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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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THE IMPACT OF DISEASE-MODIFYING MEDICATIONS ON THE LIPID PROFILE OF PATIENTS WITH ISCHEMIC HEART DISEASE

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Abstract.

Background: Ischemic heart diseases (IHD) refer to narrowing of coronary artery resulting in partial or complete stenosis making patients susceptible to myocardial infarction (MI) and stroke challenging the healthcare provider due to high risk of morbidity and mortality. The aim of this study was directed to identify the role various disease-modifying medications (DMMs) in the treatment of IHD-associated risk factors, including statins, sodium-glucose transporter (SGLT2) inhibitors, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors.

Methods: A total of 500 patients recruited from multicentre were enrolled in this randomized controlled clinical trial. The patients were subdivided into 4-treatment groups, including statin group, SGLT-2 inhibitors group, PCSK9 inhibitors group, or combination therapy group. The serum lipid parameters were measured initially and after 12 months post-therapy.

Results: The treatment groups have demonstrated reduction of lipid parameters at the end of the 12-months of study period. The combination therapy has provided the greatest reduction (-74 ± 10 mg/dL, $p<0.05$). Age and gender has slightly modulated the response to these medications.

Conclusion: The combination of DMMs carry may be a valuable tool for managing the lipid parameters reducing risk factors that prone IHD-patients to stroke and MI, suggesting additional therapeutic role for cardiovascular disease managements.

Key words. Ischemic heart diseases, lipid profiles, disease-modifying medications, statins, sodium-glucose transporter inhibitors, proprotein convertase subtilisin/kexin type 9 inhibitors.

Introduction.

Ischemic heart disease (IHD) has increasing reported as a challenging for healthcare providers, due to associated morbidity and mortality rates [1]. The key modifiable parameter in the profile of IHD is dyslipidemia [2]. The pathology of dyslipidemia invok[e the initiation and continuation of the IHD, being the leading cause atherosclerosis and hence coronary artery stenosis superimposed by increased level of low-density lipoprotein (LDL) and triglycerides alongside reduced high density lipoprotein (HDL) [3,4].

The cause of IHD is multifactorial and management require a combination of different medication to collaborate and hinder the pathology [5]. Disease-modifying medications (DMDs) are hallmark for reducing diseases pathogenesis profile to alter these risk factors [6,7]. These medications include various agents, including statins, sodium-glucose transporter (SGLT2) inhibitors, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, and ezetimib, which could alter disease progression and complications profile [8]. Because these medications decrease the concentration of lipid parameters and improve the cardiovascular functionality [5]. The cardiovascular morbidity and mortality rates were reduced by using DMMs, particularly when used in combinations [9].

Among these DMMS agents, include antiplatelet agents (e.g. aspirin and clopidogrel) which prevent intravascular coagulation and thereby preventing the complication of IHD [10]. Statins (e.g. atorvastatin and rosuvastatin) are also effective in reducing the IHD profile and complications via blocking HMG-CoA reductase inhibitors thereby reducing LDL and TG alongside increasing HDL thereby preventing plaque formation [11]. PCSK9 inhibitors (evolocumab) induced LDL reduction for high-risk patients [12]. Ezetimibe also reduced cholesterol lowering helping in reducing complications of atherosclerosis [12]. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and selective beta-1 blockers preserve the heart from cardiac remodelling due to complication of elevated blood pressue, hyperlipdemia, and coronary stenosis [13]. SGLT2 inhibitors (canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin) reducing heart failure hospitalizations and cardiovascular death [9,14]. GLP-1 receptor agonists (liraglutide) also provide cardiovascular protection [10]. However, through these interactions, insights have been approached into the complex pathophysiology of IHD and highlight the need for a global approach to patient management. Therefore, this study was designed to assess the role of currently used DMMs in the modulation of IHD profile.

Materials and Methods.

Study Design: In a multicentre, randomized controlled trial (RCT) study, we assessed the impact of disease-modifying medications on the lipid profile of IHD patients. RCT was intended to evaluate the efficacy of statins, SGLT-2 inhibitors, PCSK9 inhibitors, and in combination in managing LDL-C, total cholesterol, triglycerides, and HDL-C over 12 months. Participants were randomly assigned to one of the four treatment groups: These four approaches involve statins, SGLT-2 inhibitors, PCSK9 inhibitors, or a combination of the three medications. The choice of particular medication and their doses adhered to up-to-date, evidence-based prescriptions, and dosage modification occurred only if indicated by the therapeutic response and side effects experienced by the patient.

