherapy as initial OAD therapy, the former resulted in clearly better glycemic control than the latter.

Williams-Herman et al [10] compared different sitagliptin and metformin combinations with sitagliptin or metformin monotherapy in type 2 diabetes drug-naïve patients (n = 1091 and mean HbA1c 8.7%) in a 54 week multinational study conducted at 140 clinical sites in 18 countries. At week 54, the HbAa1c reduction was highest in the combination with high metformin dose (100 mg sitagliptin and 2000 mg metformin/day), -1.8%, followed by the combination with low metformin dose (the sitagliptin 100 mg and 1000 mg metformin/day),-1.4%, monotherapy with higher metformin dose (2000mg/day), -1,3%, monotherapy with low metformin dose (1000mg/day), - 1,0% and monotherapy with sitagliptin (100mg/day), -0,8%. Similarly, the proportions of patients with an HbA1c < 7% at week 54 were 67%, 48% (S100đM1000), 44%, 25% and 23%, respectively.

A trial of Reasner et al [6] randomized 1250 drug-naïve type 2 diabetes patients (mean baseline HbA1c 9.9%) to sitagliptin/metformin 50/500 mg bid or metformin 500 mg bid (uptitrated over 4 weeks to achieve maximum doses of sitagliptin/metformin 50/1000 mg bid or metformin 1000 bid). At week 18, mean change from baseline HbA1c was −2.4% for sitagliptin/metformin combination −1.8% for metformin monotherapy (p < 0.001). The proportion of patients with HbA1c < 7% was 49.2% and 34.2% for the former and latter groups, respectively (p < 0,001).

The extents of effects of adding sitagliptin to existing OAD(s) therapy or those of combinations of sitagliptin and metformin compared to metformin or sitaglitin monotherapy are different from study to study because patients' characteristics varied from study to study. However, the improvement of glycemic control after adding sitagliptin to existing OAD(s) or better glycemic control of sitagliptin combinations compared with metformin or sitagliptin monotherapy have been proved. The mechanisms of action of DPP-4 inhibitors are different from those of other OAD classes such as biguanide, sulfonylureas and alpha-glucosidase inhibitors. This explains additional effects of adding DPP-4 inhibitors to the other OADs on glycemic control.

V. CONCLUSIONS

The add-on of the DPP-4 inhibitor Sitagliptin in patients with type 2 diabetes inadequately control with metformin alone or OAD combinations resulted in substantial improvements of glycemic control for a period of 24 weeks.

- After 12 weeks, compared the baseline, the mean FPG, 2hPPG and HbA1c significantly decreased by 1.70 mmol/L, 2.80 mmol/L and 1.21%, respectively (p < 0,001 for all), and the proportions of patients achieving MoH 2017 FPG, 2hPPG and HbA1c targets significantly increased from 18.8%, 11.9% and 0% to 69.3%, 70.3% and 61.4%, respectively, with p < 0,001.

- After 24 weeks, compared the baseline, the mean FPG, 2hPPG and HbA1c significantly further decreased by 1.91 mmol/L, 3.42 mmol/L and 1.45%, respectively (p < 0,001 for all), and the proportions of patients achieving MoH 2017 FPG, 2hPPG and HbA1c targets were 69.3%,78.2% and 69.3%, respectively, significantly higher than the baseline with p < 0,001.

SUGGESTION:

DPP-4 inhibitors should be early added to type 2 diabetes patients who do not achieve blood glucose targets with other oral antidiabetes drug(s).

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RÉSUMÉ:

L'EFFET DES INHIBITEURS DU DIPEPTIDYL PEPTIDASE COMME SUPLÉMENT AUX DROGUES ANTIDIABÉTIQUES TYPE 2 À L'HÔPITAL NATIONAL D'ENDOCRINOLOGIE

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Objectif: Evaluation de l'effet des Inhibiteurs du Dipeptidyl Peptidase (DPP) - 4 comme supplément chez les patients diabétiques type 2 contrôlés de facon inadéquate avec des drogues antidiabétiques (ODD) en monothérapie ou en doses combinées.

Sujets et Méthode: L'Intervention thérapeutique chez 101 patients avec diabète sucré type 2 adulte, de contrôle inadéquat avec OAD en monothérapie ou en doses combinées avec d'autres produits que les inhibiteurs du DPP - 4, avec HbA1c >7 à 10%. Le HbA1c a été prélevé dès le debut de l'étude, les dosages finaux ont été le glucose plasmatique a jeun.

Le glucose en post-prandial (2hPPG), et encore le HbA1c après 12 et 24 semaines. Un inhibiteur du DPP-4 a été commencé avec la moitié ou une dose complète pour les 12 premières semaines, et s'il a été commencé moitié de la dose, une dose complète est donnée pour les 12 dernières semaines. L'autre OAD et les doses restent les mêmes pour l'étude.

Résultats: L'âge moyen et la durée du diabète sont 54.1±10.1 et 2.4±3.4 ans, respectivement. Avant de procéder a l'étude, la monothérapie avec Metformine a été appliquée chez 60.4% patients, et les doses combinées les plus usitées sont Metformine + Sulfonylurée (34.6% de patients). L'unique inhibiteur du DPP-4 est le Sitagliptin à la dose moyenne de 88 mg/jour et 88.1 mg/jour pour les premières et deuxièmes 12 semaines. Au bout de 24 semaines, le HbA1c de base, le FPG moyen, le 2hPPG, sont diminués de 1.91 mmol/L. 3.42 mmol/L et 1.45% respectivement ($p<0.001$ pour toutes les valeurs), et la proportion de patients achevant les paramètres du Ministère de la Santé 2017 en FPG, 2hPPG, et HbA1c, sont augmentés de facon remarquable, 18.8%, 11.9%, et 0% respectivement ($p<0.001$).

Conclusion: Le supplément Sitagliptin inhibiteur du DPP-4 chez les patient avec diabète sucré type 2 mal contrôlé avec le Metformine seul ou bien OAD combiné, produit des améliorations notables pour le contrôle de la glycémie pour une période de 24 semaines.

Mots clés: *Type 2 diabetes, Dipeptidyl Peptidase Inhibitor.*

EARLY OUTCOMES OF ROBOTIC SURGERY FOR COLORECTAL CANCER AT BINH DAN HOSPITAL

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Hoang Vinh Chuc*, Nguyen Phu Huu*

ABSTRACT

Introduction: Colorectal cancer (CRC) is a common malignant disease of the digestive tract, the use of robotics in CRC surgery is a new technique in Vietnam. The first cases of colectomy using da Vinci Surgical System were reported in 2002 by Weber et al[12] . Since then, several centers had reported their experience with favorable outcomes. Binh Dan hospital started to use robotics in CRC surgery in November 2016. Binh Dan is the first hospital to use Robot for surgery in adults in Vietnam. The aim of our paper is to share our early experience with robotic surgery in colorectal cancer and to provide an update on the issue. ***Materials and Methods:*** retrospective review , 44 CRC patients were operated from November 2016 to June 2017 at Binh Dan hospital using Robotic da Vinci Surgical System. ***Results:*** Of the forty-four patients with CRC: 15 colon cancers: 4 ascending colon cancers treated with right hemicolectomy, 2 left colon cancers - left hemicolectomy, 9 sigmoid colon cancers - sigmoid colectomy; 29 rectal cancers: 2 treated with anterior resection, 16 low anterior resection , 4 ultra-low anterior resection, 7 abdominoperineal resection. Staging (AJCC 7): 4(9.09%) patients with stage IIA, 32(72.73%) IIB, 4(9.09%) IIIB, 4(9.09%) IIIC. Male:female ratio was 7:4. The mean age of the patients was 62 (range 28-85) years. The mean operating time was 170 minutes for colon cancer and 203.45 minutes for rectal cancer. There was no intraoperative complication related to the use of robotics. Postoperative complications: 4 cases of incision infection and 1 case of urine retention. The mean hospital stay was 8 days (range 7-14 days). ***Conclusions:*** The use of robotics in CRC surgery is feasible and safe . We can perform robotic colorectal surgeries for patients without metastasis.

