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Clinical Effectiveness of the Fixed-Dose vs Free-Dose Triple Combinations in Patients with Uncontrolled Arterial Hypertension

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Abstract

Background: The purpose of our study was a comparative assessment of the antihypertensive effectiveness of 2 triple combination antihypertensive therapy (AHT) regimens in a free-dose and fixed-dose combination of perindopril, indapamide, and amlodipine in hypertensive patients with high cardiovascular risk and a poor response to the 2-drug combinations in the clinic practice.

Methods and Results: Our study included 143 patients (79 men and 88 women) with arterial hypertension (AH) Grades 1-3 (ESC/ESH, 2018) and high cardiovascular risk who did not achieve the target blood pressure on dual combination AHT. The mean age of patients was 55.76±9.35 years; the average duration of AH was 10.69±6.61 years. All patients underwent the examinations according to the 2018 ESC/ESH Guidelines for the management of arterial hypertension.

Patients included in the study were divided into 2 groups using the envelope method: Group 1 (n=84) received a fixed-dose, triple combination of perindopril, indapamide, and amlodipine; Group 2 (n=83) received a free-dose combination of these drugs. In both groups, treatment began after discontinuation of previous therapy, with a low dose of a triple combination of antihypertensive drugs (perindopril [5 mg/day], indapamide [1.25 mg/day], amlodipine [5 mg/day]) in the form of a fixed or free combination. The initial doses of perindopril/indapamide/amlodipine in both groups were not statistically different: 6.9±2.4/1.74±0.6/7.1±2.4 mg/day in Group 1 and 6.9±2.7/1.95±0.6/7.1±2.5 mg/day in Group 2. After 4 weeks of therapy, if necessary, the doses of drugs were increased, starting with perindopril; the next adjustment of drug doses was carried out after 12 weeks of therapy. The final treatment results were determined after 24 weeks of AHT.

Target blood pressure of <140/90 mmHg was reached by 94.4% of patients in Group 1 and 83.3% in Group 2 (χ^2=7.471, *P*=0.006). Target blood pressure of <130/80 mmHg was reached by 70% of patients in Group 1 and 42% in Group 2 (χ^2=11.61, *P*=0.0001). A significant improvement in the diurnal BP profile was also revealed during treatment. According to 24-hour ambulatory blood pressure monitoring data, both groups achieved target blood pressure in terms of the average 24-h and average daytime systolic blood pressure (SBP) and diastolic blood pressure (DBP). Regarding average nighttime SBP and DBP and normalization of average nighttime diastolic blood pressure variability, target values were achieved only in Group 1 (*P*=0.028). In both groups, 24-week triple-combination therapy led to a significant decrease in central SBP, central DBP, and pulse wave velocity. At the same time, the positive dynamics of central SBP were more pronounced in Group 1 than in Group 2, and pulse wave velocity in Group 1 reached standard values.

Conclusion: The results of our study showed that in the treatment of uncontrolled hypertension on previous therapy in AH patients with high cardiovascular risk, a single-pill triple combination of the ACEI perindopril, the CCB amlodipine, and the thiazide-like diuretic indapamide contributed to the effective daily blood pressure control, the improvement of diurnal blood pressure profile, and a positive effect on central blood pressure and pulse wave velocity, thereby having a positive impact on the prognosis and quality of life of AH patients with high cardiovascular risk.**(International Journal of Biomedicine. 2024;14(2):253-259.)**

Keywords: arterial hypertension • antihypertensive therapy • target blood pressure • single-pill triple combination

