

EFFECTS OF LISINAPRIL AND AMLODIPIN IN COMBINATION FOR THE TREATMENT OF HYPERTENSION WITH PULSE WAVE VELOCITY VP PLUS 1000 METER

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ABSTRACT¹⁷

Aim: The aim of this study was to evaluate the antihypertensive efficacy of lisinopril and amlodipine in combination which were measured by the pulse wave velocity meter. **Research objects and Methods:** 40 patients with primary hypertension, mean age 69.18 ± 10.4 years. All patients had their blood pressure, pulse wave velocity (baWPV), ankle brachial index measured by pulse wave velocity VP Plus 1000 meter before receiving the treatment. All patients were then given the Lisonorm combination pill (lisinopril 10 mg and amlodipine 5 mg) for 4 weeks. After 4 weeks, the patients was measured again with the same device (the pulse wave velocity of VP Plus 1000 meter). **Results:** After 4 weeks, the values of the Right arm blood pressure decreased: 26.58 ± 9.51 mmHg/ 8.6 ± 4.47 mmHg; Left arm blood pressure decreased: $26.88 \pm 11.27/13.55 \pm 8.15$ mmHg; Right ankle blood pressure decreased: $23.75 \pm 11.78/10.75 \pm 6.64$ mmHg; Left ankle blood pressure decreased: $30.33 \pm 16.64/13.6 \pm 9.28$ mmHg; The rate of patients with the target blood pressure was 72.5% (29/40 patients). Right baPWV decreased 593.65 ± 416.59 cm/s; Left baPWV decreased 585.4 ± 447.19 cm/s. **Conclusion:** The combination of lisinopril 10mg and amlodipine 5mg effectively had decreased the blood pressure in both extremities and pulse wave velocity, and had reduced vessel wall stiffness when it was

measured by the pulse wave velocity VP Plus 1000 meter.

Keywords: Hypertension (HTN), Combination pill (lisinopril and amlodipine), Arm blood pressure (BP), Ankle blood pressure, Brachial ankle pulse wave velocity (baWPV), Target blood pressure.

I. INTRODUCTION

Hypertension (HTN) is a leading global burden of disease risk factor and is a major cause of death worldwide, with an estimation of 10 million deaths in 2015 [8]. In general, the controlled rate of HTN is not high. In the May Measurement Month (MMM) global screening campaign in 2018 of International Society of Hypertension (ISH) which was conducted in many countries, a total of 345234 individuals were screened. A total of 32.3% individuals with HTN, of whom 55.6% were aware of HTN and 55.3% were on antihypertensive medicines, out of which 25.3% were uncontrolled. Overall 41.3% with hypertension were uncontrolled [1]. In Vietnam, MMM in 2017 was shown HTN of 28.7% of those surveyed, and 37.7% of patients receiving antihypertensive medication had uncontrolled blood pressure [11]. In low-income and middle-income countries, more 70% of the treated patients with HTN have uncontrolled blood pressure. One major reason for low levels of control is that most patients only receive monotherapy [14]

Currently, about 70% of hypertensive patients require at least 2 antihypertensive

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drugs in order to reduce blood pressure levels below the recommended target. The combination therapy should be initiated in patients with a systolic blood pressure value greater than 20 mmHg above the target or a diastolic blood pressure greater than 10 mmHg above the recommended goal. The combination therapy should also be initiated in patients at high cardiovascular risk. The combination therapy of 2 medicines increases the effects of treatment and has fewer side effects than increasing the dose of monotherapy. The most commonly used combination tablet is a renin-angiotensin system inhibition with a calcium channel blocker [5].

In current clinical practice, a routine blood pressure monitor has been used to measure blood pressure and evaluate the effects of taking medicines, the results depend on the technicians who measured and read the results, there may have device errors, in some big centers they apply 24-hour ambulatory blood pressure monitoring (ABPM) and the meter of VP Plus pulse wave velocity has that function of ABPM. This device measures the blood pressure of the extremities at the same time, measures the ankle-brachial index and records the pulse wave velocity to assess the blood pressure, cardiovascular risk, arterial stiffness, and peripheral artery disease [13].

