Research article

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Effect of lipid-lowering treatment on lipid and glycemic profile of patients with elevated lipoprotein(a) levels

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ABSTRACT

Aim: The evaluation of the effect of lipid-lowering treatment in patients with elevated levels of lipoprotein(a) [Lp(a)].

Material and methods: A prospective study including 70 patients with dyslipidemia and elevated Lp(a) levels (>30 mg/dL) attending a Lipid Clinic in Greece. Subjects were allocated to the following therapies according to the national guidelines for cholesterol management: high-intensity statin monotherapy (S; n=28), ezetimibe added to high-intensity statin (SE; n=31), and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor added to high-intensity statin plus ezetimibe (SEP; n=11). Follow-up duration was 3 months. We investigated the effect of these lipid-lowering interventions on participants' lipidemic and glycemic profile. Comparisons between groups were adjusted for the baseline levels of the studied parameters.

Results: Mean age was 51 ± 15 years, 40% were male, 39% were diagnosed with familial hypercholesterolaemia (FH), 16% with atherosclerotic cardiovascular disease (ASCVD), while 36%, 33% and 15% were at very high, high, and moderate cardiovascular risk, respectively. All interventions significantly reduced apolipoprotein B (apoB), total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C), but only PCSK9 inhibitors

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significantly reduced Lp(a) levels (SEP: -28% vs SE: +11% vs S: +17%, p<0.05). Patients in the SE group achieved the highest rates of LDL-C target attainment (SEP: 36.4% vs SE: 12.9% vs S: 3.6% for LDL-C <55 mg/dL; SEP: 36.4% vs SE: 16.1% vs S: 7.1% for LDL-C <70 mg/dL, p<0.05 for the comparison among groups). No significant effect on glycemic profile across treatment groups was noted.

Conclusions: Add-on PCSK9 inhibitors were associated with the highest rates of LDL-C target achievement compared with high-intensity statin ± ezetimibe in high-risk patients with elevated Lp(a) and were the only class to significantly lower Lp(a) levels.

KEY WORDS: *Lipoprotein(a), apolipoprotein B, total cholesterol, low-density lipoprotein cholesterol, glucose, statins, ezetimibe, PCSK9 inhibitors*

INTRODUCTION

Over the past few years several studies have focused on lipoprotein(a) [Lp(a)], a lipid molecule with atherogenic, thrombogenic and inflammatory properties.[1] Elevated Lp(a), mostly genetically determined by the *LPA* gene locus, has been identified as an important cardiovascular risk factor as well as a risk factor for calcific aortic valve stenosis (CAVS), with a prevalence rate of ~20% in the general population.[2] Currently, there are no medications specifically approved for Lp(a) lowering.[3–5] In this context, current guidelines recommend optimal control of other cardiovascular risk factors.[6] In terms of cholesterol management, statins remain the cornerstone of lipid-lowering management, but they slightly increase Lp(a) levels.[7–10] Although most lipid modifying agents do not significantly alter Lp(a) concentration,[3–5] proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors have been shown to reduce Lp(a) levels.[11–13] On the other hand, type 2 diabetes (T2D) is a well-established adverse effect of statin therapy, mostly in those with predisposing factors, such as prediabetes, obesity, and increased triglycerides, albeit not superseding its cardiovascular benefit.[14,15] Ezetimibe and PCSK9 inhibitors seem to have a neutral effect on glycemic profile.[16–20]

In this context, we aimed to evaluate the effect of hypolipidaemic therapies on the lipidemic and glycemic profile of patients with elevated levels of Lp(a) in the setting of a lipid clinic.

MATERIALS AND METHODS

This was a prospective study including 70 consecutive adult patients with elevated Lp(a) levels (>30 mg/dL) and dyslipidemia attending the Outpatient Lipid Clinic of the University Hospital of Ioannina. The study protocol was approved by the Local Institutional Ethics Committee and informed consent was obtained from each patient. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the University General Hospital of Ioannina, Greece (896/21-12-2020).