Key words: *Robotic colorectal cancer surgery, da Vinci® Surgical System, Colorectal cancer, Lower anterior resection.*

I. BACKGROUND

Colorectal cancer (CRC) is very common cancer of the digestive tract and surgery is currently the main treatment. Surgical methods have gradually developed from open surgery (major surgery) to minimally invasive therapy. Since the first laparoscopic colectomy was reported in 1991, laparoscopic surgery for CRC has been progressively performed in many centers around the world. This method has been proven to benefit the patients, with favorable long-term oncologic outcomes . However, laparoscopic resection of CRC still has some difficulties in case of narrow space of pelvis, range of motion limited by laparoscopic instruments, physiologic tremors, two-dimensional cameras (2D) and necessity of experienced assistant. The da Vinci® Robot System used in this study has three-dimensional (3D) view enhancing high-definition vision with up to 10 times magnification, the Endowrist® instruments designed to provide surgeons physical ability and a wide range of motions far greater than human hands[5,6,7]. The first cases of robot-assisted colectomy using the da Vinci system

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were reported in 2002 by Weber et al[12]. Numerous reports from many centers have shown that the results were favorable. Binh Dan Hospital used robotics in surgery for CRC from November 2016. Our goal is to share early experience in the use of robotic CRC surgery as well as to update this issue.

II. MATERIALS AND METHODS

This study is a retrospective review.

We collected data from all patients underwent robotic surgery using da Vinci system at Binh Dan hospital from November 2016 to June 2017.

We used the American Joint Committee on Cancer (AJCC) 7th edition classification for tumor staging.

Some points were considered when using da Vinci system versus traditional laparoscopy for CRC surgery:

- The operating room set-up (Figure 1).
- The trocar site placement must follow certain principles (Figure 2).
- Patient position should not be changed after docking.

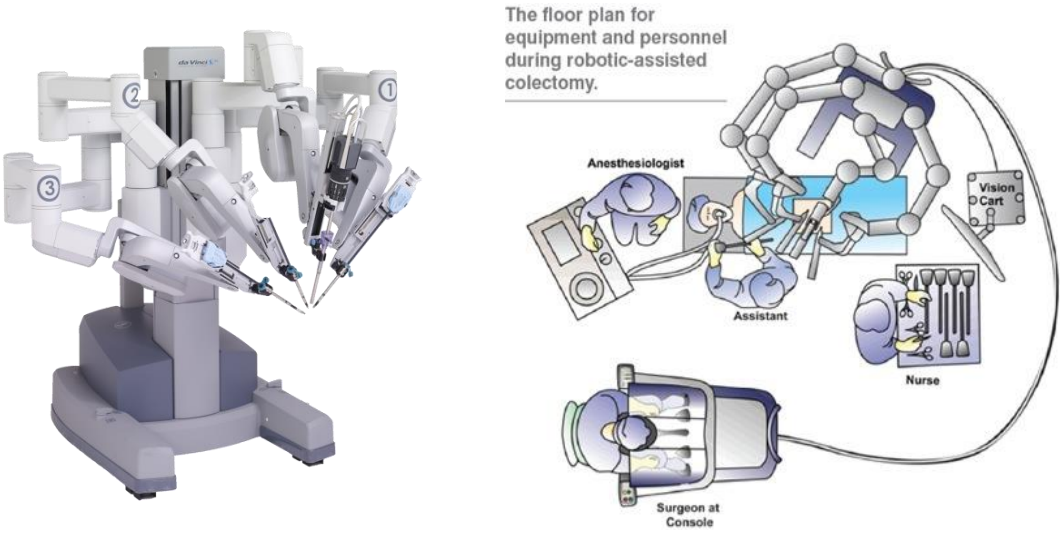

Figure 1: *Da Vinci Surgical system and operating room setup for CRC surgery*

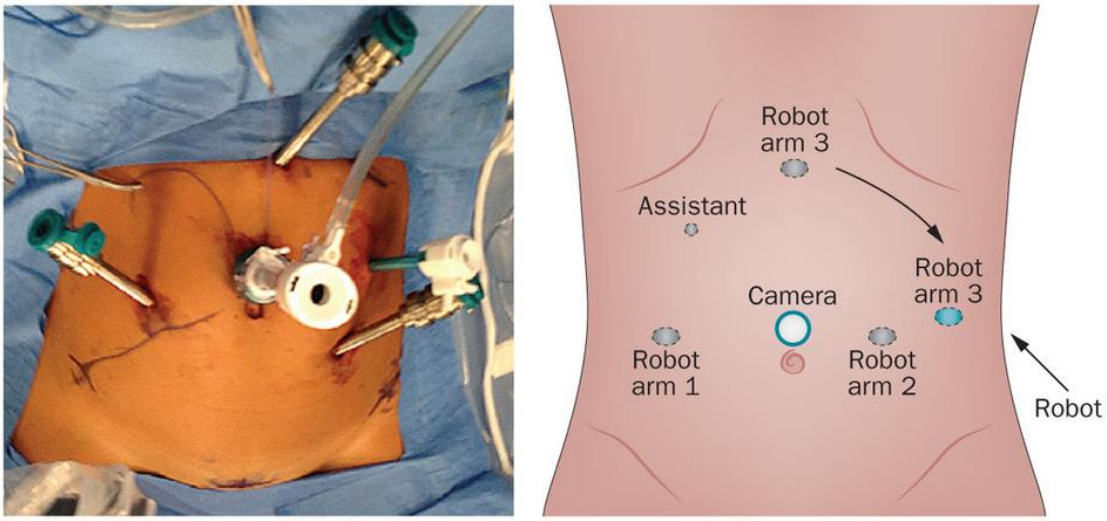

Figure 2: *Trocar site placement in CRC surgery*

III. RESULTS

The male:female ratio is 7:4. The mean age is 62 ± 11.78, the youngest is 28 and the oldest is 85.

Surgical methods: In 44 cases of CRC:

• 15 cases of colon cancer include:

o 4 cases with ascending colon cancer treated with right colectomy

o 2 cases with left upper left tumor - left colectomy

o 9 cases with sigmoid colon cancer - sigmoid colectomy

• 29 cases with rectal cancer include:

o 2 cases treated with anterior resection

o 16 cases, low anterior resection

o 4 cases, ultra-low anterior resection

o 7 cases, abdominoperineal resection

The mean number of lymph nodes harvested was 10.86 ± 6.84 (range: 2 - 22)

The mean number of positive nodes was 0.84 ± 2.65 nodes (range 0 - 16). The incidence rate of positive nodes was 9.77%.

Docking time, defined as the time from anesthesia to the onset of surgery at the console: 21.93 ± 7.49 minutes (range: 10 - 40).

Operative time, defined as the time during which the main surgeon operating at the console:

• For colonic cancer: 149,67 ± 23,94 minutes (range: 105 - 180 minutes).

• For rectal cancer: 180.69 ± 50.14 minutes (range: 120 - 330 minutes).

Total operative time, defined as the time from anesthesia to the end of surgery:

• For colon cancer: 170.05 ± 22.83 minutes (range: 135 - 205 minutes).

• For rectal cancer: 203.45 ± 52.43 minutes (range: 135 - 360 minutes).

There were no complications in robotic surgery, the blood loss during surgery was minimal.

The time that patients passed gas was 2.84 ± 0.86 post-op days (range: 1 - 4 days).

The time to feed the patients was 2.84 ± 0.86 days (range: 1 day - 4 days).

After the operation, there were four cases of incision infection (the place where the samples were collected, managed by changing wound dressings) and one case of urinary retention (patient having benign prostatic hyperplasia managed by medical

treatment, urinated after 10 days and was discharged from the hospital).

The mean postoperative hospital stay was 8 ± 1.57 days (range: 7 days - 14 days).

