RESULT OF PLATELETPHERESIS AND ANTI-PLATELET MEDICATION IN TREATMENT OF ESSITIAL THROMBOCYTHEMIA AT VIETNAM - CZECH FRIENDSHIP HOSPITAL IN 2017 - 2019

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ABSTRACT

The study was carried out in 56 essential thrombocytosis patients admitted to Vietnam - Czech hospital in Hai Phong city from 01/01/2017 to 06/2019. **Subject**: Investigation of the effectiveness of plateletpheresis and anti - platelet medication treatment (combined with hydroxyurea) in essential thrombocytosis. **Method:** prospective study with clinical intervention. **Results**: 1. The effectiveness of plateletpheresis. 1.1. Most of patients have improvement regarding symptoms related to microvascular stasis due to thrombocytosis (reduced from 58,3% to 31,8% with p < 0,05). 1.2. After 24 hours of plateletpheresis, platelet count reduced from 1,340 G/l to 736 G/l. 2. The effectiveness of anti-platelet medication after plateletpheresis: after 2 weeks of treatment, most of patients have significant improvements regarding symptoms related to microvascular stasis due to thrombocytosis (reduced from 31,8% to 3,8%).

Keywords: Essential thrombocytosis, plateletpheresis, anti - platelet medication

I. INTRODUCTION

Essential thrombocythemia is a hematopoietic malignancy, belonging to Myeloproliferative Neoplasms - MPNs, characterized by an increased number of platelets [1-3]. Complications of thrombosis and/or bleeding in patients with primary thrombocytosis affect quality of life, even in severe cases can be fatal [2, 6].

Currently, the purposes of essential thrombocythemia treatment are to reduce the number of platelets by using plateletpheresis and anti - platelet medication treatment [2-4]

Hematology and Blood Transfusion center, Vietnam - Czech Friendship hospital was built in 2007. In 2013, clinical hematology department was formed. Since 2017, plateletpheresis has been indicated for patients with essential thrombocythemia. In order to evaluate the effectiveness of plateletpheresis and anti - platelet medication (combined with hydroxyurea), we conducted this study with the purposes:

1. Evaluate the change in platelet count before and after plateletpheresis

2. Evaluate the change in clinical manifestations and effectiveness of anti - platelet medication (combined with hydroxyurea) in patients with essential thrombocythemia

II. SUBJECT AND METHOD

2.1. Subject of the study

56 patients with essential thrombocythemia were treated at Hematology and Blood

Transfusion center, Vietnam - Czech Friendship hospital from January 2017 to June 2019.

Selection criteria: patients who were diagnosed with essential thrombocythemia according to WHO 2008 and were voluntary to take part in the research.

2.2 Research methodology

2.2.1. Research design: progressive study with clinical intervention and convenient sample selection

2.2.2. Indices and research procedure

- Clinical: Ask the patients and clinical examination to detect symptoms of thrombosis or stagnation of the microcirculation: Numbness, limb paresthesia, cyanosis, headache or complications of arterial or venous occlusion.

- Tests including: counting red blood cell (RBC), white blood cell (WBC), hemoglobin. Tests were conducted at time:

+ 1st day: before plateletpheresis, right after plateletpheresis, 12 hours after plateletpheresis, 24 hours after plateletpheresis

+ Then use anti - platelet medication (aspirin or clopidogrel) and hydroxyurea: tests were done on 3rd, 7th, 14th.

Acid uric and LDH were done at hospital admission. Plateletpheresis was indicated for patients with platelets $\geq$ 1.000 G/l, using Obtia machine according to standard of the center. Treatment protocol was based on the guidance of Ministry of Health: Aspirin or clopidogrel 75 mg/24h until platelets decreases below 500 G/l. Treatment protocol of hydroxyurea was based on the guidance of Ministry of Health [2].

2.3. Data processing

Data was processed using SPSS 16.0

2.4. Ethical issue

The research was carried out in accordance with the rules of biomedical research. The research was approved by the scientific committee of Vietnam -Czech Friendship hospital.