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Abbreviations

ABPM, 24-hour ambulatory blood pressure monitoring; **AH**, arterial hypertension; **AHD**, antihypertensive drug; **AHT**, antihypertensive therapy; **ACEI**, angiotensin-converting enzyme inhibitor; **ARB**, angiotensin receptor blocker; **BP**, blood pressure; **BPV**, BP variability; **CCB**, calcium channel blocker; **CHD**, coronary heart disease; **CIMT**, carotid intima-media thickness; **CHF**, chronic heart failure; **DBP**, diastolic BP; **DBPc**, central DBP; **DBPV**, diastolic BPV; **eGFR**, estimated glomerular filtration rate; **FBG**, fasting blood glucose; **HR**, heart rate; **HDL-C**, high-density lipoprotein cholesterol; **LVDD**, left ventricular diastolic dysfunction; **LVH**, left ventricular hypertrophy; **LVMI**, left ventricular mass index; **LDL-C**, low-density lipoprotein cholesterol; **MAU**, microalbuminuria; **MBP**, mean BP; **PP**, pulse pressure; **PPc**, central PP; **PWV**, pulse wave velocity; **RAAS**, renin-angiotensin-aldosterone system; **SBP**, systolic BP; **SBPc**, central SBP; **SBPV**, systolic BPV; **SPTC**, single-pill triple combination; **TBP**, target BP; **T2DM**, type 2 diabetes mellitus; **TC**, total cholesterol; **TG**, triglycerides.

Introduction

The combined antihypertensive therapy (AHT) is the regimen of choice in patients with arterial hypertension (AH) Grades 1-3 (ESC/ESH, 2018)[1] and high cardiovascular risk. In ESH/ESC-2018 and ESH-2023 recommendations,[1,2] a double combination of antihypertensive drugs is the starting step in the treatment of AH patients with high cardiovascular risk, which accounts for 70%-80% of hypertensive patients. It is recommended to start combining AHT with a dual-combination of antihypertensive drugs, one of which is an RAAS blocker and the other - a calcium channel blocker (CCB) or a diuretic, preferably in a single pill. Often, AH patients with high cardiovascular risk are resistant to the dual-combination and require switching to a triple combination AHT, consisting of ACEI/ARB, CCB, and diuretics, also preferably in a single-pill triple combination (SPTC), to increase patient adherence to therapy.[1] According to multicenter studies, about 30% of AH patients with high cardiovascular risk need a triple antihypertensive combination.[3]

High adherence to AHT is the main requirement for achieving the target blood pressure (TBP). According to the 2018 ESH/ESH Guidelines for the management of AH,[1] the primary target SBP and DBP are <140 mmHg and <90 mmHg, respectively. At the same time, for hypertensive patients aged 18-64 years without serious renal pathology, the recommended target SBP and DBP is ≤130/80 mmHg but not lower than 120/70 mmHg.

A SPRINT study recruited 9,361 adults ≥50 years of age who were at increased risk for cardiovascular disease and had an average SBP of 130–180 mmHg. They were randomized to the SPB treatment goal of either <120 mmHg (Intensive) or <140 mmHg (Standard). In the 2015 SPRINT main results report, the primary outcome and all-cause mortality were 25% (P<0.001) and 27% (P=0.003) lower in the Intensive than in the Standard group.[4] This included a 43% reduction (P=0.005) in cardiovascular death and a 38% reduction (P=0.002) in acute decompensated heart failure. The SPRINT findings indicated that more intensive blood pressure (BP) reduction yields substantial health benefits that outweigh the risks of adverse events (hypotension, syncope, electrolyte imbalance, and acute kidney injury).[5]

The purpose of our study was a comparative assessment of the antihypertensive effectiveness of 2 triple combination AHT regimens in a free-dose and fixed-dose combination of perindopril, indapamide, and amlodipine in AH patients with high cardiovascular risk and a poor response to the 2-drug combinations in the clinic practice.

Materials and Methods

Our study included 143 patients (79 men and 88 women) with AH Grades 1-3 (ESC/ESH, 2018) and high cardiovascular risk who did not achieve the TBP on dual combination AHT. The mean age of patients was 55.76±9.35 years; the average duration of AH was 10.69±6.61 years.

Based on the anamnestic data and examination results, some associated stable clinical conditions were diagnosed (CHD [angina pectoris FC I-II], T2DM, CHF [NYHA FC I-II]), which were included in the study.

Exclusion criteria were symptomatic hypertension, acute coronary syndrome, CHF (NYHA FC>III), cardiac arrhythmia, history of myocardial infarction, renal impairment, severe co-morbidities.