In order to study the effects of the combination of the two medicines, applying new blood pressure measurement devices in clinical practice, we conducted this study with the aim of "evaluating the effectiveness of lisinopril and amlodipine in combination for the treatment of hypertension with the pulse wave velocity meter VP Plus 1000"

II. PATIENTS AND METHODS

2.1. Study setting and design

This study was a randomized clinical trial, open label, evaluating efficacy based on pre- and post-treatment criteria, was conducted from September 2020 to May 2021 at Vinh Medical University Hospital, Vinh city, Vietnam.

40 patients who were diagnosed with hypertension by mercury sphygmomanometer participated in the trial, all patients had their extremity blood pressure measured (1st time) using pulse wave velocity meter VP Plus 1000 of company OMRON COLIN, Japan, then the patient was taken an antihypertensive pill with the combination of lisinopril 10mg and amlodipine 5mg during 4 weeks (including 2 weeks at hospital and 2 weeks of medication and monitoring at home). During home medication, patients have their blood pressure monitored daily by themselves with an automatic electronic sphygmomanometer, then record and report the measurement results to the doctor and once a week, the doctor examined the patients or if the patient has a crisis of hypertensive emergency they should be treated with fast-acting drugs and excluded from the study. After 4 weeks (28 days) of combination pill, the patients have their blood pressure measured for the second time with the same pulse wave velocity meter VP Plus 1000 as measured for the first time. All patients were fully explained the benefits, possible side effects, consented to participate the study, which was performed in accordance with the Helsinki declaration. The study protocol was approved by the Scientific and Ethical Council of Vinh Medical University Hospital.

2.2. Study population

Patients who were enrolled in this study had newly detected primary hypertension with grade 2 (160-179 and/or 100-109 mmHg) who had not been taking any medication or had taken one and two-three another drugs (mono or multitherapy) but not achieve the goals (Systolic Blood Pressure-SBP \geq 140 mmHg and/or Diastolic Blood Pressure-DBP \geq 90 mmHg). Excluding the patients with the dyslipidemia, diabetes mellitus, ischemic heart diseases, cerebrovascular diseases, pregnant women at baseline and the secondary hypertension detected during treatment, the patients with hypertensive emergency at baseline and present during treatment, patients dropped out. Patients were divided into the degree of hypertension (grade 1- grade 3) based on the left arm blood pressure of the pulse wave velocity meter VP Plus 1000 and 2018 European Society of Cardiology/ European Society of Hypertension Guideline for the management of arterial hypertension 2018 (Grade 1: 140-159/90-99 mmHg; Grade 2: 160-179/100-109 mmHg; Grade 3: \geq 180/110mmHg) [4]. The hypertensive patients with grade 1 were people who had taking the monotherapy but not achieve the goals.

2.3. Study variables

Systolic blood pressure (SBP mmHg), diastolic blood pressure (DBP mmHg), pulse pressure (PP mmHg) of left arm, right arm, left ankle, right ankle; brachial-ankle pulse wave velocity (baPWV cm/s) of right and left side.

These indexes were measured twice with the same pulse wave velocity meter VP Plus 1000 of OMRON COLIN, Japan: the first measurement was done before medicine taking and the second time was measured after 4 weeks of taking Lisinopril 10mg and Amlodipine 5 mg in combination.