Patients were allocated to 3 treatment groups according to the national guidelines for the management of dyslipidemias.[21] The 10-year total cardiovascular risk was estimated with the Systematic Coronary Risk Evaluation (SCORE) 2 model in apparently healthy subjects aged 40-69 years and with the SCORE 2 old persons (OP) model in those aged ≥70 years.[22] These models are recommended for the implementation of primary prevention strategies in apparently healthy individuals.[22] They have been integrated into the 2021 ESC prevention guidelines and are now available to low, moderate, high, and very high risk regions in Europe.[22] According to these guidelines, 28 naïve patients received high-intensity statin monotherapy (S), 31 patients on stable high-intensity statin treatment received ezetimibe (SE) and 11 patients on stable high-intensity statin treatment plus ezetimibe received a PCSK9 inhibitor (evolocumab or alirocumab) (SEP) (Figure 1).

High-intensity statins were considered those expected to result in low-density lipoprotein cholesterol (LDL-C) reduction >50%, namely rosuvastatin 20 - 40 mg and atorvastatin 40 - 80 mg.[23] Follow-up duration was 3 months.

All study participants were of Caucasian origin. A complete assessment of clinical and laboratory profile was performed at baseline visit and 3 months after the initiation or modification of lipid-lowering treatment. Demographic and clinical characteristics included: i) sex, ii) age, iii) smoking history, iv) concomitant diseases with a particular emphasis on atherosclerotic cardiovascular disease (ASCVD), which included coronary artery disease, stroke, peripheral artery disease and carotid stenosis ≥50%, CAVS, and cardiometabolic risk factors, v) body mass index (BMI) and vi) blood pressure (BP). Office BP measurements were based on ESC/ESH guidelines and performed with a validated upper-arm cuff BP measurement device and

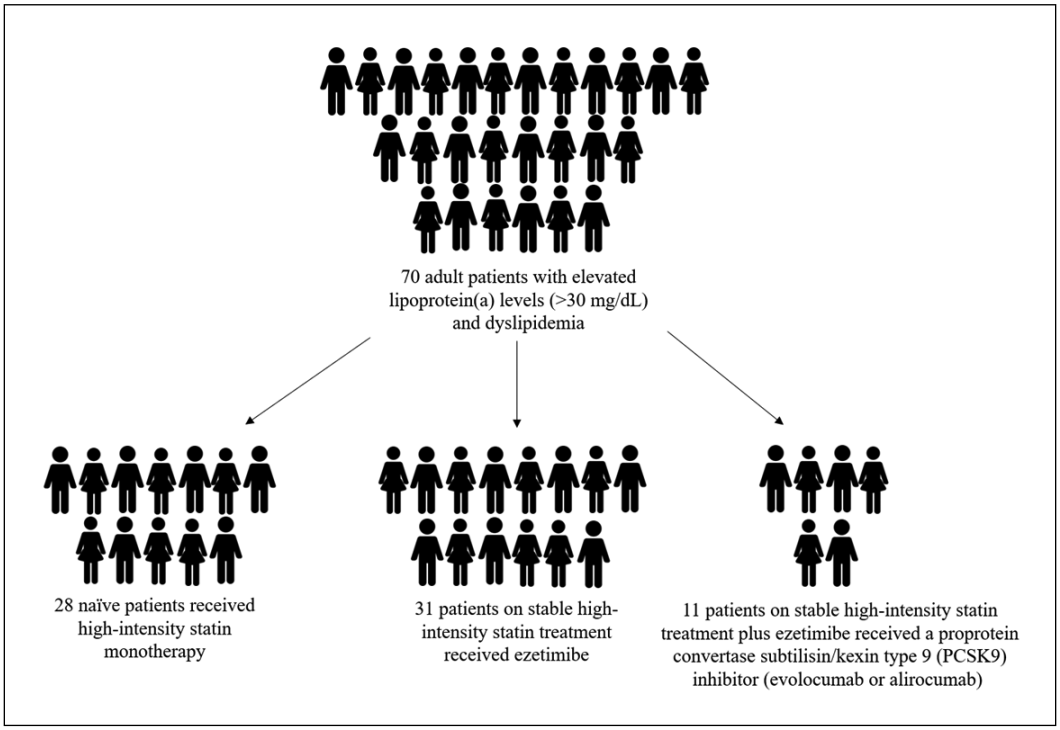

FIGURE 1 Study design and allocation groups.