Patients included in the study were divided into 2 groups using the envelope method: Group 1 (n=84) received a fixed-dose, triple combination of perindopril, indapamide, and amlodipine; Group 2 (n=83) received a free-dose combination of these drugs. In both groups, treatment began after discontinuation of previous therapy, with a low dose of a triple combination of antihypertensive drugs (perindopril [5 mg/day], indapamide [1.25 mg/day], amlodipine [5 mg/day]) in the form of a fixed or free combination. The initial doses of perindopril/indapamide/amlodipine in both groups were not statistically different: 6.9±2.4/1.74±0.6/7.1±2.4 mg/day in Group 1 and 6.9±2.7/1.95±0.6/7.1±2.5 mg/day in Group 2. After 4 weeks of therapy, if necessary, the doses of drugs were increased, starting with perindopril; the next adjustment of drug doses was carried out after 12 weeks of therapy. The final treatment results were determined after 24 weeks of AHT.

All patients underwent the following examinations: assessment of traditional risk factors, physical examination, clinical and biochemical laboratory methods, 12-lead ECG, echocardiography, and 24-hour ABPM. Office BP was measured using a mercury sphygmomanometer, according to Korotkov's method. Blood pressure was measured 3 times, and the means of these measurements were used in the analyses. The 24-hour ABPM was performed using a BR-102 plus (SCHILLER, Switzerland). BP was measured during the daytime (07:00–23:00) every 30 min and at night (23:00–07:00) every 60 min.

The pulse contour analysis was carried out using the SphygmoCor device (AtCor Medical, Australia), which obtains peripheral arterial pressure waveforms by applying an arterial applanation tonometer to the wrist. Such indicators

as the central SBP (SBPc), central DBP (DBPc), central PP (PPc), and pulse wave velocity (PWV) were analyzed.

All patients underwent echocardiography with the determination of the left ventricular mass index (LVMI), left ventricular hypertrophy[1] and left ventricular diastolic dysfunction (LVDD); ultrasound examination of the carotid intima-media thickness (CIMT), as well as the determination of the level of microalbuminuria (MAU), blood creatinine, and glomerular filtration rate (GFR) calculation according to the CKD-EPI equation.

Blood levels of TC, TG, HDL-C, LDL-C, and VLDL-C were determined in the venous blood using automatic biochemical analyzer Daytona (RANDOX, United Kingdom) and RANDOX test systems by the enzymatic colorimetric method.

Statistical analysis was performed using the statistical software «Statistica» (v10.0, StatSoft, USA). The normality of distribution of continuous variables was tested by the Kolmogorov-Smirnov test with the Lilliefors correction and Shapiro-Wilk test. Baseline characteristics were summarized as frequencies and percentages for categorical variables and as median (Me) and interquartile range (IQR [Q1; Q3]), mean±standard deviation (SD) for continuous variables. For data with normal distribution, inter-group comparisons were performed using Student's t-test. The Mann-Whitney U Test was used to compare the differences between the two independent groups (for nonparametric data). Group comparisons with respect to categorical variables were performed using chi-square test. A probability value of $P<0.05$ was considered statistically significant.

Results

At the initial stage of the study, patients in both groups did not differ in gender and age, risk factors, markers of target organ damage, biochemical parameters, and associated clinical conditions (Table 1).

Table 1.

Clinical characteristics of AH patients.

Characteristics	General group (n=167)	Group 1 (n=84)	Group 2 (n=83)
Women, n (%)	88 (52.7%)	34 (40.5%)	54 (65%)
Men, n (%)	79 (47.3%)	43 (51.2%)	36 (43.4%)
Current smoker, n (%)	30 (18.0%)	12 (14.3%)	18 (21.7%)
CHD (FC I-II)	91 (54.5%)	42 (50%)	49 (59%)
T2DM, n (%)	26 (15.6%)	12 (14.3%)	14 (16.9%)
History of stroke, n (%)	5 (3.0%)	3 (3.57%)	2 (2.4%)
CHF (NYHA FC I-II), n (%)	55 (33.0%)	28 (33.3%)	27 (32.5%)
BMI >30 kg/m^2, (n / %)	100 (60%)	50 (59,5%)	50 (60,2%)
LVH, (n / %)	138 (82.6%)	68 (81%)	70 (84.3%)
LVDD, (n / %)	38 (22.7%)	20 (25.8%)	18 (21.7%)
CIMT ≥0.9 mm, (n / %)	140 (83.8%)	68 (81%)	72 (86.7%)
MAU, n (%)	60 (36%)	33 (39.3%)	27 (32.5%)
PWV >10 m/sec, (n / %)	80 (48%)	42 (50%)	38 (45.8%)

