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DISLIPIDEMIK GIPERTENZIYADA POLIPILL TERAPIYASI: KARDIOVASKULYAR XAVFNI KAMAYTIRISH VA ORGANOPROTEKSIYANING YANGI IMKONIYATLARI

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Annotatsiya. Maqsad: Arterial gipertenziya va dislipidemiya ega, SCORE2 shkalasi bo'icha yuqori va juda yuqori yurak-qon tomir xavfli bemorlarda lizinopril/amlodipin/rozuvastatin tarkibli polipill va erkin kombinatsiyalangan terapiyaning samaradorligini qiyosiy baholash.

Material va usullar: Tadqiqotga 40–75 yoshdagi 119 nafar arterial gipertenziya va dislipidemiya bemor jalb qilindi. Bemorlar ikki guruhga randomizatsiya qilindi: 1-guruh (n=60) lizinopril/amlodipin/rozuvastatin tarkibli polipill, 2-guruh (n=59) esa perindopril/amlodipin va rozuvastatinning erkin kombinatsiyasini qabul qildi. Ko'rsatkichlar dastlabki, 12 haftalik va 6 oylik davrlarda baholandi.

Natijalar: 6 oylik davolash yakunida polipill guruhida arterial bosim, PZLP-XS, umumiy xolesterin, ApoB va aterogenlik indeksining pasayishi nazorat guruhiga nisbatan ishonchli yuqori bo'ldi. Maqsadli AB darajasiga erishish: polipill 81% vs nazorat 57%. SCORE2 bo'icha kardiovaskulyar xavf polipill guruhida 43,9%, nazorat guruhida 21,6% ga kamaydi (p<0,001). Albumin/kreatinin nisbati polipill guruhida 127 dan 36 mg/g gacha kamaydi.

Xulosa: Polipill terapiyasi yuqori va juda yuqori kardiovaskulyar xavfli bemorlarda erkin kombinatsiyaga nisbatan arterial bosim va lipid ko'rsatkichlarini samaraliroq nazorat qiladi, organoprotektiv ta'sir ko'rsatadi hamda umumiy kardiovaskulyar xavfni sezilarli kamaytiradi.

Kalit so'zlar: arterial gipertenziya, dislipidemiya, polipill, SCORE2, yurak-qon tomir xavfi, arterial qattqlik, organoproteksiya.

Abstract. Objective: To comparatively evaluate the efficacy of a fixed-dose combination (polypill) containing lisinopril/amlodipine/rosuvastatin versus free combination therapy in patients with arterial hypertension and dyslipidemia at high and very high cardiovascular risk according to SCORE2.

Material and Methods: 119 patients aged 40–75 years were randomized into two groups: Group 1 (n=60) received the polypill (lisinopril/amlodipine/rosuvastatin); Group 2 (n=59) received free combination (perindopril/amlodipine + rosuvastatin). Parameters were assessed at baseline, 12 weeks, and 6 months.

Results: At 6 months, the polypill group showed significantly greater reductions in blood pressure, LDL-C, total cholesterol, ApoB, and atherogenicity index. Target BP achieved: 81% vs 57%. SCORE2 risk decreased by 43.9% vs 21.6% ($p<0.001$). Albumin/creatinine ratio decreased from 127 to 36 mg/g in the polypill group.

Conclusion: Polypill therapy with lisinopril/amlodipine/rosuvastatin provides superior blood pressure and lipid control, demonstrates organoprotective effects, and significantly reduces overall cardiovascular risk compared to free combination therapy.

Keywords: arterial hypertension, dyslipidemia, polypill, SCORE2, cardiovascular risk, arterial stiffness, organoprotection.

Аннотация. Цель: Сравнительная оценка эффективности фиксированной дозированной комбинации (полипилль) лизиноприл/амлодипин/розувастатин и свободной комбинации у больных высокого и очень высокого сердечно-сосудистого риска по SCORE2.

Материал и методы: 119 больных 40–75 лет рандомизированы на 2 группы: 1-я ($n=60$) – полипилль; 2-я ($n=59$) – свободная комбинация. Контрольные визиты: исходно, через 12 недель и 6 месяцев.

Результаты: Через 6 месяцев в группе полипилля отмечено достоверно большее снижение АД, ХНП-ЛП, общего ХС, ApoB и индекса атерогенности. Целевого АД достигли 81% vs 57%. Риск SCORE2 снизился на 43,9% vs 21,6% ($p<0,001$). Альбумин/креатинин: 127→36 мг/г в группе полипилля.

