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Comparative Analysis of the Efficacy of a Polypill and a Free Combination of Antihypertensive Drugs and Statins in the Context of an Individualized Treatment Strategy

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Abstract

The objective of this study was to compare the effectiveness of a 6-month course of therapy using a fixed-dose combination (polypill) and a free combination of antihypertensive drugs and statins in achieving target levels of blood pressure (BP) and lipid profile in hypertensive patients with high and very high cardiovascular risk.

Methods and Results: The study included 92 patients with arterial hypertension (AH) Grades 1-3 (ESC/ESH, 2018), aged 40 to 75 years, of both sexes. The mean age of patients was 53.6±9.6 years; the average duration of AH was 9.2±7.1 years.

All patients underwent general clinical examination, the 24-hour ambulatory blood pressure monitoring (ABPM), biochemical blood tests, ECG, standard transthoracic two-dimensional echocardiography, and the carotid intima-media thickness (CIMT) of the common carotid artery assessment by duplex scanning. Arterial stiffness was determined using applanation tonometry.

All patients included in the study were randomly divided into two groups. Group 1 (n=46) received an FDC combination or "polypill" combining lisinopril/amlodipine/rosuvastatin in a single tablet. Group 2 (n=46) received the combination of perindopril/amlodipine and rosuvastatin in separate forms. The drugs were prescribed in therapeutic doses: perindopril (4–8 mg/day), lisinopril (10–20 mg/day), amlodipine (5–10 mg/day), and rosuvastatin (initial dose 10 mg/day). The final treatment results were determined after 6-month therapy. Two therapy regimens, including polypill combining lisinopril, amlodipine, rosuvastatin, and a free combination of perindopril, amlodipine, and rosuvastatin, demonstrated high antihypertensive, lipid-lowering efficacy, and metabolic neutrality in high-risk AH patients. Both treatment regimens allowed many patients to achieve the target BP; however, in Group 1, the number of patients who achieved target BP levels was greater than in Group 2. In addition to achieving target BP levels, a significant reduction in vascular stiffness was observed in Group 1. Group 1 showed high lipid-lowering efficacy. It was also found that the SCORE2 score decreased significantly in Group 1, reaching the normal range. At the same time, both treatment regimens showed high antihypertensive and organoprotective efficacy.

Conclusion: The polypill therapy demonstrated superiority over the separate regimen, resulting in a greater reduction in BP and an improvement in lipid profile. These results highlight the importance of choosing the right treatment regimen for patients with high cardiovascular risk and indicate the efficacy of polypills in this patient group. (**International Journal of Biomedicine. 2025;15(3):461-468.**)

Keywords: hypertension • cardiovascular risk • angiotensin-converting enzyme inhibitor • calcium channel blocker • statins

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Abbreviations

AH, arterial hypertension; **AA**, aortic augmentation; **AI**, atherogenic index; **ACEI**, angiotensin-converting enzyme inhibitor; **ABPM**, ambulatory blood pressure monitoring; **BP**, blood pressure; **CCB**, calcium channel blocker; **CHD**, coronary heart disease; **CVD**, cardiovascular disease; **CVR**, cardiovascular risk; **CPK-MB**, creatine phosphokinase-MB; **DH**, dyslipidemic hypertension; **DBP**, diastolic BP; **FDC**, fixed-dose combination; **HDL-C**, high-density lipoprotein cholesterol; **non-HDL-C**, non-high-density lipoprotein cholesterol; **LDL-C**, low-density lipoprotein cholesterol; **PPc**, central pulse pressure; **PWV**, pulse wave velocity; **SBP**, systolic BP; **SBPc,** central SBP; **TC**, total cholesterol; **TG**, triglycerides.