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According to the average values of SBP (171.06±17.7 mmHg) and DBP (100.06±8.7 mmHg), the patients were characterized by AH Grade 2 (Table 2).

Table 2.

Indicators of clinical, functional, and laboratory data in the study groups at the initial examination stage and after 24 weeks of AHT.

Variable	General group (n=167)	Group 1 (n=84)	Group 2 (n=83)
	M±SD Me [Q1; Q3]	M±SD Me [Q1; Q3]	M±SD Me [Q1; Q3]
Age, years	55.68±9.8 49 [58;73]	54.9±10.3 31 [54;72]	56.3±9.3 26[59;73]
AH duration, years	10.7±6.6 5 [10;44]	11.2±7.9 1 [10;44]	10.28±5.2 1 [10;26]
BMI (kg/m^2)	32.3±5.07 22.8 [32;46]	32.9±5.2 22.1 [32.7;44.2]	31.7±4.9 16.7 [31.3;46.8]
SBP, mmHg	171.06±17.7 160 [170;240]	171.3±17.2 140 [170;240]	170.7±18.2 140 [170;240]
DBP, mmHg	100.06±8.7 100 [100;140]	100.8±8.2 80 [100;140]	99.38±9.2 65 [100;140]
MBP, mmHg	122.9±9.9 120 [123;173]	122.6±8.6 106.6 [123.3;150]	123.2±11 98.3 [123.3;73.3]
PWV, m/sec	10.9±2.4 9.4 [10.8;22.8]	10.8±2.4 6.4 [10.5;19.2]	11±2.4 7 [11;22.8]
LVMI, g/m^2	139.9±32.8 136.8 [117.2;237.6]	139.19±32.7 136.6 [116,8;208.6]	140.8±32.9 137.9 [121;237.6]
CIMT, mm	1.027±0.19 1 [0.9;1.5]	1.02±0.19 1 [0.7;1.5]	1.03±0.19 1 [0.5;1.5]
FBG, mmol/L	6.14±2.29 5 [5.4;16.5]	6.28±2.5 4.1 [5.4;15.6]	6.01±2.06 4.2 [5.4;16.5]
Creatinine, µmol/L	94.5±22.2 79 [92;207]	93.79±23.6 51 [91;207]	95.2±21.02 51 [95;144]
eGFR mL/min/1.73m^2	70.25±17.1 57.15 [67.4;120.68]	73.1±17.58 28 [70;112.35]	67.66±16.4 34.8 [64;120.68]
MAU, mg/24-h	43.6±42.06 29.8 [15.1;218.8]	45.7±41.5 32.5 [16.2;212.8]	41.4±42.4 25.4 [14.7;200.0]
Uric acid, mg/dL	6.25±1.65 5.1 [6.2;11.2]	6.15±1.4 3.1 [6.2;9.4]	6.35±1.8 2.6 [6.2;11.2]
TC, mg/dL	205±47.8 169 [205;364]	202.96±47.9 97 [207;321]	202.96±47.9 102 [203;364]
TG, mg/dL	166.8±83.2 105.25 [151;407]	164.87±82.6 60 [143.5;402]	168.2±83.8 6.7 [157;407]
LDL-C, mg/dL	122.02±43.6 100 [123;274]	122.13±46.4 5 [124;246]	121.7±41.2 29 [122;274]
HDL-C, mg/dL	44.26±11.1 37 [43;97]	44.35±11.9 24 [43;97]	44.16±10.3 24 [43;80]
Atherogenic index	3.64±1.16 3 [3.4;7.1]	3.67±1.25 2 [3.4;7.1]	3.60±1.08 2 [3.4;6.9]

Against a background of 24-week treatment, the obtained indicators in 2 modes of triple combined AHT were analyzed comparatively. A highly significant reduction in BP using different types of measurements was obtained in both groups (Table 3).