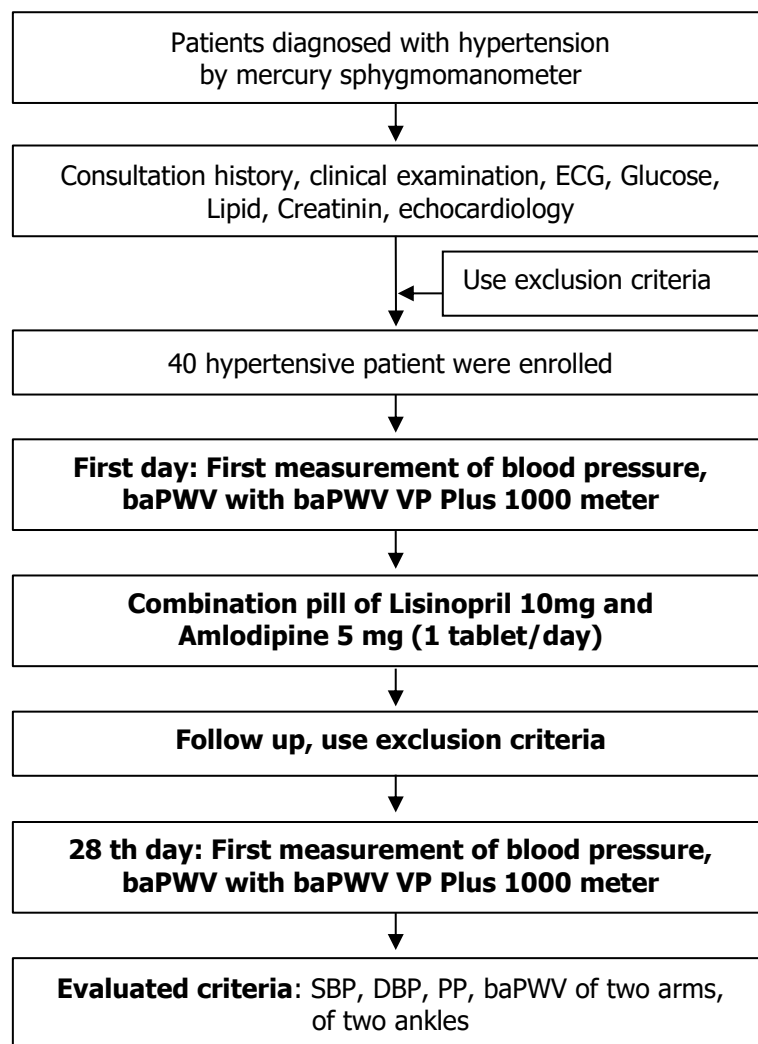
Target blood pressure was based on left arm blood pressure with pulse wave velocity meter VP Plus. Target blood pressure is in accordance with WHO 2021 < 140/90 mmHg [20].

Blood pressure response was defined as reduction of \geq 20 mmHg for SBP and/or \geq 10 mmHg for DBP [7].

Before measuring blood pressure with a pulse wave velocity meter, the patients were not allowed to drink or smoke, they rested in the supine position for 10 minutes. All metallic belongings including jewelry, metal objects, phones have to be removed. Loose-fitting clothes and loose pants were provided to ensure that patients' arms and ankles are exposed to the device's cuff, keep silent during the measurement.

2.4. Statistical analysis

Data was entered into Excel software and was analyzed with SPSS 20.0 software. Qualitative variables are expressed as frequency and percentage, whereas quantitative variables are described as mean value and standard deviation (mean \pm SD). Proportions rate were compared using *chi*² test, while the mean values were with *student T-test*. A value of $p < 0.05$ was statistically significant.



SBP = Systolic Blood Pressure, DBP= Diastolic Blood Pressure, PP= Pulse Pressure, baPWV= brachial -ankle Pulse Wave Velocity

Figure 1: Flow of the study

III. RESULTS

3.1. Baseline characteristics of patient

There were 40 patients took part in this study which completed 4 weeks treatment without dropped out. Female was 22 and male patients was 18; the mean of age was 69.18 ± 10.4 . The mean of weight was 55.72 ± 9.04 , BMI was 21.97 ± 2.56 , the mean of left arm systolic blood pressure was 159.2 ± 17.68 and left arm diastolic BP was 88.72 ± 11.3 , respectively; The rate of hypertension grade 1, 2, 3 and isolated

systolic hypertension between men and women is similar ($p > 0.05$). The grade 1 HTN patient who taken one or two medications (mono and multitherapy) but not achieve the goals was 62.5% (25/40 patients) and grade 2-3 HTN patients was 37.5% (15/40 patients). Interestingly, 92.5% of patients at the baseline who have taken medicine but have not achieved the goal. The results are summarized in Table 1.

Table 1. Baseline characteristics of patient

Variability		Male	Female	Total
Number of patients		18 (45%)	22 (55%)	40
Age (year)		67 ± 10	71 ± 9	69.18 ± 10.4
Body weight (kg)		60 ± 9	50 ± 5	55.72 ± 9.04
Height (cm)		165 ± 6	153 ± 7	15.98 ± 8.21
BMI (kg/m ²)		22.27 ± 298	21.31 ± 1.39	21.97±2.56
Number of hypertensive patients that has taken the drugs without achievement of the goals		16 (40%)	21 (52.5%)	37 (92.5%)
Left arm mean SBP (mmHg)		159.39 ± 19.58	157.75 ± 16.75	159.2 ± 17.68
Left arm mean DBP (mmHg)		92.33 ± 12	82.25 ± 7.29	88.72 ± 11.03
Isolated systolic hypertension	n (%)	9 (22.5%)	17 (42.5%)	26 (65%)
	SBP	147 ± 7	151 ± 7	149.77 ± 7.38
	DBP	83 ± 4	82 ± 5	82.19 ± 4.59
Classification	Grade 1	11 (27.5%)	14 (35%)	25 (62.5%)
	Grade 2	4 (10%)	4 (10%)	8 (20.0%)
	Grade 3	3 (7.5%)	4 (10%)	7 (17.5%)