Introduction

According to the 2010 Global Burden of Disease study, cardiovascular disease (CVD) was responsible for 15.6 million deaths worldwide, representing 29.6% of all deaths. In 2021, CVDs accounted for 20.5 million deaths, comprising approximately one-third of all global deaths.[1] According to the results of the WHO STEPS study on the prevalence of risk factors for non-communicable diseases in the Republic of Uzbekistan in July 2019, conducted among 4,320 people aged 18-69 years: In the Republic of Uzbekistan, 83.5% of deaths were from non-communicable diseases, of which 63.3% of deaths were from CVD.[2]

In 1988, Williams et al.[3] first used the term "dyslipidemic hypertension (DH)" to describe the coexistence of dyslipidemia and hypertension, initially proposed in the context of familial DH. It was suggested to be a genetic syndrome present in approximately 12% of patients with essential hypertension and 48% of hypertensive sibships.

In a scientific article published in 2012, Dalal et al.[4] introduced the term "LIPITENSION" into clinical practice, considering the prevalence of AH and dyslipidemia, the impact of these risk factors on patient prognosis, and the importance of early control.

Epidemiological data indicate that >90% of patients with hypertension in North America, Europe, and the Middle East, and >80% in Australia, Latin America, and Asia have at least one additional risk factor for CVD.[5] In particular, the prevalence of dyslipidemia in people with hypertension is 1.2–1.5 times higher than in the general population. Epidemiological studies have shown that the combination of hypertension and dyslipidemia not only contributes to the negative consequences of CVD, but also increases the risk of developing these atherosclerotic diseases by 2–3 times, as demonstrated in several studies, such as Framingham,[6] MRFIT (Multiple Risk Factor Intervention Trial),[7] INTERHEART (Interaction of Potentially Modifiable Risk Factors Associated with Myocardial Infarction in 52 Countries).[8]

In recent years, the concept of using the so-called "polypill" proposed in 2003 by Wald and Law[9] has been actively discussed at international forums. In a meta-analysis, the authors demonstrated that lowering low-density lipoprotein cholesterol (LDL-C) with statins by 1.8 mmol/L can reduce the risk of coronary heart disease (CHD) by 61% and stroke by 17%. Antihypertensive drugs included in the polypill at half the dosage help reduce diastolic blood pressure (DBP) by 11 mmHg, which leads to a 46% reduction in the risk of CHD and 63% of stroke. Thus, the polypill can reduce the risk of CHD by 88% and stroke by 80%. If a patient aged 55-64 years, who has not been diagnosed with CVD, starts taking the polypill, they will be protected from developing CHD and stroke for 10-12 years, regardless of the presence of risk factors.

In 2022, the results of the SECURE study on secondary prevention of CVD in patients with a history of myocardial infarction were published. The study involved 2,499 patients, randomly assigned to two groups. The first group took a fixed combination of drugs in the form of a polypill, including aspirin (100 mg), ACEI ramipril (2.5, 5, or 10 mg), and atorvastatin (20 or 40 mg). The second group took the same drugs separately. With a median follow-up period of 3 years, the primary combined endpoint was recorded in 9.5% of patients in the polypill group and 12.7% in the separate therapy group. Treatment adherence was significantly higher in the polypill group, resulting in a 25% reduction in the risk of endpoints (P=0.02).[10] In addition, five clinical trials were conducted to evaluate the effectiveness of the polypill in reducing the risk of death from all types of CVD: CRUCIAL, TIPS, UMPIRE, IMPACT, and Kanyini GAP.[11,12,13,14,15] In the TIPS trial, patients were given a polypill with different formulations, each containing five different drugs, to prevent CVD. This multicenter trial demonstrated that the polypill improved SBP levels compared with a combination of fewer drugs, was well tolerated, and showed improved adherence to treatment.[12]

The 2018 ESC/ESH guidelines for hypertension management recommend to initiate therapy with a combination of two antihypertensive drugs, preferably in a single-pill fixed-dose combination (FDC), for most patients.[16,17] In most clinical situations, the optimal starting fixed combination is a combination of an angiotensin II receptor blocker (ARB) or angiotensin-converting enzyme inhibitor (ACEI) with calcium channel blocker (CCB) or a diuretic, which significantly increases the effectiveness of antihypertensive therapy. An example is the combination of perindopril (4-8 mg) or lisinopril (10-20 mg) with amlodipine (5-10 mg).