Table 3.

BP parameters after 24 weeks of AHT in the study groups.

Variable	Group	Initial data	After 24-week AHT	P_1	P_2	P_3
SBP, mmHg	1	171.3±17.2	121.95±6.7	0.0001	NS	0.0001
	2	170.7±18.2	128.38±8.5	0.0001		
DBP, mmHg	1	100.8±8.2	77.23±5.59	0.0001	NS	0.0001
	2	99.38±9.2	80.89±6.38	0.0001		
MBP, mmHg	1	122.64±8.92	92.23±5.47	0.0001	NS	0.0001
	2	123.53±10.59	96.72±6.18	0.0001		
Average 24-h SBP, mmHg	1	147.23±15.37	124.53±9.64	0.0001	NS	NS
	2	145.98±20.24	127.2±13.03	0.0001		
Average 24-h DBP, mmHg	1	89.01±11.34	75.77±6.11	0.0001	NS	NS
	2	88.86±14.26	77.74±11.13	0.0001		
Average daytime SBP, mmHg	1	149.24±15.26	126.89±10.2	0.0001	NS	NS
	2	147.38±20.33	129.22±13.65	0.0001		
Average daytime DBP, mmHg	1	90.49±11.45	77.61±6.84	0.0001	NS	NS
	2	89.98±14.08	79.86±11.89	0.0001		
Average nighttime SBP, mmHg	1	141.03±20.32	118.28±10.24	0.0001	NS	0.017
	2	141.76±23.53	123.12±15.32	0.0001		
Average nighttime DBP, mmHg.	1	84.49±13.66	70.01±7.86	0.0001	NS	NS
	2	85.4±16.81	73.12±11.63	0.0001		
Average 24-h SBPV, mmHg	1	17.66±4.36	14.46±3.7	0.0001	NS	NS
	2	18.32±5.37	15.34±3.45	0.0001		
Average 24-h DBPV, mmHg	1	13.66±3.74	12.32±3.69	0.032	NS	NS
	2	13.27±3.69	12.78±3.43	NS		
Average daytime SBPV, mmHg	1	16.88±4.86	13.81±3.84	0.0001	NS	NS
	2	17.27±6.1	14.83±4.06	0.0001		
Average daytime DBPV, mmHg	1	13.28±4.18	11.73±3.93	0.023	NS	NS
	2	12.83±4.11	12.34±3.64	NS		
Average nighttime SBPV, mmHg	1	15.9±4.93	13.27±4.67	0.044	NS	NS
	2	16.06±5.52	13.22±4.06	0.006		
Average nighttime DBPV, mmHg	1	11.1±3.66	11.12±4.74	NS	NS	NS
	2	12.18±7.4	10.84±4.46	NS		
Daytime SBP load, %	1	64.87±27.2	20.06±23.31	0.0001	NS	0.021
	2	56.18±27.61	30.16±28.28	0.0001		
Daytime DBP load, %	1	49.86±29.6	15.56±16.09	0.0001	NS	0.005
	2	47.04±31.83	26.0±26.65	0.0001		
Nighttime SBP load, %	1	79.34±25.74	25.69±17.38	0.0001	NS	0.0001
	2	77.54±26.14	57.45±34.36	0.0001		
Nighttime DBP load, %	1	59.16±31.64	23.49±20.17	0.0001	NS	0.015
	2	59.64±34.54	34.96±33.69	0.0001		
Nocturnal SBP fall, %	1	5.53±9.65	6.64±7.28	NS	NS	NS
	2	3.41±8.68	4.89±8.89	NS		
HR, bpm	1	82.8±10.59	70.47±8.85	0.0001	NS	NS
	2	78.96±9.07	69.19±6.6	0.0001		