Заключение: Полипилльная терапия обеспечивает более эффективный контроль АД и липидных показателей, оказывает органопротективное действие и значительно снижает общий сердечно-сосудистый риск.

Ключевые слова: артериальная гипертензия, дислипидемия, полипилль, SCORE2, сердечно-сосудистый риск, артериальная жёсткость, органопротекция.

Kirish. Yurak-qon tomir kasalliklari (YuQTK) dunyo bo'icha o'limning yetakchi sababi bo'lib qolmoqda. 2023-yilda YuQTK bilan bog'liq yo'qotilgan sog'lom hayot yillari soni 437 million (95% UI: 401–465 million) tashkil etdi – 1990-yildagi 320 millionga nisbatan 1,4 barobar ko'p [1]. JSSTning 2019-yilda O'zbekistonda o'tkazilgan STEPS tadqiqoti natijalariga ko'ra, o'limlarning 83,5% i yuqumsiz kasalliklar, ularning 63,3% ini esa yurak-qon tomir kasalliklari tashkil etgan [2].

Framingham Heart Study tadqiqotiga ko'ra, arterial gipertenziyalı bemorlarning 80% dan ortig'ida kamida bitta qo'shimcha xavf omili mavjud bo'lib, eng ko'p uchraydigani dislipidemiya hisoblanadi [5, 6]. Ikkala holatning birgalikdagi kechishi – dislipidemik gipertenziya – kardiovaskulyar xavfni keskin oshiradi va kompleks davolash yondashuvini taqozo etadi.

Davoga past moyillik alohida muammo bo'lib: bemorlarning taxminan 50% antigipertenziv davodan bir yil ichida voz kechadi [7]. 13 139 bemorni o'z ichiga olgan meta-tahlil shuni ko'rsatdiki, polipill qabul qilgan bemorlarda davoga rioya qilish nazorat guruhiga nisbatan sezilarli yuqori ($RR=1,38$; 95% IS: 1,22–1,56; $p=0,001$), YuQTK hodisalari xavfi esa 28% ga past ($RR=0,72$; 95% IS: 0,63–0,82; $p=0,001$) [8].

ESC/ESH 2018 tavsiyalariga ko'ra, aksariyat bemorlarda davolashni fiksirlangan doza kombinatsiyasi bilan boshlash tavsiya etiladi [9, 10]. AAFI, KKB va statinning bitta tabletkada birlashtirilishi kardiovaskulyar xavfni kompleks kamaytirish imkonini beradi.

Tadqiqot maqsadi: Arterial gipertenziya va dislipidemiya mavjud, SCORE2 bo'icha yuqori va juda yuqori kardiovaskulyar xavfli bemorlarda 6 oylik davolash davomida lizinopril/amlodipin/rozuvasatin tarkibli polipillning erkin kombinatsiyaga nisbatan samaradorligini qiyosiy baholash.

Material va usullar. Tadqiqot Respublika ixtisoslashtirilgan kardiologiya ilmiy-amaliy tibbiyot markazida 2022–2024 yillarda o'tkazildi. Etika qo'mitasi tomonidan ma'qullangan (bayonnoma № 2, 2024-yil yanvar). Tadqiqotga 40–75 yoshdagi, AG I–II daraja (ESC/ESH 2018) va dislipidemiya mavjud, SCORE2 bo'icha yuqori va juda yuqori YuQTK xavf guruhidagi bemorlar jalb etildi.

Istisno mezonlari: qandli diabet 1 va 2-tur; surunkali buyrak kasalliklari; oilaviy giperxolesterinemiya; ikkilamchi va gestasion AG; aterosklerotik YuQTK; yurak aritmiyalari; og'ir metabolik, buyrak va jigar kasalliklari; tadqiqotdan bosh tortish.

Bemorlar konvertlar usuli bilan randomizatsiya qilindi: 1-guruh (n=60) polipill (lizinopril/amlodipin/rozuvasatin), 2-guruh (n=59) perindopril/amlodipin + rozuvasatinning erkin kombinatsiyasini qabul qildi. Dozalar: perindopril 4–8 mg/kun, lizinopril 10–20 mg/kun, amlodipin 5–10 mg/kun, rozuvasatin 10–20 mg/kun. Maqsadli ko'rsatkichlar: SAB <140, DAB <90 mm sim.ust.; PZLP-XS <100 mg/dl; SCORE2 <10%.