The objective of this study was to compare the effectiveness of a 6-month course of therapy using an FDC (polypill) and a free combination of antihypertensive drugs and statins in achieving target levels of blood pressure (BP) and lipid profile in AH patients with high and very high cardiovascular risk (CVR).

Material and Methods

The study included 92 patients with AH Grades 1-3 (ESC/ESH, 2018), aged 40 to 75 years, of both sexes.

Exclusion criteria were symptomatic hypertension, acute coronary syndrome, chronic heart failure (NYHA FC>II), cardiac arrhythmia, history of myocardial infarction, renal impairment, diabetes mellitus, severe co-morbidities, and condition after revascularization.

Office BP was measured using a mercury sphygmomanometer, according to Korotkov's method. Blood pressure was measured three times, and the mean of these measurements was used in the analyses. The 24-hour ambulatory blood pressure monitoring (ABPM) was performed using the Cardiospy recorder (LABTechLTD, Hungary).

Vascular stiffness was assessed by applanation tonometry using the SphygmoCor device (AtCor Medical, Australia), measuring central systolic blood pressure (cSBPc), central diastolic blood pressure (cDBPc), central pulse pressure (PPc), aortic augmentation (AA), augmentation index (AIx), and pulse wave velocity (PWV).

All patients underwent echocardiography on the Affiniti 30 ultrasound system (PHILIPS, Netherlands) with the

determination of the left ventricular mass index (LVMI), left ventricular hypertrophy [LVMI of >95 g/m² (for women) and >115 g/m² (for men)].[16] The carotid intima-media thickness (CIMT) of the common carotid artery was assessed by duplex scanning. Blood levels of lipids, urea, creatinine, uric acid, glucose, ALT, AST, and CK-MB fraction were determined using a Daytona autoanalyzer (RANDOX, UK). The estimated glomerular filtration rate (eGFR) was calculated according to the CKD-EPI (2021) equation. Microalbuminuria (MAU) in morning urine was assessed by enzymatic analysis on the MindrayBS 380 biochemical analyzer (China), with a measurement range from 30 to 300 mg/L and higher. The 10-year risk of fatal and non-fatal cardiovascular events was assessed using the SCORE2 scale.

All patients included in the study were randomly divided into two groups using the envelope method. Both groups received dual combination antihypertensive therapy with statins (ACEI+CA+statin). Group 1 (n=46) received an FDC combination or "polypill" combining lisinopril/amlodipine/rosuvastatin in a single tablet. Group 2 (n=46) received the combination of perindopril/amlodipine and rosuvastatin in separate forms. Treatment was initiated with starting doses of drugs that were titrated every two weeks to achieve target values of BP and blood lipid levels (<140 mmHg), DBP (<90 mmHg), LDL-C (<100–70 mg/dL), non-high-density lipoprotein cholesterol (non-HDL-C<100–85 mg/dL), and triglycerides TG (<150 mg/dL). A reduction in SBP, DBP, and SCORE2 risk of 10% or more, as well as a 50% reduction in LDL-C from baseline levels, was also assessed.

The drugs were prescribed in therapeutic doses: perindopril (4–8 mg/day), lisinopril (10–20 mg/day), amlodipine (5–10 mg/day), and rosuvastatin (initial dose 10 mg/day). In the event of side effects, a corresponding questionnaire was completed, indicating the reasons for the patient's exclusion from the study. All patients were examined before and after a 6-month course of pharmacotherapy.

Statistical analysis was performed using the statistical software «Statistica» (v10.0, StatSoft, USA). Baseline characteristics were summarized as frequencies and percentages for categorical variables and as mean±standard deviation (SD) for continuous variables. The Mann-Whitney U test was used to compare the differences between the two independent groups, and the Wilcoxon test (W) was used to compare the mean values of dependent samples. Group comparisons for categorical variables were performed using a chi-square test. The probability value of $P<0.05$ was considered statistically significant.