an appropriate cuff size.[24] The corresponding instruments measuring subjects' height and weight were validated and calibrated, whereas BMI was calculated as: (weight, kg) / (height, m).[2] Heterozygous Familial Hypercholesterolaemia (HeFH) was defined according to the Dutch Lipid Clinic Network (DLCN) criteria.[25]

Laboratory data included: i) fasting plasma glucose (FPG), ii) insulin (INS), iii) Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) index (FPG, mg/dL x INS, mU/L /405), iv) uric acid (UA), v) a complete lipid profile, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), LDL-C, Lp(a) and apolipoprotein B (apoB) and vi) creatinine. Blood samples were collected in the morning into sterile Vacutainer-SST II advance tubes (Becton-Dickinson, Plymouth, UK) after overnight fasting for at least 8-12 h. Tubes were refrigerated immediately after collection, were centrifuged at 4°C within 40 min of blood sampling, and then were analyzed within 2 h. Serum concentrations of TC were determined enzymatically on an Olympus AU600 Clinical Chemistry Analyzer (Olympus Diagnostica, Hamburg, Germany). HDL-C was determined by a direct assay (Olympus Diagnostica, Hamburg, Germany). LDL-C was calculated using the Friedewald formula, provided that TG levels were <400 mg/dL (4.5 mmol/L). Serum apoB and Lp(a) levels were measured with a Behring Nephelometer BN100 and with reagents from Dade Behring GmbH analyzer (Liederbach, Germany). Renal function was estimated by eGFR with CKD-EPI (CKD Epidemiology Collaboration) formula using creatinine results from a method that had calibration traceable to isotope dilution mass spectrometry.[26] The HOMA-IR has been used widely as an indirect method for quantifying insulin resistance and pancreatic β-cell function.[27] Common reference levels for HOMA-IR range from 0.7-2.[27] Lp(a) cholesterol content was estimated as 30% of Lp(a) mass and subtracted from LDL-C to obtain LDL-$C_{Lp(a)corr}$ [LDL-$C_{Lp(a)corr}$ = LDL-C – 0,3 x Lp(a)].[28] Concomitant therapy was additionally recorded.

Statistical analysis

Continuous variables were tested for normality by the Kolmogorov-Smirnov test. Data are presented as mean ± standard deviation (SD) and median [interquartile range (IQR)] for parametric and non-parametric data, respectively. For categorical values, frequency counts and percentages were applied. Chi-square (χ^2) test was performed for interactions between categorical values. The independent sample *t*-test (parametric and non-parametric) was used for the comparison of continuous numeric values between 2 groups. One-way analysis of variance (one-way ANOVA) was performed to assess the difference of the variables of interest between ≥2 groups. Multivariate analysis of covariance (MANCOVA) was used for the comparison of continuous numeric values

between ≥2 groups after adjusting for the baseline values of the investigated variable of interest. Two-tailed significance was defined as p<0.05. Analyses were performed with the SPSS v21.0 software (SPSS Statistics for Windows, Version 28.0. Armonk, New York, NY, USA: IBM Corp).

RESULTS

In total, 70 subjects were included in the present study. Subjects' baseline characteristics are presented in Table 1. Briefly, mean age was 51 ± 15 years, 40% were male, 39% were diagnosed with HeFH, 16% with ASCVD, while 36%, 33% and 15% were at very high, high, and moderate cardiovascular risk, respectively. Among patients' baseline characteristics, it is worth noting that among 3 groups, patients who received additionally ezetimibe ± PCSK9 inhibitors had an increased prevalence of arterial hypertension and T2D compared to naïve patients, while patients who finally received PCSK9 inhibitors also had an increased prevalence of cardiovascular and chronic kidney disease, compared to the patients of the other 2 groups.

All interventions significantly reduced apoB, TC and LDL-C, but only PCSK9 inhibitors reduced significantly Lp(a) (Table 2). Specifically, PCSK9 inhibitors achieved the highest reduction in LDL-C (SEP: -56% vs SE: -43% vs S: -22%, p<0.05) and Lp(a) levels (SEP: -28% vs SE: +11% vs S: +17%, p<0.05). The same was noted for the change in LDL-$C_{Lp(a)corr}$ across 3 groups (Table 2). Patients in the SEP group achieved the highest rates of LDL-C target attainment (Table 3).