SBP= Systolic Blood Pressure, DBP= Diasytolic Blood Pressure

3.2. The reduction levels of SBP, SBP, PP after 4 weeks treatment with lisinopril and amlodipine combination tablets

Reduction levels of SBP, DBP, PP at the left arm:

SBP decreased significantly by 26.88 ± 11.27 mmHg, equivalent to 16.71 ± 6.26% from 159.2 ± 17.68 mmHg to 132.32 ± 15.04 mmHg with p <0.001. SBP decreased significantly by 13.55 ± 8.15 mmHg, corresponding to 14.8 ± 7.86% from 88.72 ± 11.03 mmHg to 75.18 ± 8.23 mmHg with p<0.001. PP was significantly reduced by 13.33 ± 8.19, corresponding to 18.82 ± 11.21 from 70.48 ± 11.97 mmHg to 57.15 ± 12.74 mmHg with p <0.001. This result was presented in Table 2.

The rate of patients that achieved the target blood pressure (<140/90 mmHg) was 72.5% (29/40 patients); the rate of BP

response was 87.5% (35/40), the results in Table 3

Reduction levels of SBP, DBP, PP at the right arm:

SBP decreased significantly by 26.58 ± 9.51 mmHg, respectively 16.35 ± 4.98% from 160.8 ± 16.17 mmHg to 134.22 ± 12.74 mmHg. SBP decreased significantly by 8.6 ± 4.47 mmHg, corresponding to 10.07 ± 4.94 from 84.3 ± 7.34 mmHg to 75.7 ± 6.48 mmHg. PP significantly reduced 17.98 ± 7.81 mmHg, respectively 22.95 ± 8.41% from 75.5 ± 12.04 mmHg to 58.53 ± 8.99 mmHg with p<0.001. The reduction of parameters is shown in Table 4

Reduction levels of SBP, DBP, PP at the left ankle

SBP was significantly reduced by 30.33 ± 16.64mmHg, respectively 16.8 ± 8.54% from 177.62 ± 20.95 mmHg to 147.3 ±

19.65mmHg with $p < 0.001$. SBP decreased significantly by 13.6 ± 9.28 , equivalent to $15.22 \pm 9.41\%$ from 86.95 ± 10.28 mmHg to 73.35 ± 9.34 mmHg. PP significantly reduced 16.73 ± 12.9 , respectively $16.16 \pm 8.28\%$ from 90.68 ± 17.41 mmHg to 73.95 ± 12.61 mmHg with $p < 0.001$. The results are shown in Table 5.

Reduction levels of SBP, DBP, PP at the right ankle

SBP significantly decreased by $23.75 \pm$

11.78 mmHg, respectively $13.56 \pm 6.1\%$ from 173.1 ± 17.53 mmHg to 149.35 ± 16.03 mmHg with $p < 0.001$. SBP decreased significantly by 10.75 ± 6.64 , respectively $12.38 \pm 7.44\%$ from 85.85 ± 7.78 mmHg to 75.1 ± 8.23 mmHg with $p < 0.001$. PP decreased by 13 ± 7.68 , equivalent to 14.7 ± 7.9 from 87.25 ± 13.65 mmHg to 74.25 ± 12.54 mmHg with $p < 0.001$. The data are presented in Table 6.

Table 2. SBP, DBP, PP of left arm at baseline and after 4 weeks treatment

Variability	Baseline	AT	Δ	% red	p vs baseline
SBP (mmHg)	159.2 ± 17.68	132.32 ± 15.04	26.88 ± 11.27	16.71 ± 6.26	< 0.001
DBP (mmHg)	88.72 ± 11.03	75.18 ± 8.23	13.55 ± 8.15	14.8 ± 7.86	< 0.001
PP (mmHg)	70.48 ± 11.97	57.15 ± 12.74	13.33 ± 8.19	18.82 ± 11.21	< 0.001

AT= after treatment; SBP= systolic BP; DBP = diastolic BP; PP = Pulse Pressure.