Table 1: *Post-operated pathological staging (AJCC 7)*

	Stage	pTMN	No. of cases	%
	IIA	T3N0M0	4	9.09%
	IIB	T4aN0M0	32	72,73%
	IIIB	T3N1M0/T4aN1M0/T3N2aM0	4	9,09%
	IIIC	T4aN2aM0/T3N2bM0/T4aN2bM0	4	9,09%
Total			44	100%

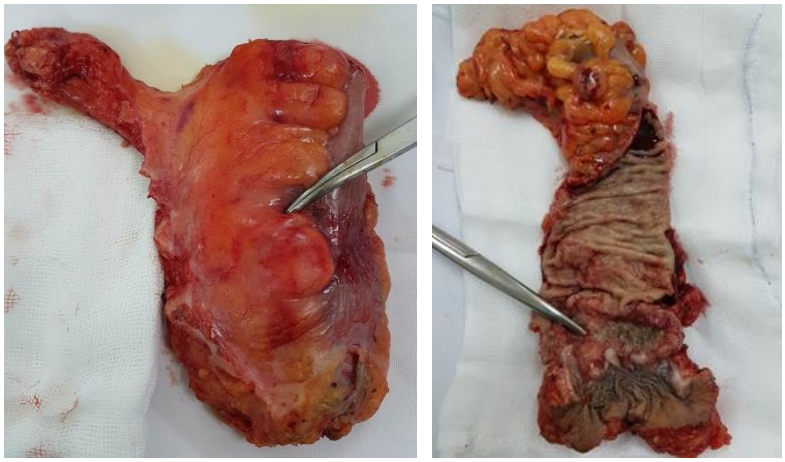

Figure 3: *Rectal cancer, Binh Dan hospital (2017)*

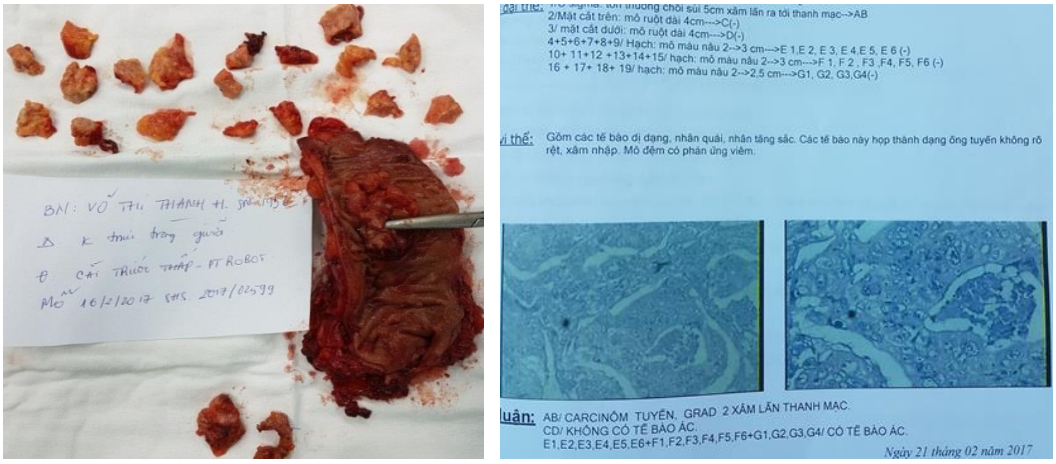

Figure 4: *Rectal cancer with lymph nodes harvested and pathology report.*

IV. DISCUSSION

The role of laparoscopic surgery has been demonstrated through numerous studies in the literature. However, this method is still limited, particularly in cases of pelvic operation. Moreover, the learning curve is quite long. Surgeons do not feel the depth, their hands may have tremors,and they need professional and experienced assistants especially when operative time is prolonged.

Robotic surgery helps to avoid these limitations and increases the feasibility of colorectal surgery. Several studies show that long-term oncologic outcomes are similar to those found in laparoscopic laparoscopy.

With lower incidence of conversion to open surgery, therefore the incidence of postoperative complications are lower. Long-term results are lower, too.

In recent decades, surgeons have applied invasive surgical techniques in colorectal surgery such as laparoscopic and robotic-assisted surgery. In the literature there are many studies on these two topics [1,3,6].

Studies have shown that long-term results are similar to conventional open surgery. Still, there remain debates on which is the best method.

In laparoscopic surgery, there are many limitations such as high rate of conversion to open surgery. Robot-assisted surgery helps surgeons overcome these obstacles and can be applied to other specialties such as urology, general surgery and gynecology [1,5].

Robotics in CRC has several advantages such as better vision in the pelvis, more precise suturing, and articulate surgical instruments.

In recent years, the number of studies on robotic surgery has increased steadily [1,2,6,7,9]. Initially the authors applied robotics for rectal surgery, then for colon cancer, but with slower progress.

Ferrara's study[3] shows that compared with laparoscopy, robotic surgery is more profitable, especially in lymph nodes harvest. In 2002, Weber [12] and colleagues were the first authors to report the results of using robotics in colorectal surgery, such as sigmoid colectomy and rectal resection. The number of lymph nodes harvested at least 12 nodes in accordance with the guidelines of the American Joint Committee on Cancer (AJCC). Da Vinci system excels in the precision compared with conventional open surgery. The endoscope is programmed to regulate the temperature to prevent fogging.

Table 2: *Some studies on robot-assisted CRC surgery*

Author	Year	Country	Number of patients
Rawlings et al[10]	2007	Illinois, United States	30
Baik et al[2]	2008	Seoul, Korea	9
Lim Y K[7]	2009	Singapore	8
Huang et al[5]	2015	Cao Hung, Taiwan	40
We	2016	HCM city, Vietnam	44

Table 3: *Patient characteristics compared with other authors*

Author	Huang et al[5]	Lim Y K[7]	We

No. of patients	40	8	44
Male:female	1:1	5:3	7:4
Age	60(32-89)	55(42-80)	62(28-85)
Total operative time (minute)	264(109-527)	192(145-250)	192,5(135-360)
Total operative time for colon cancer (minute)			170(135-205)
Total operative time for rectal cancer (minute)			203,45(135-360)
Blood loss (ml)	150(20-500)	Minimal	Minimal
Complication rate	35%	12,5%	5,68%
Lymph nodes harvested	9(0-22)	17(2-26)	10,86(2-22)
Positive lymph node	1,3(0-6)	0,3(0-2)	0,84(0-16)
Hospital stay (day)	7(5-32)	5(4-30)	8(7-14)

Robotic surgery provides better vision than laparoscopy accompanied with simulating fine movements of human hands thanks to EndoWrist system. Robots can allow surgeon to spare nerves, identify ureters and gonadal vessels, and perform suturing better.

Because of the above reasons, the sexual and urinary functions after surgery are preserved. The number of conversion to open surgery are higher in rectal cancer than in colon cancer since rectal surgery requires more difficult techniques. The causes of conversion were massive bleeding and diffuse adhesion.

Opertive time in robotic procedure is longer for both colon and rectal cancer. Longer duration is due to equipment arrangement. When the staff get familiar with setting, operative time will decrease. Combination of laparoscopic left colon mobilization with robotic dissection will reduce operative time tremendously (1.5, 6). In our study, the first docking times of the robot lasted 30 to 40 minutes because of the unfamiliarity with the instruments and the trocars site. However, this interval significantly shortened after 10 cases, usually takes about 10-15 minutes.

Our hospital stay was about 7-14 days. Most of the patients were discharged after 7 days, five cases after 10 days due to surgical site infection and urinary retention (patient with benign prostatic hyperplasia). 8 cases of patients with mid- to low-rectal cancer which Lim et al[7] operated on had hospital stay of about 4-5 days, with one case discharged after 10 days due to pneumonia on chronic obstructive pulmonary disease. 40 cases of CRC of Huang (5) el al were discharged 5 to 32 days after surgery.

Our total number of nodes was 10.86 (2-22), less than Lim YK [7] 17 (2-26), and more than Huang [5] 9 (0-22). However, our number of metastatic nodes was higher than that of Lim (Table 3), as most of our patients usually seek healthcare in the late stage of cancer.

We did not have any complications in the operation. There were five cases of postoperative complications including four cases of surgical site infections managed with antibiotics based on sensitivity, wound dressing change and were discharged after 10 days; one case of post-operative urinary

retention, in which the patient had benign prostatic hyperplasia managed by medical treatment, urinated 10 days later and was discharged. Lim [7] do not report any complications in surgery and one case of postoperative pneumonia. Huang [5] et al. documented 14/40 cases with complications including postoperative bleeding, persistent abscess, anastomosis leakage and stenosis, urethral injury and urinary retention, surgical site infection and pneumonia.

All of our margins were cancer-free and no recurrent cases of abdominal metastases were observed during the follow-up.

Some points must be considered when using robot system: The trocar sites are crucial, we need toplan carefully their placement so that after docking the robot arms can be easily manipulated without collision, and patient position would not be changed during the operation at the console.

V. CONCLUSION

Robot-assisted CRC surgery is proven to be a safe, feasible method, and initially shows good results for patients in terms of lymph node harvesting as well as manipulation in narrow spaces. We will continue to study with a larger sample size and compare it with laparoscopic surgery about the effectiveness, lymph node harvest, and recurrent incidence.

This is a great step in the surgical field of Binh Dan Hospital and of Vietnam also. With the advantages of the robot system such as the surgeon directly controls the camera, 3D vision, high resolution, excellent dexterity... robotic surgery has promising future to benefit CRC patients, to perform curative surgery, and to reduce recurrent incidence.