Among the study participants without diabetes (n=60), high-intensity statin treatment and the addition of ezetimibe to high-intensity statin had no significant effect on glycemic profile across treatment groups (Table 4). Similar results were noted for PCSK9 inhibitors, although it is worth mentioning the non-significant trend towards a decrease in HOMA-IR index by 19% (Table 4).

All therapeutic interventions were well tolerated, and no adverse events were mentioned during study.

TABLE 1. Study participants baseline characteristics.

	S	SE	SEP	Total sample
Number of patients (N)	**28**	**31**	**11**	**70**
Gender				
Male	32%	42%	55%	40%
Age				
<40	36%	16%	18%	24%
40-70	61%	74%	64%	67%
≥70	3%	10%	18%	9%
Age (years)	45 (±16)	54 (±13)	55 (±14)	51 (±15)
Smoking				
Never smoker	64%	58%	60%	61%
Former smoker	11%	16%	30%	16%
Current smoker	25%	26%	10%	23%
Arterial hypertension	11%	36% *	36%	26%
Type 2 Diabetes	4%	23% *	20%	15%
Familial Hypercholesterolaemia	21%	32%	100% *#	39%
Coronary Heart Disease	0	7%	64% *#	13%
Stroke	0	3%	9%	3%
Carotid stenosis	4%	0	9%	3%
Peripheral artery disease	0	0	18% *#	3%
Atherosclerotic Cardiovascular Disease	4%	10%	64% *#	16%
Aortic valve stenosis	0	0	9%	1%
Chronic Kidney Disease	0	0	18% *#	3%

Data are presented as N (%). Parametric variables are presented as mean ± SD and non-parametric as median (IQR).
*p<0.05 for the comparison with naïve patients treated with a high-intensity statin
#p<0.05 for comparison with patients treated with ezetimibe plus high-intensity statin
Abbreviations: S; high-intensity statin monotherapy, SE; high-intensity statin plus ezetimibe, SEP; high-intensity statin plus ezetimibe plus PCSK9 inhibitors

TABLE 2. Effect of lipid-lowering drugs on the lipidemic profile of patients with elevated Lp(a).

	Baseline Visit	After 3 Months	Absolute Change within each Group	% Change within each group
Total Cholesterol, mg/dL				
S	256 (±38)	177 (±35)	-79 (±51)‡	-31%‡
SE	176 (±23) *	151 (±23)*	-25 (±20)‡	-14%‡
SEP	217 (±52) *#	138 (±43)*	-78 (±30)‡*#	-36%‡*#
Triglycerides, mg/dL				
S	97 (57-263)	78 (45-371)	-21 (-140 to 284)‡	-22%‡
SE	105 (44-198)	81 (45-254)	-8 (-98 to 74)	-8%
SEP	96 (72-270)	79 (44-363)	-20 (-119 to 93)	-21%
High-density Lipoprotein Cholesterol, mg/dL				
S	60 (±15)	58 (±13)	-3 (±7)‡	-1%‡
SE	54 (±16)	54 (±14)	-1 (±7)	-0.2%
SEP	52 (±12)	51 (±15)	0	0
Low-density Lipoprotein Cholesterol, mg/dL				
S	174 (±34)	99 (±27)	-75 (±44)‡	-43%‡
SE	101 (±19)*	79 (±15)*	-22 (±19)‡	-22%‡
SEP	140 (±45)*#	63 (±30)#*	-78 (±37)‡*#	-56%‡*#
Low-density Lipoprotein Cholesterol corrected for Lipoprotein(a) Cholesterol, mg/dL				
S	153 (±36)	78 (±30)	-77 (±46)‡	-50%‡
SE	81 (±20) *	56 (±20) *	-25 (±20)‡*	-31%‡*
SEP	113 (±54) *#	42 (±34)*	-71 (±38)‡#	-63%‡#
Apolipoprotein B, mg/dL				
S	102 (±27)	70 (±18)	-32 (±28)‡	-31%‡
SE	85 (±26) *	65 (±13)	-20 (±20)‡	-24%‡
SEP	107 (±22) #	59 (±19)	-47 (±28)‡*	-44%‡*
Lipoprotein(a), mg/dL				
S	53.7 (30.9-168.8)	64.7 (23.6-145.0)	6 (±17)	11%
SE	57.8 (30.9-198.0)	69.1 (26.1-222.0)	10 (±18)‡	17%‡
SEP	79.2 (30.2-204.0)	48.8 (18.8-155.0)	-22 (±12)‡*#	-28%‡*#