AB simobli sfigmomanometr (Korotkov usuli, 3 o'lchov o'rtachasi); arterial qattiqlik SphygmoCor (AtCor Medical, Avstraliya); biokimyoviy tahlillar Daytona analizatori (RANDOX, Buyuk Britaniya); KFT CKD-EPI (2021); MAU Mindray BS-380 (Xitoy) yordamida baholandi. Barcha bemorlar dastlabki, 12 hafta va 6 oy o'tgach ko'rikdan o'tkazildi.

Statistik tahlil: Shapiro–Wilk (normallik); RM-ANOVA / Fridman (guruh ichi dinamika); Styudent (Welch) / Mann–Whitney U (guruhlararo); χ^2 / Fisher (kategorial); Spearman (korrelyatsiya). $p < 0,05$ statistik ahamiyatli deb qabul qilindi.

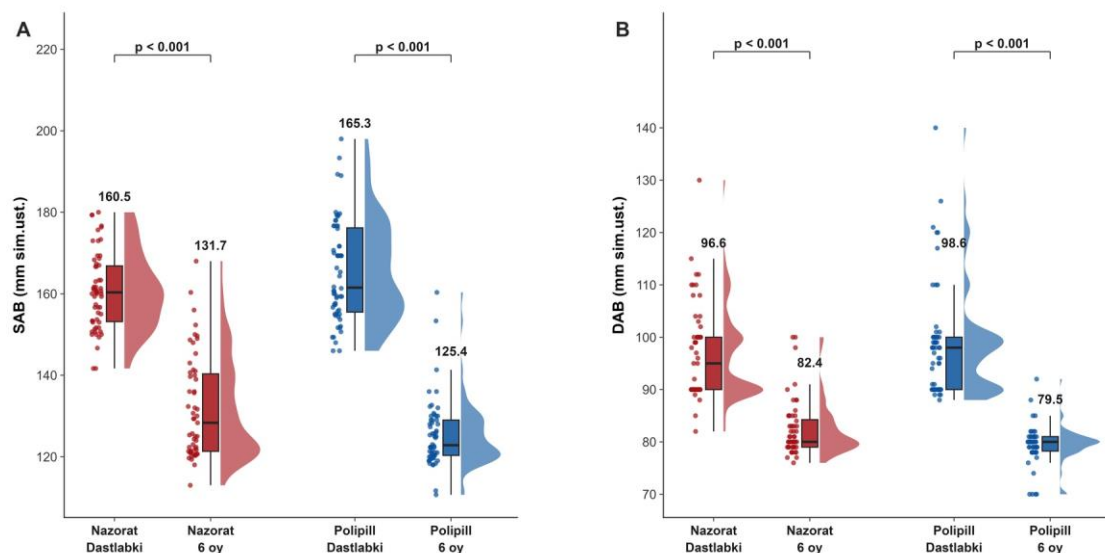
Natijalar. Guruhlarning boshlang'ich ko'rsatkichlari o'rtasida statistik ahamiyatli farqlar aniqlanmadi (1-jadval). 1-guruhda SAB $164,9 \pm 12,3$, DAB $98,2 \pm 10,1$ mm sim.ust.; 2-guruhda $160,1 \pm 9,4$ va $96,5 \pm 8,8$ mm sim.ust. PZLP-XS: $145,9 \pm 35,2$ va $143,4 \pm 29,5$ mg/dl. SCORE2 ikkala guruhda median 17 (13–22) ball.

1-jadval. Tadqiqot guruhlarining boshlang'ich klinik, metabolik va kardiovaskulyar xavf ko'rsatkichlari tavsifi