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RÉSUMÉ:

RÉSULTATS IMMÉDIATS DE LA CHIRURGIE AU ROBOT DU CANCER COLORECTAL À L'HÔPITAL BINH DAN

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Introduction: Le cancer colorectal (CRC) est une maladie maligne du tube digestif, l'usage de la robotique dans ce cancer est encore une nouvelle technique au Vietnam.

Les premiers cas de la colestomie utilisant le système Chirurgical Da Vinci sont rapportés en 2002 par Weber et al (12). Depuis lors, plusieurs centres ont rapporté leurs expériences aux résultats favorables. L'hôpital Binh Dan avait commencé la chirurgie utilisant la robotique du CRC en Novembre 2016. Binh Dan est le premier hôpital au Vietnam à utiliser les robots dans la chirurgie chez adultes.

Notre but est de communiquer notre expérience immédiate avec la chirurgie robotique dans le cancer colorectal et de fournir l'acquisition d'une nouvelle connaissance à ce sujet.

Matériel et méthode: La revue est rétrospective. 44 patients avec CRC ont été operés de Novembre 2016 à Juin 2017 à l'hôpital Binh Dan, utilisant le Système Chirurgical Da Vinci.

Résultats: Sur les quarante quatre patients avec CRC: 15 cancers du colon, 4 cancers du colon ascedant ayant subi l'hémicolectomie droite, 2 cancers du colon gauche - l'hémicolectomie gauche, 9 cancers du sigmoide - colectomie du sigmoide, 29 cancers du rectum: 2 ayant une résection antérieure, 16 une résection antérieur basse, 4 une résection très basse, 7 une résection abdominopérinéale. Les stades du cancer: (AJCC 7): 4 (9.09%) patients au stade IIA, 32 (72.73%) IIB, 4 (9.09%) IIC. Proportion M/F: 7.4. L'âge moyen des patients: 62 (26 - 85 ans). Durée d'opération: 170 minutes pour le cancer colique, et 203.45 minutes pour le cancer rectal. L'usage des robots n'a pas rapporté de complications peroprératoires. Complications postopératoires: 4 cas d'infection de la plaie d'incision, 1 cas par rétention d'urine. Le séjour moyen à l'hôpital est de 8 jours (7-14 jours).

Conclusions: La robotique en chirurgie CRC est possible et denuée d'accidents. Cette chirurgie est possible chez les patients qui n'ont pas de métastases.

Mots clés: *Robotic colorectal cancer surgery, Da Vinci Surgical System, Colorectal cancer, Lower anterior resection.*

STUDY CLINICAL MANIFESTATIONS AND COMPUTERIZED TOMOGRAPHY CHARACTERISTICS OF ACUTE ISCHEMIC STROKE PATIENTS IN THE FIRST 6 HOURS AFTER SYMPTOM ONSET

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ABSTRACT

Purpose: Describe clinical characteristics and computerized tomography (CT) signs of acute ischemic stroke (AIS) patients in the first 6 hours after symptom onset. ***Methods:*** There were 134 AIS patients in the first 6 hours at the 108 hospital from 7/2016 to 7/2017, describe the clinical characteristics of AIS patients (history of disease, neurologic deficits of sudden onset, time of onset) early CT images signs, NIHSS scores, ASPECT scores. ***Results*:** Average age: 64.35± 12.37, from 21-85. The average time is 213 minutes. Common history of disease: hypertension (55.2%) and Atrial fibrillation (27.6%). Clinical manifestations include: unilateral paresis (95.5%), aphasia (70.9%) and Facial palsy (91%). Consciousness are 68.9%. Other characteristics include headache, dizziness and gaze preference are low rate. The NIHSS score averages 17.37 ± 6.8. In the CT image: 55.22% of patients had a reduced contrast attenuation of the cerebral parenchyma, 70.89% had large blood vessels occlusion, 81.35% had a frontal cerebral artery. Average ASPECT scores 7.87± 1.39. Clinical characteristics of the vertebrobasilar arterial system stroke were coma, dizziness. Signs of large vessel occlusion were coma, gaze preference and language disorders. ***Conclusions:*** Clinical symptoms of AIS patients in the first 6 hours were abundant, however the most common signs were unilateral paresis**,** facial palsy and language disorders. Nearly half of patients with AIS in the first 6 hours had no lesions on CT imaging.

Keyword: *Acute ischemic stroke, clinical manifestations, computerized tomography image*

I. BACKGROUND

Time is the brain and to save the brain cells of the AIS patient is the race against time. In each minute, 1.9 million neurons, 14 billion synapses, and 12 km (7.5 miles) of myelinated fibers are destroyed. In vitro, the nerve cells have a rapid change after 20 minutes of ischemia. These changes were: Cellular swelling, mitochondrial decay, which changes most markedly in the fourth hour to the sixth hour [8,9].

The NINDS study (1995) confirmed that intravenous recombinant tissue plasminogen activator (rtPA - Alteplase) in the first 3 hours, helped additional 13% improvement compared with standard treatment group. The ECASS III (2008) study showed that rTPA was beneficial in AIS patients within 3 to 4.5 hours. A meta-analysis based on 12 randomized controlled trials validated the benefits of Intra-arterial rtPA within 6 hours of onset (OR 1.17, 95% CI: 1.06-1, 29; p = 0.001) [7]. Recently, the generations of mechanical thrombectomy devices had been applied for removing thrombi from the neurovasculature have expanded the treatment window for AIS patients. There were 8 reputation trials, which were

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SYNTHESIS, IMS III, MR RESCUE, MR CLEAN, ESCAPE, SWIFT PRIME, EXTEND-IA and REVASCAT, they have been analyzed and made the fundamental for American Heart Association/American Stroke Association, who have published update 2015 guideline for the early management of AIS patients regarding endovascular treatment. However, each trials had different window treatments, such as the ESCAPE trial collected patient in 12 hours, MR RESCUE and REVASCAT trial was 8 hours, and the remaining trials had window treatments was 5 to 6 hours [7]. Finally, treatment guidelines of AHA/ASA had high consensus with the treatment window 6 hours.

All clinical and invitro evidence, showed that the first 6 hours after symptom onset was the golden time for AIS treatment. Therefore, the investigation of clinical characteristics, computerized tomography AIS in the first 6 hours will have a great necessary. For the above reasons we carry the study ***"Study clinical manifestations and computerized tomography characteristics of acute ischemic stroke patients in the first 6 hours after symptom onset".*** The aim of this study was to determine clinical manifestations and computerized tomography characteristics of AIS patients in the first 6 hours after symptom onset.

II. METHODS

Consecutive patients presenting with AIS patients in the first 6 hours after symptom onset between July 2016 and July 2017 were enrolled in the study. We followed the patients until discharge.

Patient selection

Inclusion criteria were 85 years old or younger, patients arrived emergency department before 6 hours after symptom onset, have symptoms of AIS (FAST: Facial drooping; Arm weakness; Speech difficulties and time is of the essence)

Exclusion criteria included the presence of cerebral hemorrhage or patients had symptoms onset lasts over 6 hours

Imaging and clinical assessment

The clinical assessment including history and symptoms onset.

A focused medical history for patients with IAS aims to identify risk factors for atherosclerotic and cardiac disease, including the following: Hypertension, diabetes mellitus, tobacco use, high cholesterol, history of coronary artery disease, heart failure, or atrial fibrillation.

Common signs and symptoms of stroke include the abrupt onset of any of the following: Hemiparesis, monoparesis, or (rarely) quadriparesis; hemisensory deficits; monocular or binocular visual loss; visual field deficits; diplopia; dysarthria; facial droop; ataxia; vertigo (rarely in isolation); aphasia; sudden decrease in the level of consciousness. NIHSS scores were assessed on admission and discharge.

The current standard is noncontrast computed tomography (NCCT) of the head because it is fast and widely available, but we used computed tomography angiography (CTA) as soon as the patient addmission. We excluded intracranial hemorrhage and found carefully earrly sign on NCCT, calculated the ASPECTS (Alberta Stroke Program Early CT score) score.

On CTA, we have located the cerebral artery occlusion and evaluated CTA collateral score.

Statistical methods

Categorical variables were expressed with their frequency distributions and continuous variables as mean (SD) and SD [9]. IBM

SPSS 22.0 software was used to perform all of the analyses.