Results

In the event of side effects, a corresponding questionnaire was completed, indicating the reasons for the patient's exclusion from the study. All patients were examined before and after a 6-month course of pharmacotherapy.

At the initial stage of the study, patients in both groups did not differ in gender and age, BP level and markers of target organ damage. According to the average values of SBP (162.46±11.31 mmHg) and DBP (96.11±10.18), the patients were characterized by AH Grade 2. Both groups had a very high CVR, according to the SCORE2 scale (Table 1).

Table 1.

Clinical characteristics of the study patients.

Indicators	Overall n=92	Group1 n=46	*P*-value	Croup 2 n=46
Age, yrs	53.66±9.69	52.06±9.40	0.2926	56.33±7.84
Women, n (%)	33 (35%)	30 (65%)	0.8279	29 (63%)
Men, n (%)	59 (64%)	16 (34%)	0.8279	17 (36%)
AH duration, yrs	9.23±7.17	8.71±5.92	0.7948	12.5±8.28
SBP, mmHg	162.46±11.31	165.82±12.54	0.3788	161.8±9.89
DBP, mmHg	96.11±10.18	99.23±10.61	0.1400	96.43±9.21
MBP, mmHg	119.13±9.40	122.19±10.25	0.3421	118.22±7.78
BMI, kg/m²	30.79±5.39	30.81±5.50	0.4413	31.45±5.34
LVH	46 (50%)	19 (41%)	0.1444	27 (58%)
Atherogenic index	4.34±1.43	4.63±1.39	0.9362	4.23±1.43
PWV, m/s	10.82±3.20	11.59±3.25	0.1187	10.63±3.0
SCORE2, score	18.13±8.46	17.73±8.25	0.7263	21.8±8.75

Against a background of 6-month treatment, a significant improvement in the office BP indicators were revealed in both groups, regardless of the treatment regimen (Table 2). However, the reduction percentage in SBP and DBP was significantly more pronounced in Group 1 than in Group 2, although the differences were not statistically significant. Achievement of the target levels of SBP and DBP was recorded in 91% and 97% of patients in Group 1 and in 76% and 76% in Group 2 ($P<0.001$ in both cases), and simultaneous achievement of target levels of SBP and DBP - in 91% of patients in Group 1 and 50% of patients in Group 2 ($P=0.0000$).

Table 2.

The efficacy of 6-month therapy in study groups.

Indicators	Overall n=92	Group 1 n=46	P_1	Group 2 n=46
SBP, mmHg	162.46±11.31 126.14±10.44	165.82±12.54 121.23±5.23	0.3788	161.8±9.89 131.04±12.0
P_2	0.0001	0.0000		0.0000
DBP, mmHg	96.11±10.18 80.20±4.42	99.23±10.61 78.54±3.05	0.1400	96.43±9.21 81.86±4.96
P_2	0.0001	0.0000		0.0000
MBP, mmHg	119.13±9.40 95.82±6.37	122.19±10.25 93.37±4.62	0.3421	118.22±7.78 98.26±6.97
P_2	0.0001	0.0003		0.0006
Δ% SBP	-22.00±8.29	-26.53±5.72	0.1615	-15.87±8.36
Δ% DBP	-15.73±9.28	-20.17±7.26	0.2713	-13.55±9.79
Δ% MBP	-18.74±7.92	-23.18±5.64	0.4413	-14.67±8.13
Achieving target BP levels				
SBP DBP SBP and DBP	81 (88%) 82 (89%) 81 (88%)	42 (91%) 45 (97%) 42 (91%)	0.0003 0.0000 0.0000	26 (76%) 26 (76%) 23 (50%)

The numerator shows the results before treatment. the denominator shows the results after 6 months of therapy. P_1 is for Group 1 vs. Group 2 before treatment; P_2 is for Group 1 vs. Group 2 after treatment.