Parametric variables are presented as mean ± SD and non-parametric as median (IQR).
‡p<0.05 for the comparison within each group
*p<0.05 for the comparison with patients treated with a high-intensity statin
#p<0.05 for comparison with patients treated with ezetimibe plus high-intensity statin
Abbreviations: S; high-intensity statin monotherapy, SE; high-intensity statin plus ezetimibe, SEP; high-intensity statin plus ezetimibe plus PCSK9 inhibitors

DISCUSSION

The present study shows that add-on PCSK9 inhibitors achieved the highest rates of LDL-C target attainment compared with high-intensity statin monotherapy ± ezetimibe in patients with Lp(a) levels ≥30 mg/dL. Moreover, PCSK9 inhibitors were the only class to significantly lower Lp(a). Interestingly, no differences were noted regarding the effect of these lipid-lowering interventions on the participants' glycemic profile.

Elevated Lp(a) is the most common inherited lipid disorder associated with ASCVD.[29] About 90% of the Lp(a) levels is autosomal dominantly inherited and strongly

TABLE 3. Effect of lipid-lowering drugs on achieving LDL-C target.

	LDL-C target reached after 3 months of lipid-lowering intervention			
	<55 mg/dL	<70 mg/dL	<100 mg/dL	<115 mg/dL
S (N=28)	3.6%	7.1%	21.4%	32.1%
SE (N=31)	12.9%	16.1%	32.2%	41.9%
SEP (N=11)	36.4%*	36.4%*	45.4%*	NA

*p<0.05 for the comparison among groups for each LDL-C target
Abbreviations: LDL-C; Low-density lipoprotein cholesterol, S; high-intensity statin monotherapy, SE; high-intensity statin plus ezetimibe, SEP; high-intensity statin plus ezetimibe plus PCSK9 inhibitors, NA; not applicable

TABLE 4. Effect of lipid-lowering drugs on the glycemic profile of patients with elevated Lp(a).

	Baseline Visit	After 3 Months	Absolute Change within each Group	% Change within each group
Glucose, mg/dL				
S	90 (±8)	91 (±12)	1 (±11)	1%
SE	97 (±11) *	98 (±10) *	0	0
SEP	91 (±6)	90 (±10)	-1 (±11)	-1%
Insulin, μU/mL				
S	7.2 (2.8-151.4)	7.3 (3.3-123.3)	0.4 (-28.1 to 18.4)	6%
SE	6.7 (2.8-42.0)	8.3 (2.9-30.3)	0.1 (-21.8 to 18.8)	1%
SEP	10.8 (3.1-55.9)	9 (2.4-37.1)	-1.8 (-27.5 to 6.4)	-17%
HOMA Insulin Resistance Index				
S	1.7 (0.4-38.1)	1.6 (0.6-42.6)	-0.1 (-1.5 to 4.5)	-6%
SE	1.7 (0.7-10.0)	2.1 (0.7-7.6)	0	0
SEP	2.6 (0.7-12.0)	2 (0.5-9.0)	-0.5 (-6.3 to -0.6)	-19%