III. RESULTS

3.1. Baseline characteristics

Table 1: *Baseline characteristics*

Characteristics		***No.of Patients (n=134)***	***Rate (%)***
Age (years)	Mean ($\overline{X}$ ±SD)	64.35± 12.37	
	Min	21	
	Max	85	
Age groups (years)	≤ 40	4	3.0
	40-59	40	29.9
	≥ 60	90	67.1
Gender	Female	55	41.0
	Male	79	59.0
Time (minute)	Mean ($\overline{X}$ ±SD)	213.38 ± 92.54	
	Min	15	
	Max	360	
	Mode	300	
Blood vessels of the brain	*Anterior circulation*	109	81.35
	Posterior circulation	25	18.65

Mean age was 64.35± 12.37 years. The highest age is 85, the lowest is 21. The age group most encountered is over 60 years old. There were 55 women (41%). Mean time was 213.38 ± 92.54 minute, the fastest is 15 minute and the limit is 360 minute. The anterior cerebral circulation system had accounted 81.35%.

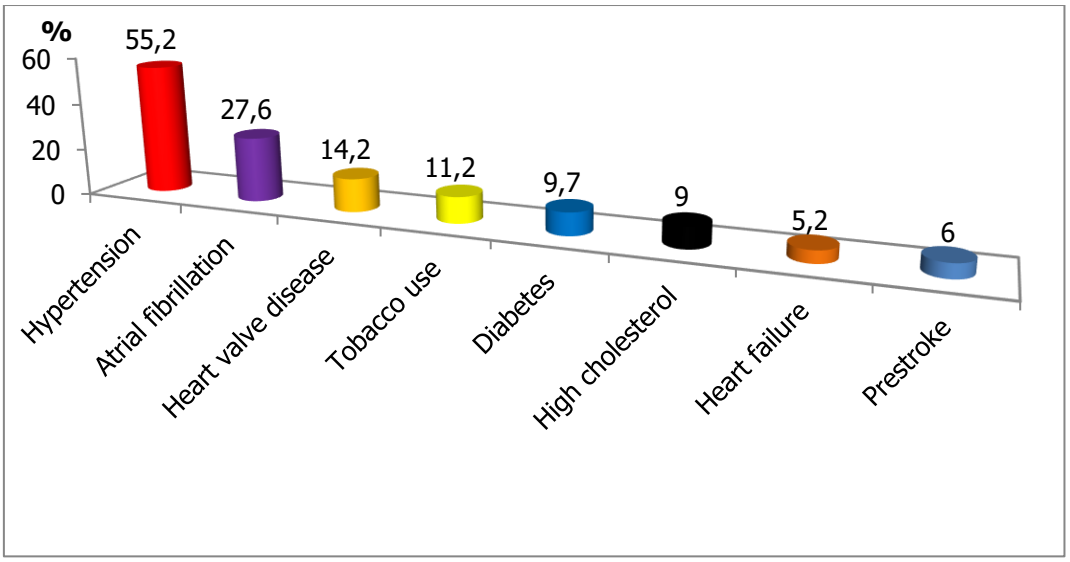

Figure 1. *Medical history of ischemic stroke*

Hypertension (55.2%) and atrial fibrillation (27.6%) were the most common medical history of ischemic stroke patients. Less medical history were diabetes, heart valve disease, smoking history.

3.2. Clinical manifestations

Table 2: *Clinical signs of AIS patients in the first 6 hours after symptom onset*

Clinical manifestations	AIS Patients		Anterior circulation		Posterior circulation		p
	No. of Patients n=134	Rate 100%	No. of Patients n=109	Rate 81,35%	No. of Patients n=25	Rate 18,65%	
coma	16	11.94	2	1.83	14	56.0	<0.05
dizziness	16	11.94	3	2.75	13	52.0	<0.05
vomiting	11	8.21	8	7.34	3	12.0	>0.05
gaze preference	15	11.2	13	11.92	2	8.0	>0.05
Aphasia	95	70.89	79	72.48	16	64	>0.05
unilateral paralysis	128	95.5	108	99.08	20	80.0	<0.05
Facial palsy	122	91.0	100	91.74	22	88.0	>0.05

The common clinical signs of AIS patients in the first 6 hours were unilateral paralysis (95.5%), facial palsy (91.0%) and aphasia (70.9%). Other manifestations were dizziness, coma, vomitting. The coma, dizziness were more common in patients at posterior cerebral circulation occlusion with p <0.05.

Table 3: *NIHSS score of patient on addmission*

NIHSS score		No. of Patients ***(n=134)***	***Rate (%)***
NIHSS	Mean ($\overline{X}$ ± SD)	17.37±6.8	
NIHSS groups	< 6	7	5.22
	6 - 15	44	32.83
	16 - 29	75	55.97
	≥30	8	5.98

The mean NIHSS score was 17.37. The highest NIHSS score was 42 points, the lowest score was 2 points, the mode NIHSS score was 21. Mostly patients with NIHSS scores from 16 to 29 with 55.97%. The proportion of patients with NIHSS scores below 6 and over 30 accounts about 10%.

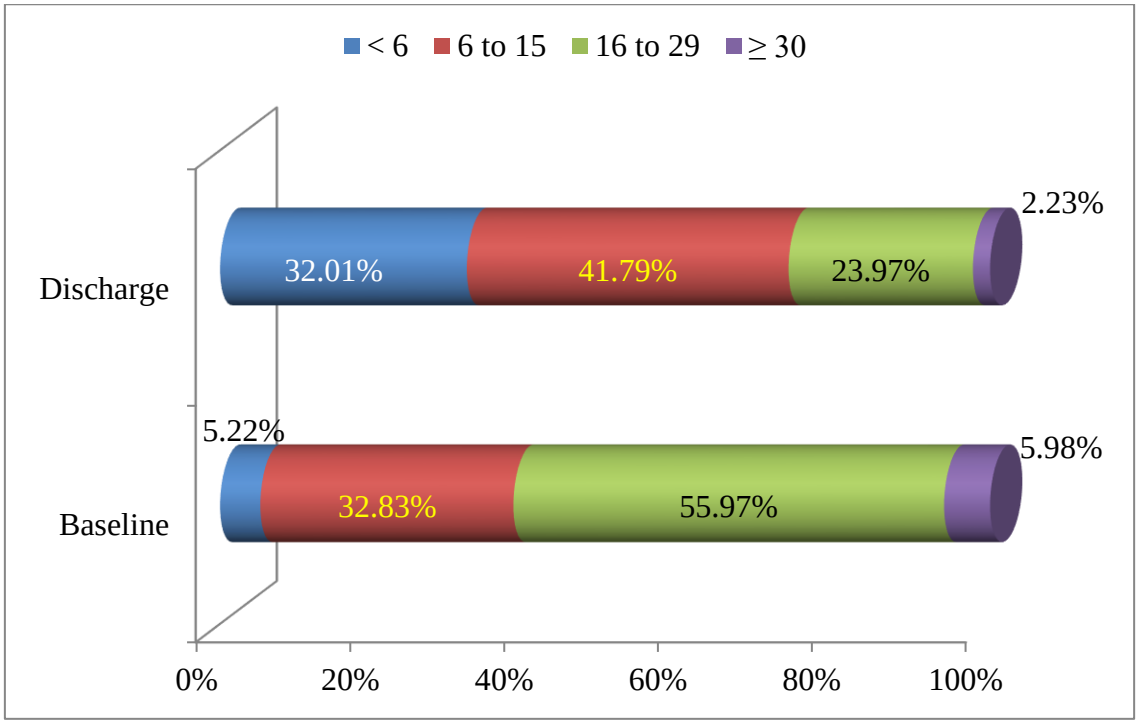

Figure 2: *Distribution of NIHSS scores at baseline and discharge*

NIHSS data at admission are needed to assess the stroke severity of the population treated, and are helpful to place into perspective the NIHSS discharge data. NIHSS discharge from <6 was 32.01%

3. 3. Computerized tomography characteristics

Table 4: *Computerized tomography characteristics of acute ischemic stroke patients in the first 6 hours after symptom onset*

Characteristics	*No. of Patients (n=134)*	*Rate (%)*
Hypoattenuation	74	55.22
Normal	60	44.78
Large vessel occlussion	95	70.89
Lacunar stroke	39	29.11
Anterior cerebral circulation	109	81.35
Posterior cerebral circulation	25	18.65

With AIS patients in the first 6 hours after symptom onset, CT image was normal about 44.78%. The large vessel occlusion stroke had accounted for 70% and anterior cerebral circulation occlussion was 81.35%.