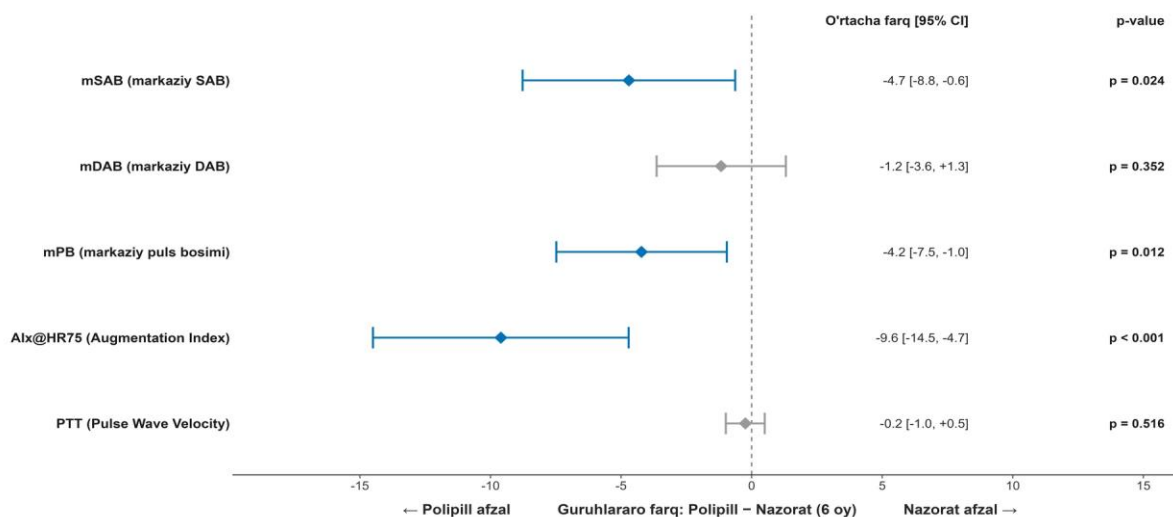
Ko'rsatkichlar	Umumiy n=119	1-guruh n=60	2-guruh n=59	p
SAB, mm sim.ust. (M $\pm$ SD)	162,8 $\pm$ 11,1	164,9 $\pm$ 12,3	160,1 $\pm$ 9,4	>0,05
DAB, mm sim.ust. (M $\pm$ SD)	97,6 $\pm$ 9,6	98,2 $\pm$ 10,1	96,5 $\pm$ 8,8	>0,05
YuQS, ta/daq (M $\pm$ SD)	76,5 $\pm$ 10,0	74,0 $\pm$ 12,0	77,8 $\pm$ 10,1	>0,05
PZLP-XS, mg/dl (M $\pm$ SD)	144,2 $\pm$ 31,7	145,9 $\pm$ 35,2	143,4 $\pm$ 29,5	>0,05
Dislipidemiya IIa, n(%)	13 (10,9%)	7 (12,3%)	6 (10,2%)	>0,05
Dislipidemiya IIb, n(%)	103 (86,5%)	50 (87,7%)	53 (89,8%)	>0,05
Nasliy moyillik, n(%)	115 (95%)	58 (96%)	57 (95%)	>0,05
Chekish, n(%)	42 (35%)	25 (41%)	17 (28%)	>0,05
Giperurekemiya, n(%)	71 (59%)	36 (60%)	35 (58%)	>0,05
KF PTT >10 m/s, n(%)	64 (53%)	35 (58%)	29 (48%)	>0,05
MMAS-8 (Q1–Q3)	2 (0–3)	2 (0–3)	1 (0–2)	>0,05
SCORE2, ball, Me (Q1–Q3)	17 (12–22)	17 (13–22)	17 (13–22)	>0,05

Izoh: KFPTT – karotid-femoral puls to'liqini tarqalish tezligi; M $\pm$ SD – o'rtacha $\pm$ standart og'ish; Me (Q1–Q3) – median (kvartilar orali'i).

Farmakoterapiya fonida ofisdagi AB har ikki guruhda ishonchli pasaydi. 6 oy yakunida 1-guruhda SAB 165,3±12,3 dan 125,4±8,1 mm sim.ust., DAB 98,6±10,1 dan 79,5±3,7 mm sim.ust. gacha; 2-guruhda SAB 160,5±9,4 dan 131,7±12,3, DAB 96,6±8,8 dan 82,4±5,3 mm sim.ust. gacha kamaydi ($p<0,001$) (1-rasm). Maqsadli AB ko'rsatkichlariga erishish tahlili: SAB 118–130 / DAB 70–80 mm sim.ust. ga 12 haftada polipill guruhida 27%, nazorat guruhida 18%; 6 oyda esa polipill guruhida 81%, nazorat guruhida 57% bemor erishdi. Maqsadli ko'rsatkichlarga erisha olmagan bemorlar ulushi 6 oy yakunida polipill guruhida 5%, nazorat guruhida 26% ni tashkil etdi ($\chi^2=12,95$; $p=0,0015$).