Parametric variables are presented as mean ± SD and non-parametric as median (IQR).
*p<0.05 for the comparison with patients treated with a high-intensity statin
Abbreviations: S; high-intensity statin monotherapy, SE; high-intensity statin plus ezetimibe, SEP; high-intensity statin plus ezetimibe plus PCSK9 inhibitors

determined by a single gene, the *LPA* gene.[3] By the age of 2 the *LPA* gene is fully expressed.[30] Afterwards, Lp(a) levels are stable over time and seem not to be affected by diet, physical activity, or other environmental factors.[6] Evidence from experimental, observational, and genetic studies has demonstrated that increased Lp(a) is associated with increased risk for coronary heart disease (CHD), ischemic stroke, PAD, heart failure, CAVS, mitral valve stenosis and possibly retinopathy in diabetic patients.[31–37] Although Lp(a) thresholds (>30 mg/dL or >50 mg/dL; >75nmol/L or >125 nmol/L, respectively) were initially proposed, there is a linear relationship between Lp(a) levels and ASCVD.[6]

There are no medications specifically approved for Lp(a) lowering yet.[3–5] Specifically, novel therapies targeting apo(a), such as antisense oligonucleotides or silent RNAs, are effective in lowering Lp(a) by >90%, but their cardiovascular benefit is yet to be determined.[3,38,39] However, a few available therapeutic agents have a modest effect on Lp(a).[3–5] Although the effect of statin treatment on Lp(a) levels remains an area of controversy, it seems that statins slightly increase Lp(a) levels.[7–10] Most other lipid modifying agents, including ezetimibe do not significantly alter Lp(a) concentration,[3–5] except for PCSK9 inhibitors, which have been shown to reduce Lp(a) levels, by ~ 20-30%.[11–13]

Our results concerning the effect of high intensity statins, ezetimibe and PCSK9 inhibitors on patients with elevated Lp(a) levels agree with past evidence derived from the general population. Similar to our study, statins reduce LDL-C by 30-63%,[40] TGs by 14-33%,[41] and increase HDL-C up to 10%[42] in patients with hypercholesterolemia, with atorvastatin 40-80 mg and rosuvastatin 20-40 mg being the most potent ones. Nevertheless, the effect of statin treatment on Lp(a) levels remains an area of controversy. Statin trials have shown mixed results regarding their impact on Lp(a) levels. A large meta-analysis of 6 trials including 5256 patients randomized to various statins or placebo indicated that most statins increase Lp(a) by 8-24%, although a significant heterogeneity in the response of Lp(a) levels to statin administration, as well as between different statins was reported.[43] On the other hand, another meta-analysis of 39 trials including 24,448 patients randomized to receive various statins or placebo indicated a non-significant trend towards an increase in Lp(a) by 0.1% in statin groups (vs placebo), with no significant differences among statins or different intensities of statins.[44] Similarly, our study indicated a non-significant increase in Lp(a) levels in the group of patients who received a high intensity statin by 11%. Ezetimibe, a cholesterol absorption inhibitor, has a modest LDL-C lowering efficacy; 17% when used alone[45] and 14-25% when used in combination with statins.[46] Its effect on Lp(a) remains also controversial.[47] In a meta-analysis of 7 randomized controlled trials with ezetimibe monotherapy in 2237 patients with primary hypercholesterolemia, ezetimibe significantly reduced Lp(a) levels by 7.1%, whereas another meta-analysis including 11 double-blind randomized controlled trials with 1926 hypercholesterolemic adults, showed that ezetimibe, either as monotherapy vs placebo or in combination with statin vs statin monotherapy, did not significantly alter Lp(a) concentration.[47] In contrast to this evidence, our study showed that the addition of ezetimibe on high-intensity statin treatment significantly increased Lp(a) levels by 10%. This could be attributed at least in part to the small sample size of the study or to the different design of our study including only patients with elevated Lp(a) levels. On the other hand, our results are in agreement with past evidence derived from FOURIER and the ODYSSEY OUTCOMES trials[48–55] showing that PCSK9 inhibitors are highly effective in lowering LDL-C levels by ~60% in patients on statin therapy, as well as Lp(a) levels by 20-30%.[11,12,56] Of interest, the cardiovascular efficacy of these drugs have been shown superior in individuals with elevated Lp(a).[57] According to a post hoc analysis of the ODYSSEY OUTCOMES trial referring to statin-treated patients with LDL-C ~70 mg/dL, alirocumab was associated with a higher reduction in risk for major adverse cardiovascular events (MACE) in patients with mildly elevated Lp(a) levels (≥13.7 mg/dL) (adjusted treatment HR: 0.68, 95% confidence interval: 0.52-0.90) in comparison with those having lower Lp(a) levels (adjusted treatment HR: 1.11, 95% confidence interval: 0.83-1.49).[57] Similarly, according to a post hoc analysis of the FOURIER trial, patients with higher baseline Lp(a) levels (>37 nmol/L) experienced greater absolute reductions in Lp(a) with evolocumab and tended to derive greater coronary benefit (HR: 0.77, 95% confidence interval: 0.67-0.88) in comparison with those having lower baseline Lp(a) levels (HR: 0.93, 95% confidence interval: 0.80-1.08).[58]