Table 5: *Early signs of acute ischemic stroke patients*

Early sign on NCCT	*No. of Patients (n=134)*	*Rate (%)*
Cortical sulcal effacement	19	25.6
Loss of grey-white matter differentiation	18	24.3
Loss of the insular ribbon	23	31.1
Obscuration of the lentiform nucleus	15	20.3
Obscuration of the Sylvian fissure	20	27.0
Hyperattenuation of large vessel	17	22.9

There were 74 patients with AIS, who have early sign on NCCT, accounted for 55.22%. Signs of early ischemic were cortical sulcal effacement (25.6%); loss of grey-white matter differentiation (24.3%); loss of the insular ribbon (31.1%); and hyperattenuation of large vessel (22.9%, eg: hyperdense middle cerebral artery sign).

Table 6: *ASPECT score for territory of middle cerebral artery*

ASPECT score		*No. of Patients (n=63)*	*Rate (%)*
ASPECT	Mean ($\overline{X}$ ± SD)	7.87±1.39	
	Min	3	
	Max	10	
	Mode	8	
ASPECT groups	≤ 5	4	6.35
	6 - 7	20	31.75

	≥ 8	39	61.90

The ASPECT score was calculated for AIS patients with blood supply location of the middle cerebral artery (including internal carotid artery occlusion and segmental M1), which was 63 patients. In the first 6 hours, there were 4 patients with ASPECT score below 5, accounted for 6.35%. The most patients with ASPECT score above 6. The mean ASPECTS score was 7.8.

Table 7: *Located occlussion of artery*

Location of artery	***No. of Patients (n=134)***	***Rate (%)***
The segmental M1 of middle cerebral artery	34	*25.37*
The internal carotid artery	29	21.64
The segmental M2 of middle cerebral artery	8	5.97
The anterior cerebral artery	5	3.73
The Vertebrobasilar	19	14.18
The small vessel occlussion	39	29.11

In patients with large vessel occlussion, mainly middle cerebral artery occlussion (M1 segment 25.37%, M2 segment 5.97%) and the internal carotid artery (21.64%). The posterior cerebral artery consists of the basilar artery, vertebral artery and posterior cerebral artery occupied 14.18%. Patients with small blood vessels included the anteriorl and posterior cerebral circulatory system.

IV. DISCUSSION

4.1. Baseline characteristics

Baseline characteristics of all patients are given in Table 1, it has shower mean age was 64.35± 12.37 years. The highest age was 85, the lowest was 21. The age group most encountered was over 60 years old. There were 55 women (41%). Mean time was 213.38 ± 92.54 minute, the fastest is 15 minute and the limit is 360 minute. The anterior cerebral circulation system had accounted 81.35%. The mean age in our study was similar to the SWIFT trial in 2012 by Saver J.L. et al. [7]. Thereby the mean age of the group 65.4 ± 14.5, Merci group 67.1 ± 11.1. Earlier research by Nguyen Hoang Ngoc at 108 hospital showed that the mean age was 64.7, our results are quite similar due to the same location, where had collected data [2].

About time, the fastest time from onset to admission at emergency department was 15 minutes, the latest time was 6 hours, the mean time was about 213 minutes. The result was similar Nguyen Hoang Ngoc et al. at 108 hospital [2].

The anterior cerebral circulation system had accounted 81.35%. Thus, the anterior cerebral circulation system occlusion had caried large proportion, the same result of Nguyen Hoang Ngoc et al [2], Saver J.L. et al. [7] and Daniel Behme & partner in Germany [5].

The medical history of AIS patients has always been emphasized. Our result showed that hypertension (55.2%) and atrial fibrillation (27.6%) were the most common medical history of AIS patients. Less medical history were diabetes, heart valve disease, smoking history. The rate of hypertensive patients was consistent with description of

Nguyen Van Tuyen (46.5%) [4]. However, the rate of atrial fibrillation in our study was lower (Nguyen Van Tuyen 40.7%, and Nguyen Quang Anh (64.3%). The medical histories were also reported similarly of Nguyen Hoang Ngoc et al. [2].

4.2. Clinical manifestations

The common clinical signs of AIS patients in the first 6 hours were unilateral paralysis (95.5%), facial palsy (91.0%) and aphasia (70.9%). Other manifestations were dizziness, coma, vomitting. The coma, dizziness were more common in patients at posterior cerebral circulation occlusion with p <0.05. In our study, the all level of paralysis had noted so that the rate paralysis of AIS patients was rather higher than result of Do Duc Thuan et al study, which had noted high level of paralysis. The rate severe paralysis patients of Do Duc Thuan et al study was 79.24% [3]. The European study about compare clinical signs between anterior and posterior cerebral circulation showed that the rate paralysis of AIS patients of anterior cerebral circulation accounted 96% was higher than posterior cerebral circulation with 80% [10]. The symptoms of aphasia, facial drops were similar to Do Duc Thuan et al study and The European study. Thus classic symptoms such as paralysis, aphasia and facial drops were noted.

Interestingly, there was a difference in clinical manifestations between anterior and posterior cerebral circulation occlusion. We found that coma, dizziness was more common in patients with posterior circulation with p <0.05. The gaze preference signs were quite specific for large vesel occlusion, which we had noted of anterior cerebral circulation occlusion stroke were more than posterior. However the number of AIS patients, who had this sign was not much so that was no statistically significant difference. The trial of Peter Vanacker et al in Euro had showed that coma and eye movement disorders were common of posterior occlusion. The others sign as unilateral paralysis, sensory disorders and language disorders were more common in the anterior cerebral circulation [10].

The mean NIHSS score was 17.37. The highest NIHSS score was 42 points, the lowest score was 2 points, the mode NIHSS score was 21. Mostly patients with NIHSS scores from 16 to 29 with 55.97%. The proportion of patients with NIHSS scores below 6 and over 30 accounts about 10%. The most studies had reported a mean NIHSS of 17 instead study of Military 103 Hospital [3], or 108 Hospital [2] or Euro [5, 10]. We had patients with basilar artery occlusion with deep coma when admission so the NIHSS score was recorded highest 42.

At 108 hospital, we have applied mechanical thrombectomy to revascularization AIS with large vessel occlusion brough good results, which showed on *Figure 2*. NIHSS data at admission are needed to assess the stroke severity of the population treated, and are helpful to place into perspective the NIHSS discharge data. NIHSS discharge from <6 was 32.01%. This result was similar of Daniel Behme & partner in Germany [5].

4.3. Computerized tomography characteristics

In terms of CT image with AIS patients in the first 6 hours after symptom onset, CT image was normal about 44.78%. The large vessel occlusion stroke had accounted for 70% and anterior cerebral circulation occlussion was 81.35%. The studies at 103 hospital previously had reported that up to 39.62% of patients with normal CT image [3].

There were 74 patients with AIS, who have early sign on NCCT, accounted for 55.22%. Signs of early ischemic were cortical sulcal effacement (25.6%); loss of grey-white matter differentiation (24.3%); loss of the insular ribbon (31.1%); and hyperattenuation of large vessel (22.9%, eg: hyperdense middle cerebral *artery* sign). Similar results of the study by the authors at the 103 hospital [3].

The ASPECT score was calculated for AIS patients with blood supply location of the middle cerebral artery (including internal carotid artery occlusion and segmental M1), which was 63 patients. In the first 6 hours, there were 4 patients with ASPECT score below 5, accounted for 6.35%. The most patients with ASPECT score above 6. The mean ASPECTS score was 7.8. This rate is quite similar to previous research by Nguyen Hoang Ngoc et al at 108 Hospital [2].

Regarding the position of vessel occlusion in our study, patients with large vessel occlussion, mainly middle cerebral artery occlussion (M1 segment 25.37%, M2 segment 5.97%) and the internal carotid artery (21.64%). The posterior cerebral artery consists of the basilar artery, vertebral artery and posterior cerebral artery occupied 14.18%. Patients with small blood vessels included the anteriorl and posterior cerebral circulatory system. Patients with small vessels occlusion including the anterior and posterior cerebral circulation**.** Similar results trila of Behme D. & cs in 2014 with 129 AIS patients, in which MCA: 48%; ICA: 33%, basilar artery occlusion: 16% [5]. This was also the result of TREVO 2: 60% and SWIFT: 61% [7]

V. CONCLUSIONS

Results from 134 AIS patients in the first 6 hours after symptom onset at 108 Hospital, showed: common clinical signs of AIS patients include unilateral paralysis, aphasia and facial palsy, central ventricular episodes. On CT images, nearly 45% patients showed normal of mainly with large vesel occlusion in anterior cerebral circulation. There were significant differences in clinical symptoms between the anterior and posterior circulation stroke.