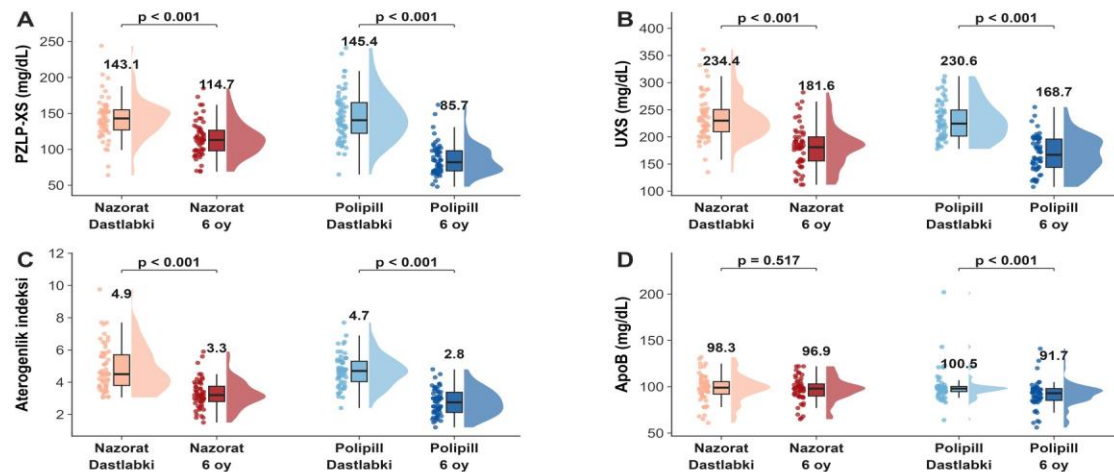


1-rasm. Farmakoterapiya davomida polipill (1-guruh) va nazorat (2-guruh) guruhlarida ofisdagi arterial bosim dinamikasi.



2-rasm. Farmakoterapiya davomida ofis AB bo'icha maqsadli ko'rsatkichlarga erishish darajasi, guruhlararo qiyosiy dinamika (%).

Markaziy gemodinamika va arterial qattqlik bo'icha: markaziy SAB guruhlararo farqi -4,7 mm sim.ust. ($p=0,024$); markaziy puls bosimi -4,2 mm sim.ust. ($p=0,012$); augmentatsiya indeksi -9,6% ($p<0,001$). KFPTT bo'icha farq -0,2 m/s, statistik ahamiyatga ega bo'lmadi (3-rasm).



3-rasm. Markaziy gemodinamika va arterial qattqlik ko'rsatkichlarining 6 oylik dinamikasi (forest plot, guruhlararo farq).

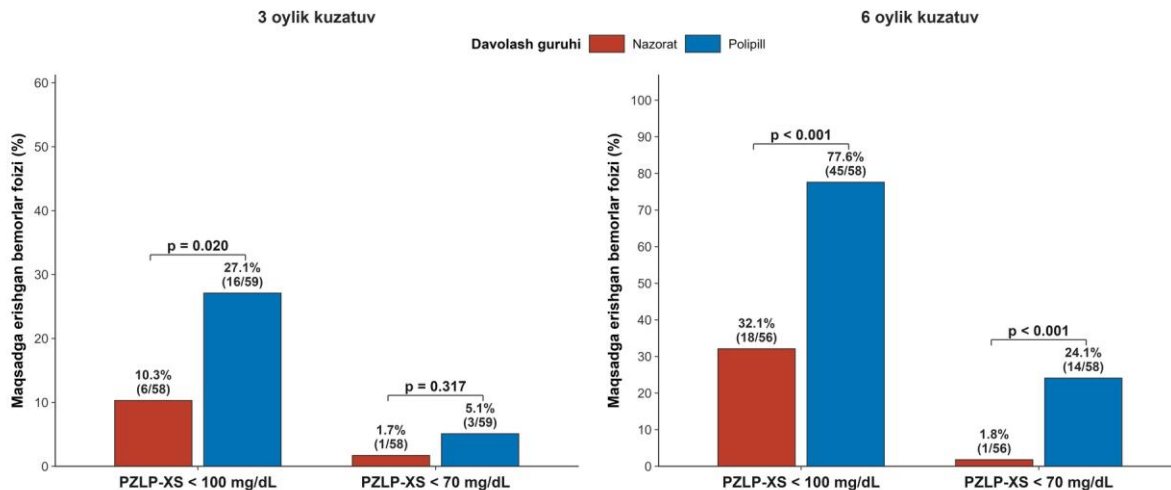
Biokimyoviy ko'rsatkichlar bo'icha: ALT, AST, KFK va glyukozada klinik ahamiyatli o'zgarishlar kuzatilmadi. Polipill guruhida kreatinin $82,7 \pm 21,1$ dan $70,6 \pm 13,7$ mkmol/l ($p < 0,001$), KFT $82,1 \pm 16,8$ dan $92,9 \pm 15,6$ ml/min/ $1,73m^2$ ($p < 0,001$) gacha o'zgardi. Albumin/kreatinin 127 dan 36 mg/g gacha kamayib, 12 haftadan nazorat guruhiga nisbatan statistik ahamiyatli farq qayd etildi ($p < 0,05$), 6 oyda ham saqlanib qoldi ($p < 0,01$) (2-jadval).