The diurnal BP profile also improved significantly during treatment. According to ABPM data, both groups demonstrated a significant decrease in the average 24-h, daytime, and nighttime SBP and DBP, with significant benefits in Group 1 for 24-hour DBP, daytime DBP, and nighttime DBP (P=0.0101, P=0.0226, and P=0.0120, respectively). In addition, the reduction in variability of daily SBP was also more pronounced in Group 1 (P=0.0248). 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.

Table 3.

The diurnal BP profile during 6-month therapy in study groups.

Indicators	Overall	Group 1	P_1	Group 2
24-hour SBP, mmHg	142.29±11.24 121.63±12.07	143.91±13.0 120.76±7.51	0.3523 0.3523	139.75±9.0 125.82±14.5
P_2	0.0000	0.0001		0.0045
24-hour DBP, mmHg	86.89±9.29 70.45±9.37	88.15±10.50 71.10±7.62	0.2005 0.0101	83.06±7.80 75.73±9.32
P_2	0.0000	0.0001		0.0001
Daytime SBP, mmHg	144.19±12.18 124.01±11.98	146.63±13.9 120.97±5.59	0.0784 0.1141	140.06±9.72 127.26±15.26
P_2	0.0000	0.0001		0.0001
Daytime DBP, mmHg	89.08±10.08 73.70±9.49	90.86±11.56 71.91±10.61	0.0910 0.0226	84.12±8.07 78.23±10.01
P_2	0.0000	0.0001		0.0001
Nighttime SBP, mmHg	135.78±13.10 115.82±13.93	136.5±14.03 116.82±7.97	0.8650 0.7565	137.12±12.20 119.71±17.13
P_2	0.0000	0.0001		0.0001
Nighttime DBP, mmHg	80.65±9.10 65.44±9.26	81.32±9.04 65.17±7.12	0.6030 0.0120	79.87±9.22 70.08±10.03
P_2	0.0000	0.0001		0.0001
Daily SBPV, mmHg	16.43±3.79 11.43±2.23	17.06±4.0 11.92±2.26	0.3897 0.0248	16.65±3.50 13.01±2.32
P_2	0.0000	0.0002		0.2743
Daily DBPV, mmHg	13.37±3.27 9.38±2.15	13.76±2.96 9.58±2.11	0.5892 0.3867	13.37±3.55 9.19±2.19
P_2	0.0005	0.0045		0.0014
Daytime SBPV, mmHg	16.22±4.12 10.57±2.66	17.10±4.07 10.91±2.57	0.2420 0.6491	16.01±4.02 11.18±3.08
P_2	0.0001	0.0001		0.0018
Daytime DBPV, mmHg	12.55±3.49 8.67±2.61	12.91±3.44 8.87±2.88	0.7278 0.4763	12.84±3.55 8.48±2.32
P_2	0.0005	0.0055		0.0014
Nighttime SBPV, mmHg	14.03±5.32 8.32±2.66	14.66±5.39 8.27±2.48	0.4354 0.1235	14.63±5.23 9.15±2.93
P_2	0.0001	0.0000		0.0034
Nighttime DBPV, mmHg	11.33±4.67 7.14±2.71	11.20±4.23 7.53±2.47	0.6527 0.3141	10.73±5.11 8.11±3.00
P_2	0.0001	0.0000		0.0153

The numerator shows the results before treatment. The denominator shows the results after 6 months of therapy. P1 is for Group 1 vs. Group 2; P2 is for before treatment and after 6 months of therapy inside each group. SBPV, SBP variability; DBPV, DBP variability;

Table 3 (continued).

The diurnal BP profile during 6-month therapy in study groups.