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RÉSUMÉ:

LES CARACTÉRISTIQUES CLINIQUES, DU CT CÉRÉBRAL, CHEZ LES PATIENTS AVEC ICTUS THROMBOTIQUE AIGU AU COURS DES 6 PREMIÈRES HEURES APRÈS L'INSTALLATION DES SYMPTÔMES

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Objectif: Decrire les caractéristiques cliniques, et du CT cérébral, de l'ictus cérébral aigu au cours des 6 premières heures après l'installation des symptômes.

Méthode: 134 patients avec AIS suivi au cours des 6 premières heures a l'hôpital 108 de Juliet 2016 à Juliet 2017, avec la description des caractéristiques cliniques:

Histoire de la maladie, survenue brusque des deficits neurologiques, temp de survenue et les images précoces enregistrées au CT, les scores NIHSS, aussi bien que les scores ASPECT.

Résultats: L'âge moyen: 64.35±12.37 (de 21 à 85 ans). Le temps moyen: 213 minutes. L'histoire de la maladie la plus fréquemment rencontrée: (55.2%) et la fibrillation atriale (27.26%). Les caractéristiques cliniques: Hémiparésie (95.5%), aphasie (70.9%), et hémiparalysie faciale (91%). Conscience conservée: 68.9%.

Les autres caractéristiques moins fréquentes: Céphalée, tournoiement, émission de gaz… Les scores NIHSS sont en moyenne 17.37±6.8. Pour les images du CT: 55.22% patients ont une atténuation de contraste dans le parenchyme cérébral, 70.89% montrént l'occlusion des grands vaisseaux, 81.35% intéressant l'artère cérébrale frontale. Le score ASPECT: 7.87±1.39. Les caractéristiques cliniques de l'ictus du système arteriel vertébrobasilaire sont le coma, ou le tournoiement. Les signes d'occlusion des grands vaisseaux sont le coma, l'émission de gaz et les désordres de la phonation.

Conclusion: Les symptôms cliniques des patients avec AIS au cours des 6 premières heures sont riches, cependant les signes les plus fréquemment rencontrés sont l'hémiparalysie faciale, et les troubles du langage.

Environ la moitié des patients avec AIS au cours des 6 premières heures ne montrent pas de lésion au CT,

Mots clés: *Acute ischemic stroke, clinical manifestation, computerized tomography image.*

STUDY OF EFFECTS OF WILLUGHBEIA COCHINCHINENSIS (WC) TO REVERSE ANXIETY DISODERS IN MICE

Cao Tien Duc*, Le Van Quan*

ABSTRACT

Object: to investigate effects of WC to ameliorate disoders in anxiety-like behaviors of mice. ***Materials and methods:*** in the present study, 50 Swiss mice were induced anxiety-like behaviors by scopolamine. Behaviors of mice treated with and without WC at doses 100mg/kg, 150mg/kg and 200mg/Kg and/or scopolamine were tested using the open field test. ***Results:*** WC at dose 150mg/kg and 200mg/kg induced an significant increase in time spent, number of entries and travel distances in the center area of open field in animals with scopolamin-induced anxiety-like behaviors. ***Conclusion:*** WC 150mg/kg and 200mg/kg might ameliorate deficits in anxiety like symtoms in experimental animals.

Keywords: *Anxiety, mice, willughbeia cochinchinesis*

I. INTRODUCTION

Anxiety disorder is one of comon symptoms in mental disoders such as depression, phobia, etc. In a recent study, it has suggested that 33.7% of the population are affected by an anxiety disorder during their lifetime [1]. Furthermore, ratio of females with anxiety disorder is higher than this of male with this symptom [2]. In treatment, benzodiazepines have been suggested to be effective to anxiety disorders. However, these drugs might induce drug independence when they are used a long time [3]. Thus, it is nessesary to investigate new natural plants or drugs for treating anxiety disorders.

It has suggested that anxiety-like disorders might relate to activities of achetylcholine. Thus, scopolamine, a antagonist to acetylcholinergic receptors, might be used to induce anxiety-like behaviors in experimental animals [4]. In the present study, we used this animal model to investigate effects of a new natural plant, WC, to meliorate dificits in anxiety-like behaviors in mice.

II. MATERIALS AND METHODS

2.1. Subjects

50 Swiss mice (150-250g body weight) were used in the present study. Animals were housed in individual cages, maintained in controlled temperature and 12 h light/dark cycles with free access to water and food. The present study was conducted at department of physiology, Vietnam Military Medical University. All procedures were performed in accordance with The Animal Center Guidelines for the Care and Use of Laboratory Animals at the Vietnam Military Medical University.

2.2. Materials

WC was isolated by Department of Pharmacy, Ho Chi Minh City University of Medicine and Pharmacy and was supplied in power form. WC power was dissolved in saline using a Magnetic Stirrer.

2.3. Animal grouping and drug treatments

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Date of scientific judgment: 23/3/2018
Reviewed date: 30/3/2018

Animals were separated randomly into 5 experimental groups, 10 mice for each group: group 1 (control group): mice were ip and p.o treated saline; group 2 (scopolamin group): mice were i.p treated scopolamin 1,5mg/Kg and p.o treated saline at 0,1ml/10g; group 3, group 4 and group 5 (WC groups): mice were i.p injected scopolamin 1,5mg/Kg and p.o WC 100mg/Kg, 150 mg/Kg and 200mg/Kg, respectively. WC and saline were orally administered at 60 minutes and scopolamin and saline were i.p injected at 30 minutes before the behavioral task.

2.4. Open field test

60 minutes after drug treatments, mice were placed in the center of a open field box. Open field box was a square box (40 × 40 × 60 cm), covered with polypropylene sheets inside the wooden box (figure 1). Animals were allowed to free explore inside open field box for 5 minutes. Behaviors of animals were recorded using a digital video system. Data was analyzed offline by ANY-maze software (Stoelting Co., Wood Dale, IL, USA).

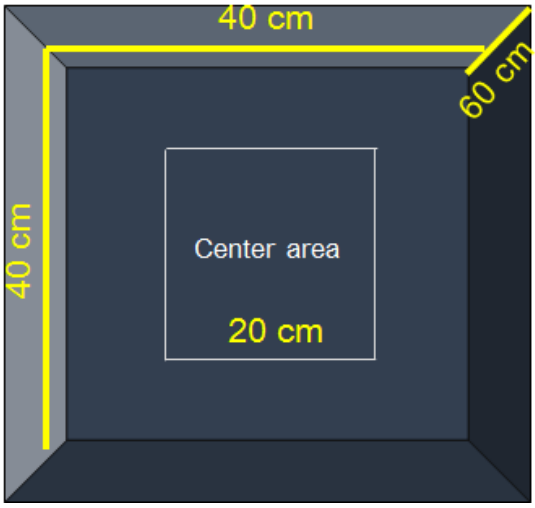

Figure 1. *Open field box*

2.5. Research indicators

In the present study, the open field are was seperated into two areas: a center area and a periphery zone (figure 1). To investigate anxiety-like behaviors in mice, we concentrated to analyze activities of animals in the center area of the open field apparatus. These were:

- Time spent in the central zone (s).
- Numbers of entries into the central area
- Travel distances in the central area (m)

2.6. Data analysis

Time spent in the central area; numbers of entries into average speed of locomotion in the central zone were analyzed by one-way analysis of variance (ANOVA) followed by the Tukey's post-hoc test for multiple comparisons, using SPSS 19.0. Results were considered to be statistically significant at $p < 0.05$. All results were expressed as mean ±SEM.