The result is used to improve the effectiveness in treatment of patients with essential throbomcythemia.

III. RESULT

3.1. Changes in platelet count before and after plateletpheresis

3.1.1. Common features of patients

Table 3.1. Age, gender of patients

Age Gender	20 - 30		31 - 40		41 - 50		51 - 60		>60		Total	
	SL SL	%	SL	%	SL	%	SL	%	SL	%	SL	%
Male	2	3,6	5	8,9	7	12,5	6	10,7	3	5,4	23	41,0
Female	3	5,3	11	19,7	8	14,3	7	12,5	4	7,1	33	59,0
Total	5	8,9	16	28,6	15	26,8	13	23,2	7	12,5	56	100

Comments: patients aged 31- 60 accounted for the highest with 78,6%. Female patients accounted for 59%, male was 41%.

Table 3.2. Features of blood stagnation and microcirculation after 24 hours of plateletpheresis

Symptom Quantity	Numbness		Acrocyanosis		Limb pain		Headache	
	Quantity	%	SL	%	SL	%	SL	%
Patient	4	7,8	1	1,8	1	1,8	12	21,4

Comment: After 24 hours of plateletpheresis, 7,8% of patients had numbness, 1,8% had Acrocyanosis, 1,8% had limb pain and 21,4% had a headache

3.1.2. Peripheral blood indices

Table 3.3. Number of Platelets before and after plateletpheresis

Time Platelet value	Before n = 56 (1)	Right after n = 56 (2)	after 12h n = 56 (3)	After 24h n = 56 (4)
Platelet count $\overline{X}$ ± SD	1.240 ± 461	782 ± 246	710 ± 257	736 ± 289
p	$P_{1-2}< 0,01$	$P_{2-3}< 0,05$	$P_{3-4}< 0,05$	$P_{1-4}< 0,001$

Comments: Platelet count before plateletpheresis was 1.240 ± 461 G/l, right after plateletpheresis was 782 ± 246 G/l and 24h after plateletpheresis was 736 ± 289 G/l this has statistical significance $P < 0,01$

Table 3.4. WBC count and hemoglobin before and after plateletpheresis

		Before	Right after	After 12h	After 24h
WBC $\overline{X}$ ± SD	Quantity (G/l)	12,9 ± 7,7	11,9 ± 7,2	12,4± 7,6	11,1±6,8
	p	$P_{1-2}> 0,05$	$P_{2-3}> 0,05$	$P_{3-4}>0,05$	$P_{1-4}> 0,05$
Hb $\overline{X}$ ± SD	Quantity (g/l)	123±25	116±21	117±28	114±23
	p	$P_{1-2}> 0,05$	$P_{2-3}>0,05$	$P_{3-4}> 0,05$	$P_{1-4}> 0,05$

Comments: There was no change in WBC count and hemoglobin before and after plateletpheresis with $p > 0,05$

3.1.3. Comparison of effectiveness of plateletpheresis in patients with platelets >1.500 G/l and ≤ 1.500G/l

Table 3.5: Comparison of effectiveness of plateletpheresis in patients with platelets >1.500 G/l and ≤ 1.500G/l

Platelet count	Before	Right after	After 12h	After 24h
PLT >1.500 G/l $\overline{X}$ ± SD	1.645± 492	1.046 ± 217	896 ± 112	945 ± 108
PLT ≤ 1.500 G/l $\overline{X}$ ± SD	1.324 ± 286	792 ± 112	710 ± 116	705 ± 106

Comments: Patients with PLT > 1.500G/l at the time before, right after, after 12h and after 24h were: 1.645 ± 492 G/l;1.046 ± 217G/l;896 ± 112G/l;945 ± 108G/l, respectively. Patients with PLT ≤ 1.500 G/l at the time before, right after, after 12h and after 24h were: 1.324 ± 286G/l;792 ± 112G/l; 710 ± 116G/l; 705 ± 106G/l, respectively.