T2D development is the caveat of statin therapy, mainly concerning high-intensity statins. A meta-analysis of clinical trials (13 randomized controlled endpoint trials of statins with 91140 participants) showed that statins were associated with an increased risk of newly developed diabetes, with the absolute risk increase by statins being 0.4%.[14,15,59] It is worth noting, however, that the increase in T2D development risk mainly concerns patients with predisposing factors, such as prediabetes and obesity and definitely this risk does not supersede the cardiovascular benefit of statins.[14,15,59] In our study high-intensity statin treatment had no significant effect on the participants' glycemic profile, but its small size and short follow-up, along with the lack of data on glycosylated hemoglobin test (HbA1C) levels consist major limitations. Our results showing a neutral effect of the addition of ezetimibe on the glycemic profile of patients with elevated Lp(a) levels are similar to past evidence in the general population. In the IMPOVE-IT Trial the addition of ezetimibe to simvastatin vs simvastatin alone did not increase the risk of new-onset diabetes (HR: 1.04, 95% confidence interval: 0.94-1.15).[20] Furthermore, the results for PCSK9 inhibitors are also in agreement with the data from clinical trials so far. Published clinical studies to date have not demonstrated any correlation between PCSK9 inhibition, insulin resistance, plasma glucose levels, pancreas insufficiency, or increased rates of T2M.[16–19]

It is worth noting that this is the first study concerning exclusively patients with elevated Lp(a) levels, especially considering the association between very low Lp(a) levels and incident T2D, an association derived from large prospective epidemiological cohorts with robust durations of follow-up.[60] T2D prevalence in our study (15%) was similar to that of a previous retrospective study (11%) conducted in our clinic and including 1241 patients with dyslipidemia.[61] In addition, a non-significant trend towards a reduction in HOMA index was noted with PCSK9 inhibitors which lowered modestly Lp(a) in our study. Therefore, more evidence is needed to investigate the causality between Lp(a) and T2D and whether Lp(a) reduction by

treatment modalities can lead to incident T2D.[60]

The major limitations of this study were its small sample size and follow-up, along with the lack of data on dietary habits and physical activity of the patients. Another limitation is the lack of Lp(a) values before any therapeutic intervention in patients receiving ezetimibe or PCSK9 inhibitors. On the other hand, this study is a real-world study conducted in an outpatient lipid clinic, investigating the effect of the available lipid-lowering therapies in dyslipidemic patients with elevated Lp(a) levels.

CONCLUSIONS

Add-on PCSK9 inhibitors were associated with the highest rates of LDL-C target attainment compared with high-intensity statin treatment ± ezetimibe, and the only class to significantly lower Lp(a) in patients with elevated Lp(a) levels. Although these interventions did not affect participants' glycemic profile, longer follow up is needed.

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Conflict of Interest

ADK has received personal fees from Novartis, outside the submitted work. FB has received honoraria and personal fees from Amgen, Novartis, Novo Nordisk and Viatris, outside the submitted work. GL has received honoraria, grants and non-financial support from Angelini, Bayer, Menarini, and Sanofi, outside the submitted work. EL reports personal fees and non-financial support from Amgen, personal fees from Servier, personal fees from Boehringer-Ingelheim, personal fees and non-financial support from AstraZeneca, personal fees from MSD, personal fees from Lilly, personal fees and non-financial support from Bayer, personal fees from Novartis, personal fees from Chiesi, outside the submitted work. CT and AT report no conflicts of interest associated with the present work.