Sample Size Calculation: The sample size was calculated to determine if there was a significant difference in lipid profiles between the treatment groups. This calculation was based on the

resultant changes in the primary outcome of LDL-C. We used a standard variation in LDL changes of 20 mg/dL, alpha level of 0.05, and power of 0.90 to detect a 15 mg/dL difference between any two groups. According to these parameters, we assumed that 100 patients per group would be needed, 20% dropouts, therefore we included 500 patients in our study.

Inclusion and Exclusion Criteria:

Adults aged 18 years and over diagnosed with IHD who had undergone coronary angiography or non-invasive imaging were included in this study. Participants were eligible if they had dyslipidemia defined by LDL-C >100 mg/dL or HDL-C <40 mg/dL in men and <50 mg/dL in women, or triglyceride >150 mg/dL. Furthermore, participants had to consent and agree to participate. Exclusion criteria included patients with a history of hypersensitivity or contraindication to study medications, pregnant or breastfeeding women, those with a known liver or kidney dysfunction, those participating in another clinical trial that may be affecting lipid levels.

Data Collection: Data collection included demographic characteristics, medical history, and an assessment of the participants' lipid profile at the baseline. Subsequent reassessment of adherence, side effects and interim lipid profile data was carried out at 3, 6, 9 and 12 months after enrolment. To assess changes in lipid profile at 12 months all baseline measurements were repeated at the last visit.

Outcome Measures: Primary Outcome: Change in LDL-C levels from baseline to 12 months.

Secondary Outcomes: Changes in HDL-C, total cholesterol, and triglyceride levels. Incidence of cardiovascular events (e.g., myocardial infarction, stroke), medication adherence rates, and side effect profiles.

Ethical Considerations: The study protocol was reviewed and approved by the Scientific committee. Consent was obtained in writing before enrolment for all participants. The study was subject to the Declaration of Helsinki and Good Clinical Practice guidelines.

Adjustment for Multiple Comparisons: To ensure the accuracy of the results, we considered the risk of making Type I errors due to multiple comparisons. To address this issue, we applied the Bonferroni correction method to adjust the p-values in both the primary and secondary outcome analyses. Alternatively, if it was deemed more suitable based on the number of comparisons and the correlation among outcomes, we utilized a less conservative approach known as the Benjamini-Hochberg procedure to control the false discovery rate.

Statistical Analysis: All statistical analyses were conducted using GraphPad Prism (V9, USA). Data are represented as mean ± standard deviation. Before analysis, data were evaluated for normality using the Shapiro-Wilk test One-way analysis of variance (ANOVA) was applied to determine significant differences between studied groups at p value less than 0.05 followed by post-hoc Tukey's test to recognize the specific pairwise differences.

Results.

Compared to baseline levels, the plasma LDL-C concentration revealed that all medications have significantly (P<0.05) reduced the plasma concentration of LDL-C after 12 months of continuous use. The reduction of LDL-C level after treatment was significant in comparison to baseline levels (P<0.05), the lowest value was with SGLT-2 and the highest was with PCSK9, statin or combination therapy (Figure 1).

Analysis of lipid parameters revealed significantly greater TC reduction of in PCSK9 inhibitors or combination therapy groups compared to statin or and being lowest with SGLT-2 inhibitors (Figure 3). However, the reduction of TG was significantly better in SGLT-2 inhibitors or combination therapy groups compared to statin or PCSK9 inhibitors. The HDL-C elevation was significantly the lowest with PCSK9 inhibitors compared to SGLT-2 inhibitors or combination therapy (Figure 2).

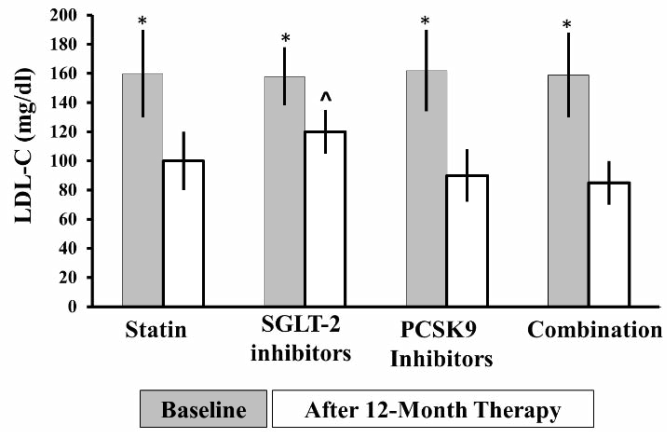

Figure 1. *Serum LDL-C concentration at baseline versus after 12 months of using either statins, PCSK9 inhibitors, SGLT-2 inhibitors, or a combination therapy. Data expressed as mean ± standard deviation. *^ indicate significant differences at p<0.05 using One-Way-ANOVA with post-hoc analysis. * as compared to after 12-months of therapy within the group. ^ as compared to after 12-months of therapy between the groups.*