3.1.4 Side effects of plateletpheresis

Table 3.6 Side effects of plateletpheresis

Complication Patient	Blood vessel rupture		Dizziness		Mild hypotension	
	Quantity	%	Quantity	%	Quantity	%
Complication/total patient (n=56)	3	5,4	2	3,6	1	1,8

Comments: There was 5,4% of patients having blood vessel rupture, 3,6 % having dizziness and 1,8% having mild hypotension

3.2. Effectiveness of treatment using anti - platelet medication combined with hydroxyurea

Table 3.7 Clinical manifestations after treatment with anti - platelet medication combined with hydroxyurea

Time Symptom	Before		After 3 days		After 7 days		After 14 days	
	SL	%	SL	%	SL	%	SL	%
Numbness	4	7,1	2	3,6	1	1,8	0	0
Acrocyanosis	1	1,8	1	1,8	1	1,8	0	0
Limb pain	1	1,8	1	1,8	1	1,8	0	0
Headache	12	21,4	5	8,9	3	5,4	1	1,8

Comments: Anti - platelet medication combined with hydroxyurea helps to reduce clinical symptoms and complications after 14 days.

IV. DISCUSSION

4.1. Effectiveness of plateletpheresis
4.1.1. General features

Age and gender of patients are presented in table 3.1. The result shows that age from 31 - 60 is the most common, accounting for 78,6%. Female has a higher percentage with 59%, while male is 41%. This is in accordance with the study by Nguyen Ha Thanh, National Institute of Hematology and Blood Transfusion which showed the percentage of 45,4 ± 10,2, youngest age was 18, highest was 84 years old [1]. Female patients accounted for 54%, male patients accounted for 46%.

4.1.2. Changes in PLT count before and after plateletpheresis

Plateletpheresis is a supporting treatment which helps to reduce quickly PLT count, improve clinical symptoms, reduce complications and improve the effectiveness of chemotherapy [2,3,5].

Because plateletpheresis has short effect, we evaluate the effectiveness in 24 first hours, then evaluate the effect of anti - platelet medication combined with hydroxyurea.

4.1.3. Arterial or venous occlusion after 24 hours of plateletpheresis

It can be seen that plateletpheresis helps to improve quickly symptoms relating to arterial occlusion: after 24 hours, numbness, acrocyanosis reduce from 18,5% to 7,6% ($P<0,05$); headache reduces from 35,5% to 21,8% ($P< 0,05$), total of patients having symptoms reduce from 58,3% to 31,8% ($P<0,05$).

Our result is similar to the result of other researchers such as Dutcher which showed: after 24 hours of plateletpheresis, acrocyanosis reduced from 23% to 10% and headache reduced from 25% to 8% [4]. According to Tefferi, symptoms of numbness, acrocyanosis reduced from 28,4% to 12% after plateletpheresis [6].

4.1.4. Changes in some peripheral blood indices

- Change in PLT count before and after plateletpheresis

Table 3.3 shows that at right after, after 12 hours, 24 hours of plateletpheresis, PLT reduce in compared with the time before plateletpheresis. The greatest reduction is at right after plateletpheresis (from 1.240 ± 461

to 782 ± 246 G/l with P < 0,001). After 12h: 710 ± 257 G/l and after 24h: 736 ± 289 G/l.

The level of PLT count reduction can be seen at right after, after 12 hours and 24 hours. The time right after plateletpheresis has the lowest PLT count.

According to Dutcher, PLT count reduces at an average of 53% after 24h. Our research has the same result [4].

- Table 3.4 shows the number of WBC and hemoglobin before and after plateletpheresis. There is a mild reduction in the number of WBC and hemoglobin at the time right after, after 12h and after 24h, which has no statistical significance P<0,05 [2,5,6].

Therefore, this method does not change the number of WBC and hemoglobin in patients. If patients have anemia, plateletpheresis can be applied[2][4][5].