Indicators	Overall	Group 1	P_1	Group 2
Daytime SBP load,%	56.82±26.39 27.66±28.42	62.80±25.84 23.23±6.4	0.0323 0.0057	47.01±25.83 31.91±38.80
P_2	0.0001	0.0001		0.0003
Daytime DBP load,%	46.43±27.18 22.20±25.17	49.84±29.04 17.73±10.84	0.2670 0.0198	37.37±25.03 26.97±33.52
P_2	0.0001	0.0001		0.0004
Nighttime SBP load,%	79.16±22.51 30.81±29.78	79.58±21.11 23.56±14.98	0.8728 0.9442	83.18±24.05 38.06±38.23
P_2	0.0001	0.0001		0.0001
Nighttime DBP load,%	50.12±3041 28.64±28.34	52.10±28.17 26.73±11.84	0.4839 0.0045	48.75±32.68 30.54±38.42
P_2	0.0001	0.0001		0.0039

The numerator shows the results before treatment. The denominator shows the results after 6 months of therapy. P1 is for Group 1 vs. Group 2; P2 is for before treatment and after 6 months of therapy inside each group.

One of the important markers of vascular damage in hypertension is indicators of central BP and PWV. In both groups, 6-month therapy led to a significant decrease in SBPc, DBPc, PPc, and PWV. At the same time, the AA parameter significantly decreased only in Group 1 (Figure 1).

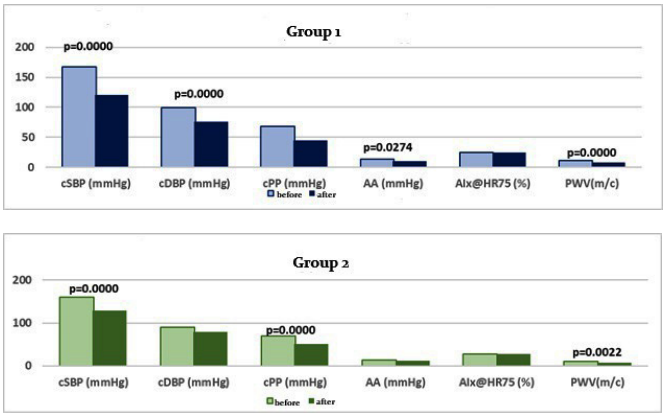

Figure 1. *Parameters of central hemodynamic and vascular stiffness before and after 6-month therapy in the study groups.*

Against the background of 6-month therapy in both groups, no adverse impact on metabolic parameters, including glucose, uric acid, and creatinine, as well as liver enzyme levels, was observed, indicating the metabolic neutrality of the therapy (Figure 2).

In general, positive dynamics of lipid profile parameters were shown in both groups. However, it should be noted that in Group 1, the levels of TC, LDL-C, non-HDL-C, TG, and AI, as well as the level of ApoB, were reduced more significantly than in Group 2. In addition, a significant increase in HDL-C was observed in Group 1 compared to Group 2 (53.3±12.0 mg/dL and 44.1±4.5 mg/dL after treatment, P<0.0001). Despite a

significant decrease in CVR, according to the SCORE2 scale in both groups, the most pronounced results and target levels were recorded in Group 1: from 18.7±8.2 points to 9.1±5.9 points in Group 1 (*P*=0.0001) and from 19.8±8.7 to 14.3±8.0 points in Group 2 (*P*=0.0093) (Figure 3).

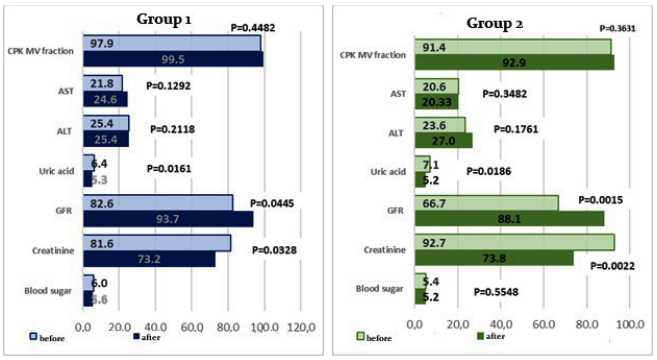

Figure 2. *Metabolic parameters before and after 6-month therapy in the study groups.*