2-jadval. Farmakoterapiya fonida metabolik va buyrak funksiyasi ko'rsatkichlari dinamikasi

Ko'rsatkich	Guruh	Dastlabki	12 hafta	6 oy	p (guruh ichi)
Kreatinin, mkmol/l	Polipill	$82,7 \pm 21,1$	$74,3 \pm 17,0$	$70,6 \pm 13,7$	$< 0,001$
	Nazorat	$79,6 \pm 17,1$	$77,0 \pm 15,3$	$74,8 \pm 14,9$	$> 0,05$
	t-test	$p = 0,380$	$p = 0,364$	$p = 0,112$	
KFT, ml/min/ $1,73m^2$	Polipill	$82,1 \pm 16,8$	$88,1 \pm 15,1$	$92,9 \pm 15,6$	$< 0,001$
	Nazorat	$83,1 \pm 17,6$	$83,2 \pm 19,6$	$89,1 \pm 19,5$	$< 0,05$
	t-test	$p = 0,761$	$p = 0,130$	$p = 0,243$	
MAU, mg/l (Me Q1-Q3)	Polipill	103 (90-206)	96 (40-142)	37,5 (30-91)	$< 0,001$
	Nazorat	121 (74-152)	100 (50-167)	45 (32-82)	$< 0,001$
	Mann-Whitney	$p = 0,137$	$p = 0,481$	$p = 0,199$	
Albumin/kreatinin, mg/g	Polipill	127 (59-168)	70 (38-124)*	36 (26-51)**	$< 0,001$
	Nazorat	155 (136-199)	120 (38-216)	57 (27-102)	$< 0,001$
	Mann-Whitney	$p = 0,073$	$p = 0,010^*$	$p = 0,002^{**}$	

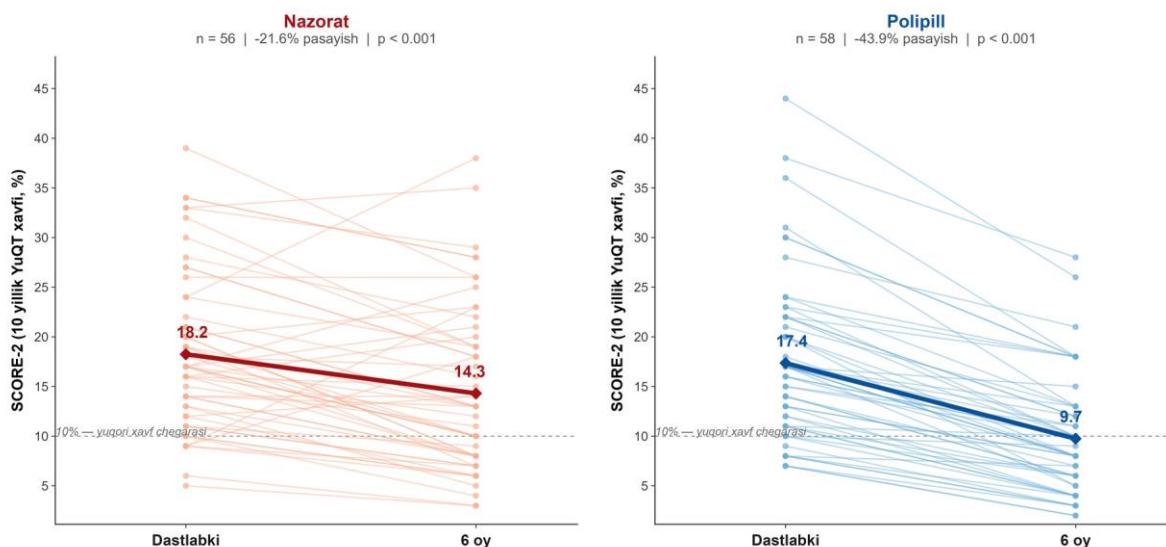
Izoh: * $p < 0,05$; ** $p < 0,01$ – polipill guruhida nazorat guruhiga nisbatan. KFT – ko'ptokchalar filtratsiyasi tezligi; MAU – mikroalbuminuriya.