Δ= (Baseline BP, PP - AT BP, PP); % red = Δ/baseline

Table 3: The achievement rate of the target blood pressure and rate of BP response

HTN grade	Male		Female		Total	
	TBP	BPR	TBP	BPR	TBP	BPR
Grade I	11 (27.5%)	9 (22.5%)	12 (30%)	12 (30%)	23 (57.5%)	21 (52.5%)
Grade II	4 (10%)	4 (10%)	1 (2.5%)	3 (7.5%)	5 (12.5%)	7 (17.5%)
Grade III	0 (0%)	3 (7.5%)	1 (2.5%)	4 (10%)	1 (2.5%)	7 (17.5%)
Total	15 (37.5%)	16 (40%)	14 (35%)	19 (45.7%)	29 (72.5%)	35 (87.5%)

TBP = Target blood pressure; BPR = Blood Pressure Response

Table 4. SBP, DBP, PP of right arm at baseline and after 4 weeks treatment

Variability	Baseline	AT	Δ	% red	p vs baseline
SBP (mmHg)	160.8 ± 16.2	134.2 ± 12.7	26.58 ± 9.51	16.35 ± 4.98	< 0.001
DBP (mmHg)	84.3 ± 7.34	75.7 ± 6.48	8.6 ± 4.47	10.07 ± 4.94	< 0.001
PP (mmHg)	75.5 ± 12.04	58.53 ± 8.99	17.98 ± 7.81	22.95 ± 8.41	< 0.001

Table 5. SBP, DBP, PP of left ankle at baseline and after 4 weeks treatment

Variability	Baseline	AT	Δ	% red	p vs baseline
SBP (mmHg)	177.62 ± 20.95	147.3 ± 19.65	30.33 ± 16.64	16.8 ± 8.54	< 0.001
DBP (mmHg)	86.95 ± 10.28	73.35 ± 9.34	13.6 ± 9.28	15.22 ± 9.41	< 0.001
PP (mmHg)	90.68 ± 17.41	73.95 ± 12.61	16.73 ± 12.9	16.16 ± 8.28	< 0.001

Table 6. SBP, DBP, PP of right ankle at baseline and after 4 weeks treatment

Variability	Baseline	AT	Δ	% red	p vs baseline
SBP (mmHg)	173.1±17.53	149.35±16	23.75±11.78	13.56± 6.1	<0.001
DBP (mmHg)	85.85 ± 7.78	75.1 ± 8.23	10.75 ± 6.64	12.38 ± 7.44	<0.001
PP (mmHg)	87.25±13.62	74.25±12.54	13 ± 7.68	14.7 ± 7.9	<0.001

3.3. Levels of reduction in baPWV after 4 weeks treatment with combination tablet from lisinopril and amlodipine

The brachial-ankle pulse wave velocity (baPWV) on the right decreased significantly by 593.65 ± 416.59 cm/s, respectively 23.47 ± 10.23% from 2384.87 ± 677.04 cm/s to 1791.22 ± 419.85 cm/s with p<0.001

baPWP on the left decreased significantly by 585.4 ± 447.19 cm/s, respectively 22.71 ± 11.56% from 2405.78 ± 717.96 cm/s to 1820.38 ± 446.28 cm/s with p<0.001. The data was presented in Table 7

Table 7. Baseline baPWV and after treatment

baPWV (cm/s)	Baseline	AT	Δ	% red	p vs baseline
The right	2384.87± 677.04	1791.22 ± 419.85	593.65 ± 416.59	23.47 ± 10.23	p<0.001
The left	2405.78 ±717.96	1820.38 ± 446.28	585.4 ±447.19	22.71 ± 11.56	p<0.001

IV. DISCUSSION

4.1. The reduction levels of SBP, SBP, PP after 4 weeks treatment of combination bill from lisinopril and amlodipine

Combination low dose drugs treatment increases efficacy and reduces adverse effects [10]. Combination therapy provides greater antihypertensive power than the use of high doses of monotherapy [5]. A study by Wald D.S et al, in a meta-analysis of 42 clinical trials with 10,968 patients receiving monotherapy and a combination dose from any 2 classes of thiazides, beta-blocker, angiotensin-converting enzyme inhibitor, and calcium channel blockers over 1 drug alone to compare the effects of combining drugs with doubling dose. This study had concluded that the extra blood pressure reduction from combining drugs from 2 different classes is approximately 5 times

greater than doubling the dose of 1 drug. [19]. Currently, the most recommended drug combination is the combination of an inhibitor of the renin-angiotensin system (ACE inhibitors, angiotensin II receptor blockers) with a calcium channel blocker or diuretic [5]. The combination of an ACE inhibitor and a long-acting calcium channel blocker enables effective blood pressure control, end-organ protection, and a reduced rate of cardiovascular events [6],[9].