***4.1.5.* Comparison of plateletpheresis in patients with PLT ≤1.500 G/l and ≥ 1.500 G/l.**

In order to evaluate whether elevated PLT affects the effectiveness of plateletpheresis, we evaluate two groups of patients: Patients have PLT > 1.500 G/l and patients have PLT ≤ 1.500 G/l at the time before, right after, after 12h and after 24h, which are shown in table 3.5. In group of patients with PLT > 1.500 G/l , PLT count reduce from 1.645 G/l -> 1.046 G/l -> 896 G/l -> 945 G/l. In group of patients with PLT >1.500 G/l, the reducing rate is the same with plateletpheresis. Similarly, group ≤ 1.500 G/l have the same result.

Thus, the increase in PLT count does not affect the effectiveness of PLT reducing technique of plateletpheresis [4].

4.1.6. Side effects of plateletpheresis

Side effects were presented in table 3.6. There were 3 cases of blood vessel rupture with 5,4%, 2 patients had dizziness with 3,6%, 1,8% of patients had mild hypotension

(does not affect plateletpheresis). Our result is similar to other researches.

***4.2.* Effectiveness of treatment using anti - platelet medication combined with hydroxyurea**

Table 3.7 shows the symptoms at the time 3 days, 7 days and 14 days: numbness: 7,1% -> 3,6% ->1,8% -> 0%; acrocyanosis: 1,8% -> 1,8% -> 1,8% -> 0%; limb pain: 1,8% -> 1,8% -> 1,8% -> 0%; headache: 21,4% -> 8,9% -> 5,4% -> 1,8%.

After treatment with anti - platelet medication combined with hydroxyurea, most of symptoms disappear after 14 days [3].

Thus, it can be seen that plateletpheresis and anti - platelet medication (combined with hydroxyurea) is effective treatment, improving clinical symptoms relating to blood stagnation and microcirculation, which helps to improve the life quality of patients [1-3].

V. CONCLUSION

Some conclusion can be drawn out:

1.Changes in PLT count before and after plateletpheresis

- PLT count before plateletpheresis: 1.240 ± 461 G/l reduce to: right after: 728 ± 246 G/l, after 12h: 710 ± 257 G/l, after 24h: 736 ± 289 G/l.

2.Changes in clinical symptoms and effectiveness of anti - platelet medication (combined with hydroxyurea)

- Reduce clinical symptoms including numbness, acrocyanosis, limb pain, and headache

- All of these symptoms disappear after 14 days of treatment.

RECOMMENDATION

There should be frequent indication of plateletpheresis for patients with essential thrombocythemia.

REFERENCES

1. **Binh, V.D., Thanh, N.H., Huong, V.L., Tri, N.A. (2016)** A study on essential thrombocythemia at the National Institute for Hematology and Blood Transfusion in 2016. Medical Journal, 446, 826-834.
2. **Vietnam Ministry of Health (2016)** Essential thrombocythemia, guidance on diagnosis and treatment, 61 - 66.
3. **Carobbio, A., Thiele, J., Passanonti, F. (2011)** A Risk factors for arterial and venous thrombosis in WHO - defined essential thrombocythemia and international study of 891 patient. Blood, 117, 5,857 - 5,859.
4. **Dutcher. JP (2013)** Therapeutic Cytapheresis, plasma pheresis and plasma exchange in neoplastic disease of the blood. Springer New York, p 1241 - 1249.
5. **Szczeporkowski, Z.M; Winter, J.L; Brandazenko, N., et al. (2010)** Guidelines on the use of therapeutic apheresis in clinical fractice - Evidence based approach from the apheresis applications committee of the American Society for Apheresis. Journal of clinical apheresis, 25(3), 83-177.
6. **Tefferi, A. and Babri, T. (2015)** Polycythemia vera and essential thrombocythemia: 2015 update on diagnosis risk- stratification and management. American Journal of hematology, 90(2), 162-173.