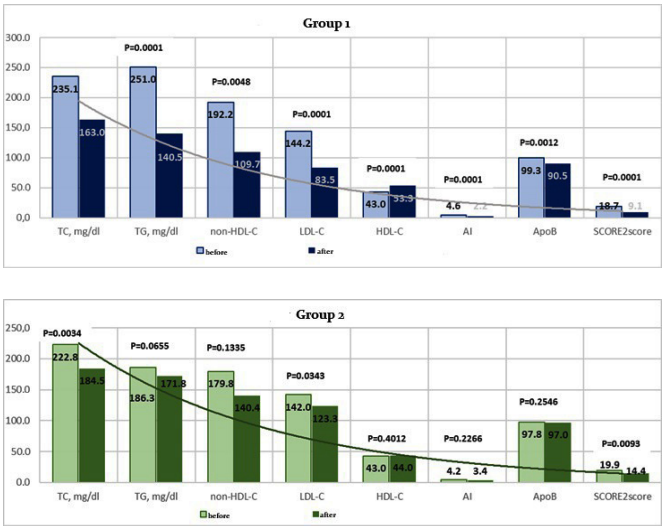

Figure 3. *Lipid profile parameters and SCORE2 scores before and after 6-month therapy in the study groups.*

Overall, patients in both groups achieved their target lipid profile values. However, patients in Group 1 achieved all target lipid profile values, and accordingly, their SCORE2 scores were significantly more reliable than those in Group 2 (Figure 4). The target TC level was achieved in 69% and 45% of patients in Groups 1 and 2, respectively (*P*=0.0203). In Group 1, the target level of TG was achieved in 71% of patients, compared to 39% in Group 2 (*P*=0.0016). Achievement of non-HDL-C levels was recorded in 41% of patients in Group 1 and 17% in Group 2 (*P*=0.0117), and LDL-C levels in 80% and 26%, respectively (*P*=0.0000). Achievement of the target AI was detected in 78% of patients in Group 1 and 41% of patients in Group 2 (*P*=0.0003), and target ApoB in 86% versus 65%, respectively (*P*=0.0145). Target score levels on the SCORE2 scale were observed in 84% of patients in Group 1 and 43% in Group 2 (*P*=0.0000).

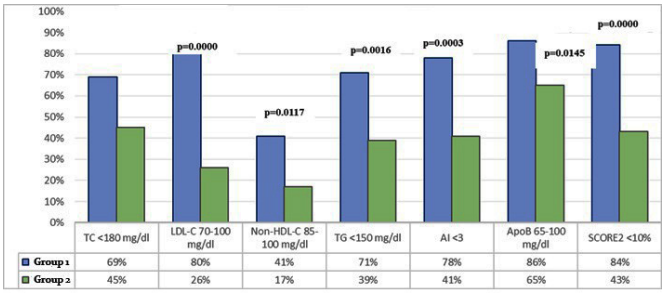

Figure 4. *Achievement of target lipid profile parameters after 6-month therapy in study groups.*

Discussion

When considering the specific effects of antihypertensive drugs in the context of their combined use, we should again turn to the results of the ASCOT study,[18,19] which demonstrates a new approach to the strategy of modern antihypertensive therapy. The ASCOT study included more than 19,000 patients, which allowed a new assessment of the effect of "new" classes of antihypertensive drugs, such as CCB and ACEI, in reducing CVR. The effectiveness of antihypertensive therapy in the ASCOT-BPLA study[20] demonstrated that the combination of amlodipine with perindopril is significantly superior to the combination of atenolol and a diuretic (bendroflumethiazide) in reducing CVR. It showed a reduction in the risk of coronary events by 13%, fatal and nonfatal stroke by 23%, cardiovascular mortality by 24%, new cases of renal failure by 15% and cases of diabetes mellitus by 30%.