About the effects of the combination of 2 drugs single-pill between ACE inhibitor and calcium channel blocker, there are several types, such as the combination of lisinopril and amlodipine, between perindopril and amlodipine, there are some studies that have proven by measuring blood clinic pressure with a mercury machine or 24-hour ABPM.

Study by MUR Naidu et al in 2000 evaluating blood pressure by electronic sphygmomanometer with the aim of the present study was to compare in a double blind, randomized, crossover design, the efficacy and safety of the long acting calcium channel antagonist amlodipine and the long acting ACE inhibitor lisinopril, individually and in combination in mild to moderate hypertension; 24 patients with DBP between 95 and 104 mmHg received amlodipine 2.5 mg and 5 mg, lisinopril 5 mg and 10 mg, and their combination as per a prior randomization schedule. Supine and standing BP and heart rate were recorded at weekly intervals for 4 weeks. The result of this study showed that amlodipine 5 mg and lisinopril 10 mg monotherapy achieved the target BP in 71% and 72% patients respectively. The combination of 2.5 mg amlodipine with 5 mg lisinopril produced a much more significant lowering of BP in a higher percentage of patients than that with an individual low dose [12].

Study of Attila Ko'nyi in 2016 on 2241 patients who were measured by mercury sphygmomanometer. This patients with mild/moderate hypertension and hypercholesterolemia, at high-/very high-cardiovascular risk, received lisinopril-amlodipine (10/5, 20/5 or 20/10 mg/day) plus rosuvastatin (10 or 20 mg/day). The **results of this study showed that** at 6 months, 91% of 2241 evaluable patients achieved blood pressure target (<140/90 mmHg); low-density lipoprotein cholesterol targets, <3, <2.5 and 1.8 mmol/l, were achieved by 67, 49 and 40% of patients, respectively [2].

The study of Sergeyv V Nedogoda et al in 2018: The 24-week open-label multi-center observational study involved 60 patients who received dual combination antihypertensive

combination therapy for 6 months. All patients underwent 24 h blood pressure (BP) monitoring, applanation tonometry (determination of the augmentation index and central BP), measurement of the pulse wave velocity and laboratory tests before and after switching to the fixed-dose combination of lisinopril + amlodipine + rosuvastatin. The results showed that the office BP decreased 14.3% in SBP and 18.5% in DBP. According to the 24h ABPM data, the SBP has decreased by 16.1% and DBP by 21.8% [16].

The study of Semagina et al included 30 untreated non-diabetic hypertensive patients with NAFLD (diagnosed according to ASSLD Practice Guidelines, 2012) and metabolic syndrome. The treatment was initiated with lisinopril 10 mg/amlodipine 5 mg with doubling of dose after 4 weeks to achieve target office BP < 140/90 mm Hg. The effects on 24-h, day- and night-time brachial and central BP were evaluated with compared oscillometric BPLab VASOTENS system (OOO Petr Telegin, Nizhny Novgorod, Russia). Treatment duration was 12 weeks. BP result at clinic is $134.5 \pm 8.4 / 85.6 \pm 7.6$; After 24 hours, brachial BP decreased from $143.5 \pm 6.2/89.2 \pm 5.4$ to $132.3 \pm 5.8/80.8 \pm 4.6$, from $144.4 \pm 7.0 / 92.1 \pm 5.3$ to $134.5 \pm 6.6 / 83.7 \pm 6.1$ at night from $132.3 \pm 6.6 / 79.1 \pm 5.9$ to $117.6 \pm 5.2 / 69.4 \pm 5.0$ mmHg (for all $p < 0.05$) [15].