Lipid spektri dinamikasi: 6 oy yakunida PZLP-XS polipill guruhida 145 dan 85 mg/dl, nazorat guruhida 143 dan 114 mg/dl gacha kamaydi. Aterogenlik indeksi 4,7 dan 2,8 ga, ApoB 100,5 dan 91,7 mg/dl gacha kamaydi (4-rasm).



4-rasm. 6 oylik farmakoterapiya davomida lipid spektri dinamikasi (Raincloud diagrammasi; juftlashgan t-test).

PZLP-XS maqsadli darajasiga (<100 mg/dl) 6 oyda polipill guruhida 77,6%, nazorat guruhida 32,1% bemor erishdi; <70 mg/dl ga esa polipill guruhida 24,1%, nazorat guruhida atigi 1,8% ($p < 0,001$) (5-rasm).



5-rasm. PZLP-XS bo'icha maqsadli ko'rsatkichlarga erishish darajasining qiyosiy dinamikasi (%; 12 hafta va 6 oy).

SCORE2: polipill guruhida 17,4 dan 9,7 gacha – 43,9% kamaydi ($p < 0,001$); nazorat guruhida 18,2 dan 14,3 gacha – 21,6% kamaydi ($p < 0,001$). Polipill terapiyasi umumiy kardiovaskulyar xavfni nazorat guruhiga nisbatan ikki barobar ko'proq kamaytirdi.

SCORE2 bo'icha yurak-qon tomir xavfining individual dinamikasi 5-rasmda keltirilgan. Polipill guruhida o'rtacha SCORE2 ko'rsatkichi 17,4 dan 9,7 gacha kamaydi (43,9% regressiya; $p < 0,001$); nazorat guruhida esa 18,2 dan 14,3 gacha (21,6% regressiya; $p < 0,001$). Polipill terapiyasi umumiy kardiovaskulyar xavfni nazorat guruhiga nisbatan ikki barobardan ko'proq kamaytirdi.

Muhokama. Olingan natijalar polipill terapiyasining arterial bosim nazorati, lipid almashinuvi, markaziy gemodinamika, arterial qattqlik, buyrak funksiyasi va umumiy kardiovaskulyar xavfni kamaytirish bo'icha erkin kombinatsiyaga nisbatan ustunligini tasdiqladi. Maqsadli SAB/DAB darajalariga 81% polipill guruhida vs 57% nazorat guruhida erishildi – bu ESC/ESH [9] va ESC/EAS [11] tavsiyalangan fiksirlangan kombinatsiyalar strategiyasining amaliy samaradorligini isbotlaydi.

Markaziy SAB, puls bosimi va augmentatsiya indeksining polipill guruhida yanada yaqqolroq kamayishi tomir devorining struktura-funksional holatiga keng ta'sir ko'rsatilayotganini bildiradi. Bu ASCOT-BPLA [12] xulosalari bilan uyg'unlashadi. PZLP-XS maqsadli darajasiga polipill guruhida 77,6% vs nazorat guruhida 32,1% erishildi – ASCOT-LLA [13] ma'lumotlari bilan mutanosib.

SCORE2 ning 43,9% ga kamayishi bir vaqtning o'zida bir nechta modifikatsiyalanuvchi xavf omillariga kompleks ta'sir ko'rsatilayotganligini aks ettiradi. Albumin/kreatinin nisbatining 127 dan 36 mg/g gacha kamayishi nefroprotektiv ta'sirning mavjudligini ko'rsatadi. Metabolik xavfsizlik to'liq ta'minlandi. Natijalar Webster [14] meta-tahlili va PolyIran [15] tadqiqoti bilan to'liq mos keladi.

Xulosa. Arterial gipertenziya va dislipidemiya bilan kechuvchi, SCORE2 bo'icha yuqori va juda yuqori kardiovaskulyar xavfga ega bemorlarda lizinopril/amlodipin/rozuvastatin tarkibli polipill terapiyasi erkin kombinatsiyaga nisbatan yuqori klinik samaradorlikni namoyon etdi: arterial bosim va lipid spektrini samaraliroq nazorat qildi, markaziy gemodinamika va arterial qattqlikni yaxshiladi, mikroalbuminuriyani kamaytirdi hamda SCORE2 bo'icha umumiy kardiovaskulyar xavfni 43,9% ga pasaytirdi.