III. RESULTS

3.1. Changes of time spent in the central area of the open field

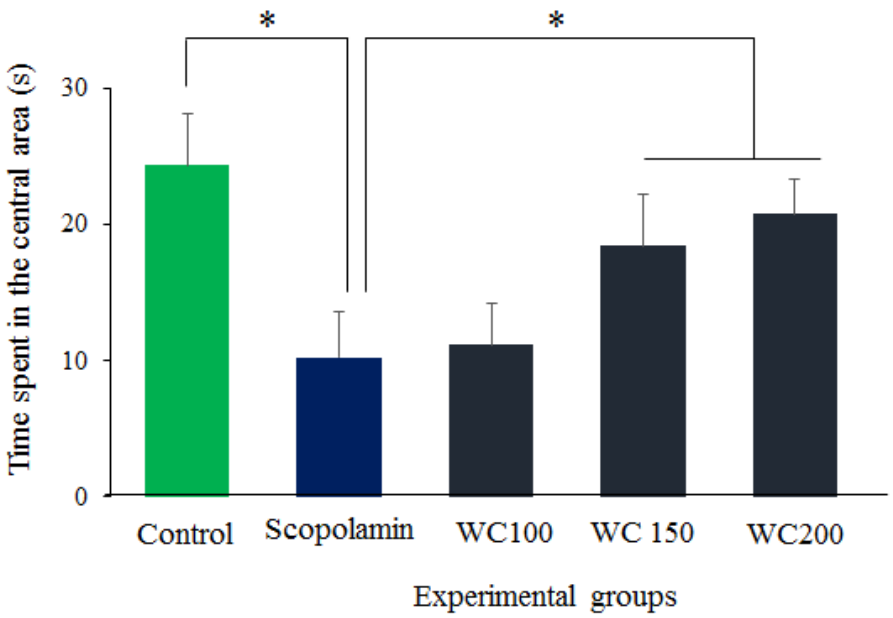

Figure 2. *Time spent in the center area*

Time spent of mice in the center area is used to assess exploring abilities as well as anxiety-like behaviors of mice. In the Fig. 2, time spent in the central area of animals treated by scopolamine was significant shorter than this of animals treated by saline ($p<0,05$). After animals treated by WC, there were gradual increases in time spent in the central area. However, significant differences were found only in animals treated by WC at doses150mg/kg and 200mg/kg ($p<0,05$).

3.2. Changes in numbers of entries to the central area

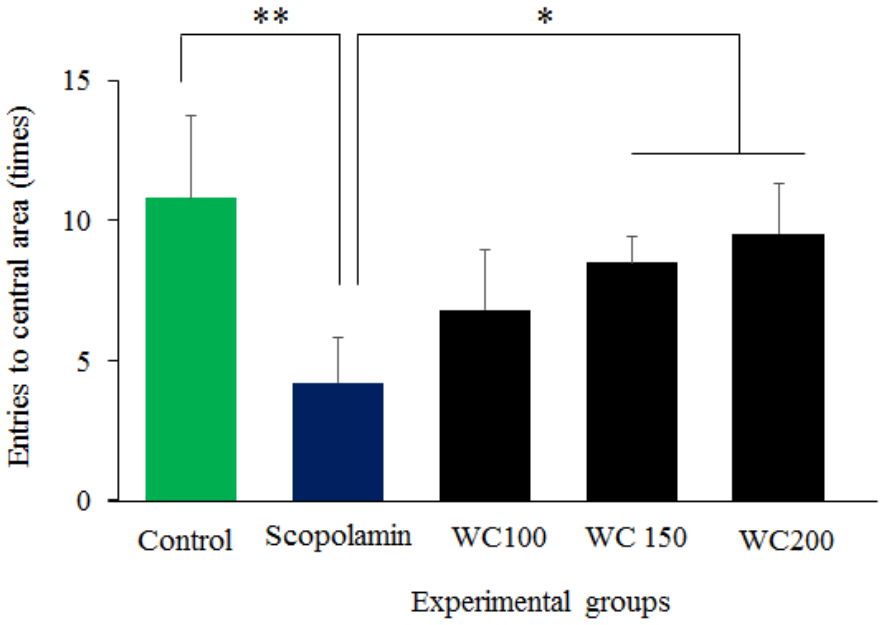

Figure 3. *Entries to the central area*

Fig. 3 indicated results of entries of mice into the central area. Results showed that number of entries into the central area of mice treated by scopolamine was significant lower than this of mice treated by saline (control group) ($p<0.01$). Furthermore, there were gradual increases in entries of mice into central areas following treatments of WC at doses 100mg/kg; 150mg/kg and 200mg/kg. However, there were significant differences in numbers of entries into the central area of mice treated by WC at doses 150mg/kg and 200mg/Kg ($p<0.05$).

3.3. Changes in travel distances in the central area

Fig. 3 showed travel distances in the central ares of mice in experimental groups. Results showed that mean travel distance in the central area of mice treated by scopolamin was significant shorter than this of mice treated by saline ($p<0.01$). After treatments of WC, travel distances in the central area of mice increased gradually. However, treval distances of mice in the central areas increased significantly in groups WC 150 and WC 200 only ($p<0.01$).

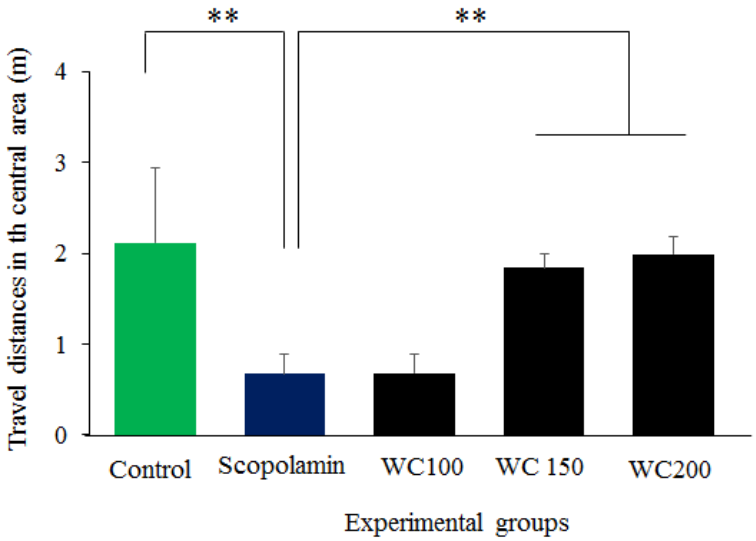

Figure 4. *Travel distances in the central area*

IV. DISCUSION

Open field is one of common behavioral tests which are employed to investigate anxiety-like disorders in rodent animals. In the open field test, the time spent and number of entries to the center of arena are often used to measure behaviors relating to anxiety disorders in mice. In general, due to life characteristics of mice, they avoid the center of open field arena. Increases in time spent and numbers of entries into the central areas of the open fields might indicate a decrease in anxiety behaviors [5].

In the present study, we found evidence of effects of WC to decrease anxiety disorders in mice. These were: treatments of WC at doses 150mg/kg and 200mg/kg induced increases in time spent, numbers of entries and travel distances in the center of open field arena. These results are consistent with previous studies which have concentrated to investigate anxiety disorders in mice. Anchan et al showed that GPR30 activation decreases anxiety in the open field which was expressed by a greater distance and higher number of entries into the central area in the open field [6]. Similarly, by the some way, they have demonstrated that γ-aminobutyric

acid transporter-1 also is involved in decreases of anxiety like behaviors in mice [7]. From above results, our study showed a direct evidence for effects of WC to decreasing anxiety like behaviors in mice.

V. CONCLUSION

In the present study, we focused to study effects of WC to anxiety disorders in mice. We found that: After treatments of WC at doses 150mg/kg and 200mg/kg, there were increases in time spent in the center of arena, greater travel distances and higher numbers of entries into the central of open field area. These results provided new evidences for using new natural plants in the treatments of anxiety disorders in humans.

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RÉSUMÉ:

ÉTUDE SUR LE WILLUGHBEIA COCHINCHINENSIS (WC) DANS LE TRAITEMENT DES TROUBLES DE L'ANXIÉTÉ CHEZ LE RAT

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Objectif: Etudier l'effet thérapeutique du Willughbeia cochinchinensis dans l'amélioration des troubles de l'anxiété chez le rat.

Matériel et méthode: Donner le Scopolamine à 50 rats Suisses pour provoquer des agissements de l'anxiété, un nombre de rats est ensuite soumis au WC (dose de 100mg/kg, 150mg/kg, et 200mg/kg), le test étant "le champ ouvert" (open field test).

Résultats: Aux doses 150mg/kg, et 200mg/kg, l'augmentation est signifiante de la durée du temps, des entrée multiples et des distances parcouruées enregistrée au centre du champ ouvert chez les rats soumis à la Scopolamine.

Conclusion: Le WC à150mg/kg, et 200mg/kg pourraient améliorer les symptômes d'anxiété chez les animaux d'expérience.

Mots clés: *Anxiety, mice, Willughbeia cochinchinensis.*

CONTENTS
REVUE MÉDICALE N°1 - 2018

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