On the issue of evaluating the effectiveness of a combination pill between the ACE inhibitor perindopril and the calcium antagonist amlodipine. Research by Vinay. K. Bahl- The STRONG (SafeTy & efficacy analysis of coveRsyl amlodipine in uncOntrolled and Newly diaGnosed hypertension) study was a prospective, observational, multicenter trial, on the treatment of HTN with fixed-dose

perindopril and amlodipine (4mg/5mg) 1 times/day for 60 days. A total of 1250 study patients included: 32.6% with newly diagnosed hypertension; 40.5% had hypertension not controlled by monotherapy; and 26.9% of hypertension was inadequately managed with another combination therapy. Mean SBP/DBP decreased significantly from baseline ($167.4 \pm 15.2 / 101.4 \pm 9.1$ mmHg) in 60 days ($-41.9 \pm 34.8 / -23.2 \pm 21.8$ mmHg; $p < 0.0001$). Target BP was achieved in 66.1% of patients in the total population, 68.3% of patients untreated, 68.4% of patients uncontrolled with monotherapy, and 59.9% of patients was poorly managed with combination therapy. In 161 patients with SBP > 180 mmHg at baseline (new diagnosis: $n = 50$; uncontrolled on monotherapy: $n = 53$; inadequate management on combination therapy: $n = 58$), BP was reduced by $63.2 \pm 32.5 / 29.0 \pm 21.9$ mmHg ($p < 0.0001$) at day 60. The fixed combination pill was safe and well tolerated. All 1175 patients who completed the 60-day study (94%) adhered to their regimen [18].

In our study, at the time of patient enrollment, most of our patients had previously received monotherapy or multiple antihypertensive therapy but have not achieved the target, this rate was quite high, accounting for 92.5 % (37/40 patients), date in Table 1. After taking lisinopril 10mg and amlodipine 5mg for 4 weeks; SBP, DBP, PP decreased significantly ($p < 0.001$) and the achievement rate of target blood pressure was quite high (72.5%) and the rate of blood pressure response was high with 87.5%. Thereby, we founded that the achievement rate of the target BP after treatment with combination pill from lisinopril 10 mg and amlodipine 5 mg was higher than

monotherapy and other antihypertensive therapy.

4.2. Reduction levels of baPWV after 4 weeks treatment with combination pill from lisinopril and amlodipine

The assessment of the degree of reduction in baPWV is a new issue in evaluating the effect of antihypertensive drugs on the stiffness of the vessel wall, assessing the vasodilator ability of the drug. To evaluate this index, only the VP Plus 1000 pulse wave velocity meter was used, which was an outstanding benefit of this device in addition to measuring the ABI index to detect peripheral artery disease.

The number of studies on this issue to date is still few, with only a few studies on AT1 receptor blockers as monotherapy.

A study by Tetsuya Nakamura et al, in 2005 that examined the angiotensin receptor blocker with valsartan on arterial wall stiffness. Brachial - ankle pulse wave velocity (baPWV) was measured in 28 women and 25 men with HTN (mean age: 62 ± 2). The study showed that The value of baPWV $1,794 \pm 46$ cm/s before valsartan ($n = 39$) decreased to $1,663 \pm 45$ cm/s after valsartan administration ($p = 0.048$, $n = 31$) statistically significant $p < 0.05$ and at a similar mean SBP (149 ± 2 vs 146 ± 1) 3 mmHg, $p = 0.304$) [17].

A study by Azra Mahmud and John Feely on 12 hypertensive patients with mean age 49 ± 11 years to evaluate the effectiveness reducing arterial stiffness, pulse velocity and blood pressure of angiotensin II receptor blocker valsartan 80mg/day for 2 weeks then increased to 160 mg/day for 2 additional weeks versus captopril ACE inhibitor 50 mg/day initially for 2 weeks then increased to 100 mg/day for 2 additional weeks and combination for 2 weeks supplement for all

patients. The results of the study showed that the reduction in pulse wave velocity with captopril and valsartan was independent. Combined therapy reduced PWV and AI (augmentation index) the pulse wave velocity was significantly reduced with combination therapy compared with monotherapy [3].

In our study, the combination pill from lisinopril 10 mg and amlodipine 5 mg reduced very significantly baPWV and the arterial stiffness in hypertensive patients. Therefore, baPWV can be used to assess the degree of vascular protection, reduction the cardiovascular risks in hypertensives patients.

V. CONCLUSION

The combination pill of lisinopril 10 mg and amlodipine 5 mg (Lisonorm 10/5mg) was effective in reducing extremity blood pressure and pulse wave velocity and arterial stiffness in hypertensives patients when measured by a wave velocity meter VP Plus 1000. It is necessary to use this technique to evaluate the reduction of vascular stiffness in hypertensive patients in order to reduce cardiovascular risks.

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