ΠΕΡΙΛΗΨΗ

Μελέτη επίδρασης της υπολιπιδαιμικής αγωγής στο λιπιδαιμικό και γλυκαιμικό προφίλ ασθενών με αυξημένα επίπεδα λιποπρωτεΐνης(α)

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Σκοπός: Σκοπός της μελέτης ήταν η αξιολόγηση της επίδρασης των υπολιπιδαιμικών φαρμάκων στο λιπιδαιμικό και γλυκαιμικό προφίλ ασθενών με αυξημένα επίπεδα λιποπρωτεΐνης(α) [Lp(a)].

Υλικό και μέθοδοι: Προοπτική μελέτη στην οποία συμμετείχαν 70 ασθενείς με δυσλιπιδαιμία και αυξημένα επίπεδα Lp(a) >30 mg/dL που παρακολουθούνται στο Εξωτερικό Ιατρείο Διαταραχών του Μεταβολισμού των Λιπιδίων και Παχυσαρκίας του Πανεπιστημιακού Γενικού Νοσοκομείου Ιωαννίνων. Έγινε έναρξη αγωγής με ισχυρή στατίνη σε 28 ασθενείς (ομάδα S), προσθήκη εζετιμίμπης σε 31 ασθενείς που ελάμβαναν ισχυρή στατίνη (ομάδα SE) και προσθήκη αναστολέα PCSK9 σε 11 ασθενείς που ελάμβαναν συνδυασμό ισχυρής στατίνης με εζετιμίμπη (ομάδα SEP), σύμφωνα με τις διεθνείς κατευθυντήριες οδηγίες για την επίτευξη των προτεινόμενων στόχων που αφορούν την χοληστερόλη των χαμηλής πυκνότητας λιποπρωτεϊνών (LDL-C). Η διάρκεια της παρακολούθησης ήταν 3 μήνες και μελετήθηκε η επίδραση των παραπάνω παρεμβάσεων στο λιπιδαιμικό και γλυκαιμικό προφίλ των ασθενών που συμμετείχαν στη μελέτη. Οι συγκρίσεις μεταξύ των ομάδων διορθώθηκαν για τα αρχικά επίπεδα των παραμέτρων που μελετήθηκαν.

Αποτελέσματα: Από τα 70 άτομα που συμμετείχαν στη μελέτη (51 ± 15 ετών, 40% άνδρες), το 39% είχε οικογενή υπερχοληστερολαιμία, το 16% είχε εγκατεστημένη καρδιαγγειακή νόσο, ενώ το 36%, 33% και 15% ανήκε στην κατηγορία του πολύ υψηλού, υψηλού και μέτριου καρδιαγγειακού κινδύνου, αντίστοιχα. Όλες οι παρεμβάσεις

μείωσαν σημαντικά τα επίπεδα της ολικής χοληστερόλης, LDL-C και απολιποπρωτεΐνης Β, ενώ μόνο η χορήγηση των PCSK9 αναστολέων συσχετίστηκε με σημαντική μείωση των επιπέδων της Lp(a) (SEP: -28% vs SE:+11% vs S:+17%, p<0.05). Οι ασθενείς που έλαβαν PCSK9 αναστολείς πέτυχαν τα υψηλότερα ποσοστά επίτευξης των στόχων της LDL-C (SEP: 36.4% vs SE: 12.9% vs S: 3.6% για LDL-C <55 mg/dL; SEP: 36.4% vs SE: 16.1% vs S: 7.1% για LDL-C <70 mg/dL, p<0.05 για τη σύγκριση μεταξύ των ομάδων). Καμία από τις παρεμβάσεις δεν είχε σημαντική επίδραση στο γλυκαιμικό προφίλ των ασθενών της μελέτης.

Συμπεράσματα: Τα αποτελέσματα της μελέτης επιβεβαιώνουν την υψηλότερη αποτελεσματικότητα της επιπρόσθετης χορήγησης PCSK9 αναστολέων στην επίτευξη των στόχων της LDL-C αλλά και στη μείωση της Lp(a) συγκριτικά τη χορήγηση υψηλής έντασης στατίνης ± εζετιμίμπης σε ασθενείς υψηλού κινδύνου με αυξημένα επίπεδα Lp(a).

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