Etik jihatlar. Tadqiqot protokoli Respublika ixtisoslashtirilgan kardiologiya ilmiy-amaliy tibbiyot markazi Etika qo'mitasi tomonidan ko'rib chiqilib, ma'qullangan (bayonnoma № 2, 2024-yil yanvar). Tadqiqot Xelsinki deklaratsiyasining 2013-yilgi tahririga muvofiq amalga oshirildi. Barcha ishtirokchilardan yozma xabardor qilingan rozilik olindi. Ma'lumotlar faqat ilmiy maqsadlarda ishlatildi, bemorlarning shaxsiy ma'lumotlari maxfiy saqlandi.

Manfaatlar to'qnashuvi: Mualliflar manfaatlar to'qnashuvi mavjud emasligini ma'lum qiladilar.

Moliyalashtirish: Tadqiqot tashqi moliyaviy ko'mak olmagan holda amalga oshirildi.

ADABIYOTLAR

1. Stark B.A. et al. Global, Regional, and National Burden of Cardiovascular Diseases and Risk Factors in 204 Countries and Territories, 1990–2023. *J Am Coll Cardiol.* 2025;86(22):2167–2243. <https://doi.org/10.1016/j.jacc.2025.08.015>.
2. World Health Organization. Prevalence of Risk Factors for Noncommunicable Diseases in the Republic of Uzbekistan, 2019. WHO/EURO:2022-6795-46561-67569. Geneva: WHO; 2022.
3. GBD 2021 Risk Factors Collaborators. Global burden and strength of evidence for 88 risk factors in 204 countries, 1990–2021. *Lancet.* 2024;403(10440):2162–2203. [https://doi.org/10.1016/S0140-6736\(24\)00933-4](https://doi.org/10.1016/S0140-6736(24)00933-4).
4. Wang W. et al. Global Burden of Disease Study 2019: metabolic risk factors are the leading drivers of ischemic heart disease. *Cell Metab.* 2021;33(10):1943–1956.e2. <https://doi.org/10.1016/j.cmet.2021.08.005>.
5. Williams R.R., Hunt S.C., Hopkins P.N. et al. Familial dyslipidemic hypertension: evidence from 58 Utah families. *JAMA.* 1988;259(24):3579–3586. <https://doi.org/10.1001/jama.1988.03720240041032>.
6. Kannel W.B. Fifty years of Framingham Study contributions to understanding hypertension. *J Hum Hypertens.* 2000;14(2):83–90.

7. Burnier M. Drug adherence in hypertension. *Pharmacol Res.* 2017;125:142–149. <https://doi.org/10.1016/j.phrs.2017.08.015>.
8. Memon R.A. et al. Effect of the polypill on adherence and prevention of cardiovascular diseases: a meta-analysis of randomized controlled trials. *Cureus.* 2023;15(1):e34134. <https://doi.org/10.7759/cureus.34134>.
9. Williams B., Mancia G., Spiering W. et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J.* 2018;39(33):3021–3104. <https://doi.org/10.1093/eurheartj/ehy339>.
10. Kónyi A., Sárszegi Z., Hild G., Gaszner B. Safety and effectiveness of combined antihypertensive and cholesterol-lowering therapy in high-/very high-risk patients. *J Comp Eff Res.* 2016;5(4):355–364. <https://doi.org/10.2217/cer-2016-0003>.
11. Mach F. et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias. *Eur Heart J.* 2020;41(1):111–188. <https://doi.org/10.1093/eurheartj/ehz455>.
12. Dahlöf B. et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required (ASCOT-BPLA). *Lancet.* 2005;366(9489):895–906. [https://doi.org/10.1016/S0140-6736\(05\)67185-1](https://doi.org/10.1016/S0140-6736(05)67185-1).
13. Sever P.S. et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients (ASCOT-LLA). *Lancet.* 2003;361(9364):1149–1158. [https://doi.org/10.1016/S0140-6736\(03\)12948-0](https://doi.org/10.1016/S0140-6736(03)12948-0).
14. Webster R. et al. Effectiveness of fixed dose combination medication ('polypills') compared with usual care: individual patient data meta-analysis of 3140 patients. *Int J Cardiol.* 2016;205:147–156. <https://doi.org/10.1016/j.ijcard.2015.12.015>.
15. Roshandel G., Khoshnia M., Poustchi H. et al. Effectiveness of polypill for primary and secondary prevention of cardiovascular diseases (PolyIran). *Lancet.* 2019;394(10199):672–683. [https://doi.org/10.1016/S0140-6736\(19\)31791-X](https://doi.org/10.1016/S0140-6736(19)31791-X).