Previous studies have demonstrated significant benefits of combination therapy over monotherapy in the treatment of hypertension. According to a meta-analysis by Wald and Law,[21] combination drugs reduce BP and the risk of cardiovascular complications better than monotherapy. In particular, the combination of ACEI with CCB has proven to be particularly effective in lowering BP in high-risk patients.[22,23] Moreover, in low- and middle-income countries, combination therapy also demonstrates high efficacy, despite challenges related to drug availability and treatment adherence.[24]

The high efficiency of the combination of CCB with ACEI is due to several factors. Firstly, CCB has a pronounced arterial vasodilation effect, and secondly, ACEI neutralize the effects of the the renin-angiotensin-aldosterone system (RAAS). The combined use of CCB and ACEI neutralizes counter-regulatory mechanisms that can reduce the effectiveness of therapy. ACEI suppresses the activity of the RAAS and the sympathetic adrenergic system, which is triggered as a result of CCB's vasodilating action. In turn, the negative sodium balance caused by CCB is eliminated due to the action of ACEI. In addition, the combination of these drugs significantly reduces the incidence of side effects. For example, a side effect of CCB, such as ankle swelling, is reduced substantially when used in conjunction with ACEI. It has also been demonstrated that the use of CCB reduces the incidence of dry cough, a common side effect of ACEI.[25,26]

The efficacy of the combined effect on BP and dyslipidemia was confirmed in the ASCOT-LLA study, where the addition of 10 mg atorvastatin to antihypertensive therapy resulted in an additional 36% reduction in the risk of nonfatal myocardial infarction and CHD death and a 29% reduction in the risk of all cardiovascular events.[9] Moreover, there is evidence that the addition of a statin enhances antihypertensive therapy.[27,28]

It is worth noting that ACEI and CCB are metabolically neutral antihypertensive drugs, which makes their combination particularly attractive for patients with lipid, carbohydrate, and purine metabolism disorders. The efficacy and safety of the drugs included in the polypill were studied in by Kónyi et al.,[17] which used an FDC of lisinopril and amlodipine (5/10 mg, 5/20 mg, and 10/20 mg) with the addition of rosuvastatin (10 or 20 mg). The study included 2241 patients with AH Grades 1–2, hypercholesterolemia, and high or very high CVR associated with diabetes mellitus, metabolic syndrome, and lower extremity arterial disease.

The results of our study show that the polypill, combining perindopril, amlodipine, and rosuvastatin, demonstrates a more pronounced reduction in BP than separate therapy. These data are consistent with the findings of the study by Cicero et al.,[29] who also noted the high effectiveness of FDC in controlling blood pressure. Moreover, the improvement in lipid profile observed in our patients is consistent with the data of Cequier et al.,[30] who showed that FDCs are effective not only in reducing BP but also in improving lipid metabolism.

Conclusion

Two ACEI/CCB/statin therapy regimens, including polypill combining lisinopril, amlodipine, rosuvastatin, and a free combination of perindopril, amlodipine, and rosuvastatin, demonstrated high antihypertensive, lipid-lowering efficacy, and metabolic neutrality in high-risk AH patients. Both treatment regimens allowed many patients to achieve the target blood pressure; however, in Group 1, the number of patients who achieved target blood pressure levels was greater than in Group 2. In addition to achieving the target blood pressure levels, a significant decrease in SBPc and DBPc, as well as PWV and aortic augmentation in Group 1, indicates a reduction in vascular stiffness. At the same time, a significant decrease in the blood levels of TC, LDL-C, TG, and atherogenic index in Group 1 confirms the lipid-lowering efficacy of the polypill treatment regimen. A significant increase in the HDL-C level in Group 1 indicated the superiority of the polypill over the combination of perindopril and amlodipine plus rosuvastatin in separate forms. It was also found that the SCORE2 score decreased significantly in Group 1, reaching the normal range. At the same time, both treatment regimens showed high antihypertensive and organoprotective efficacy.

The polypill therapy demonstrated superiority over the separate regimen, resulting in a greater reduction in BP and an improvement in lipid profile. These results highlight the importance of choosing the right treatment regimen for patients with high cardiovascular risk and indicate the efficacy of polypills in this patient group.

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. The data was only used for study purposes without individual details identifying the patient.

Competing Interests

The authors declare that they have no competing interests.

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