P_1 – between initial data and data after 24-week AHT; P_2 – between Groups 1 and 2 for initial data; P_3 – between Groups 1 and 2 for data after 24-week AHT

However, the reduction percentage in SBP and DBP was significantly more pronounced in Group 1 than in Group 2 (ΔSBP: -27.76±5.95% versus -24.46±9.85% (*P*=0.024); ΔDBP%: -22.61±6.87% versus -18.1±10.17% (*P*=0.004); Δ MAD: -24.47±5.27% versus -21.23±8.52% (*P*=0.011)). TBP of <140/90 mmHg was reached by 94.4% of patients in Group 1 and 83.3% in Group 2 (χ^2=7.471, *P*=0.006). TBP of <130/80 mmHg was reached by 70% of patients in Group 1 and 42% in Group 2 (χ^2=11.61, *P*=0.0001).

A significant improvement in the diurnal BP profile was also revealed during treatment. According to ABPM data, both groups achieved TBP in terms of the average 24-h and average daytime SBP and DBP. Regarding average nighttime SBP and DBP and normalization of average nighttime diastolic BP variability, target values were achieved only in Group 1 (*P*=0.028).

A significant decrease in daytime/nighttime SBP load and DBP load was noted in both groups, but it was more pronounced in Group 1 (Table 3) with the achievement of standard values, which is associated with the possibility of protecting target organs.

One of the important markers of vascular damage in hypertension is indicators of central BP (SBPc, DBPc, and PPc) and PWV. In both groups, 24-week triple-combination therapy led to a significant decrease in SBPc, DBPc, and PWV. At the same time, the positive dynamics of SBPc were more pronounced in Group 1 than in Group 2 (Table 4), and PWV in Group 1 reached standard values.

Table 4.

Indicators of central BP and PWV after 24 weeks of AHT in the study groups.

Variable	Group	Initial data	After 24-week AHT	P_1	P_2	P_3
SBPc, mmHg	1	161.85±21.55	134.27±12.84	0.0001	NS	0.027
	2	156.77±18.75	139.66±17.98	0.0001		
DBPc, mmHg	1	91.78±12.32	80.9±8.11	0.0001	NS	NS
	2	88.16±12.5	82.54±10.5	0.0001		
PPc, mmHg	1	72.36±20.67	54.29±13.21	0.0001	NS	NS
	2	70.77±18.7	56.24±16.43	0.0001		
PWV, m/sec	1	10.86±2.53	8.49±2.02	0.0001	NS	0.028
	2	10.9±2.56	9.2±2.12	0.0001		

P_1 – between initial data and data after 24-week AHT; P_2 – between Groups 1 and 2 for initial data; P_3 – between Groups 1 and 2 for data after 24-week AHT

In general, the 2-treatment regimens were well tolerated; only 1 patient from Group 2 reported swelling of the ankles after 12 weeks of therapy.

Discussion

Despite the widespread availability of effective antihypertensive drugs, most AH patients remain uncontrolled and do not reach the TBP. Non-compliance with pharmacotherapy is an important reason for poor BP control. According to the results of studies conducted in recent years, only ~40% of AH patients receive AHT, of which only ~10%-35% achieve the TBP of <140/90 mmHg, which is clear evidence of unsatisfactory control of hypertension.[6] Uncontrolled hypertension increases the risk of all-cause and cardiovascular mortality. A review of 28 studies in 15 countries found that 45.2% of AH patients were not taking medications, and 83.7% had uncontrolled hypertension.[7] Achieving TBP in the short term is the goal of therapy and may lead to improved cardiovascular outcomes. Clinical studies have shown that BP can be adequately controlled with a combination of up to 4 antihypertensive drugs.[8] In AH persons with high cardiovascular risk, it is recommended that combined AHT be initiated and doses titrated rapidly.[9] In cases of resistance to the dual combination of AHT, the most appropriate is a triple combination of AHT.

Studies have shown that, compared with dual-component therapy, triple AHT provides better BP control and significantly reduces cardiovascular complications.[10,11] At the same time, a fixed combination allows one to achieve goals faster and improve treatment adherence than a free combination of drugs.[10-13] Triple combinations, namely an ACEI, a CCB, and a diuretic, optimally control hypertension with fewer dose-related side effects.[9-13] In addition, when combined, each component can reduce the adverse effects of other components.[14] A recent meta-analysis of 44 studies compared a fixed combination of AHT with a free combination of AHT.[14,15] In this study, patients receiving fixed-dose combination therapy had significant reductions in SBP and DBP after 12 weeks of follow-up, as well as positive effects on PP and improved adherence to treatment, resulting in better BP control.

The PETRA study (n=11209) showed that a 3-month fixed antihypertensive combination of perindopril/indapamide/amlodipine was sufficient to achieve TBP at the lowest doses in almost half of all enrolled patients.[16] In addition, the fixed combination has a good effect on vascular stiffness parameters, which leads to improved microcirculation and a reduction in cardiovascular complications. The combination of perindopril/indapamide/amlodipine reduces the glomerular filtration rate and MAU in AH patients, promoting nephroprotection.[13,16,17] The high antihypertensive and organ-protective effectiveness of the fixed triple combinations (perindopril/indapamide/amlodipine) was shown in the PETRA, TRIO, PIONIST, TRICOLOR, and PAINT studies.[16-20]

Our previous study[21] demonstrated the achievement of a TBP <140/90 mmHg in more than 92% of patients with uncontrolled hypertension on 24-week therapy with SPTC (perindopril/indapamide/amlodipine and telmisartan/hydrochlorothiazide/amlodipine); TBP <130/80 mmHg was achieved in more than 82% of patients. In the present study, the primary TBP was achieved in 94.4% of patients in the SPTC group. The recommended TBP <130/80mmHg was achieved in 70% of patients treated with an SPTC and 42% of patients receiving a separate combination of perindopril/indapamide/amlodipine. Such different percentages of patients achieving

TBP are explained by differences in AH patient samples. The present study included patients with a longer duration of hypertension, higher SBP values, and a higher incidence of coronary artery disease than in the previous work.

A recent population-based retrospective cohort study found that the primary outcome (death or hospitalization for acute myocardial infarction or stroke) was lower in patients receiving SPTC.[7] SPTC (perindopril/indapamide/amlodipine) is more economical than the free-dose combination of perindopril/indapamide/amlodipine.[22] Although several studies have been conducted on combination AHT, comparing fixed-dose and free-dose combination therapy still requires more research.[23]

AH patients often have comorbidities that require multiple medications, so SPTC therapy may help overcome this problem, reduce dosing complexity, and improve treatment efficacy.[14] According to the WHO Quality-of-Life Scale (WHOQOL-BREF), patients receiving the perindopril/indapamide/amlodipine in SPTC significantly improved their quality of life compared to patients receiving the free-dose combination.[13] In another study, SPTC showed significant control of depression and effective control of BP.[13,24]

Thus, studies have shown that one-third of AH patients require 3 AHDs to control BP. Inadequate doses of drugs, irrational combinations, complex treatment regimens, and many pills reduce treatment adherence, leading to poor BP control. Reducing the burden of taking pills using SPTC and subsequently switching to polypill, with the addition of a statin and/or acetylsalicylic acid, will allow achieving the TBP and reducing cardiovascular risk.[2]

The results of our study showed that in the treatment of uncontrolled hypertension on previous therapy in AH patients with high cardiovascular risk, an SPTC of the ACEI perindopril, the CCB amlodipine, and the thiazide-like diuretic indapamide contributed to the effective daily BP control, the improvement of diurnal BP profile, and a positive effect on central BP and PWV, thereby having a positive impact on the prognosis and quality of life of AH patients with high cardiovascular risk.

Ethical Considerations

The study protocol was reviewed and approved by the Ethics Committee of the Republican Specialized Centre of Cardiology. All participants provided written informed consent.

Competing Interests

The authors declare that they have no competing interests.

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