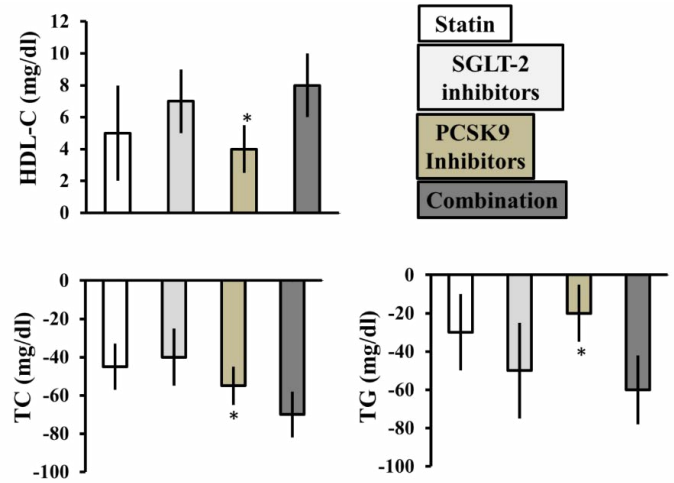

Figure 2. *Concentration changes of lipid parameters after 12 months of using either statins, PCSK9 inhibitors, SGLT-2 inhibitors, or a combination therapy. Data expressed as mean ± standard deviation. * indicate significant differences at p<0.05 using One-Way-ANOVA with post-hoc analysis. * as compared to after 12-months of therapy within the group.*

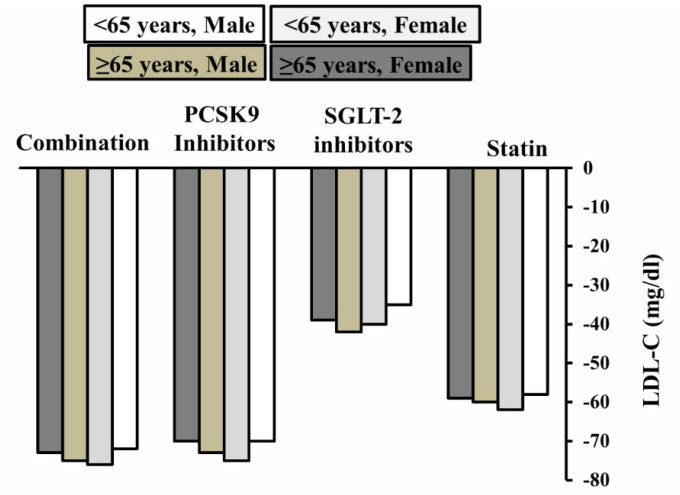

Figure 3. *Subgroup analysis of LDL-C Reduction by age and gender. Data expressed as an average reduction of LDL-C after 12 months of using either statins, PCSK9 inhibitors, SGLT-2 inhibitors, or a combination therapy with stratification of results based on age and sex.*

Table 1. *Incidence of cardiovascular events and medication adherence rates.*

Treatment Group	Cardiovascular Events (n)	Adherence Rate (%)
Statins	5	92
SGLT-2 Inhibitors	4	89
PCSK9 Inhibitors	3	95
Combination	2	90

Stratification of the results based on age and sex have revealed greater LDL-C reduction of in <65 years, female group using PCSK9 inhibitors or combination therapy and being lowest with SGLT-2 inhibitors (CI95%, Figure 3).

The incidence of cardiovascular events was lowest in the combination therapy group, which also maintained high adherence rates, though PCSK9 inhibitors had the highest adherence (Table 1).

Discussion.

The findings of the present study confirmed that the LDL levels were reduced in all treated groups, and hence markedly improve the cardiovascular disease profile. Moreover, combination of DMMs (Statin, SGLT-2 inhibitors, PCSK9 inhibitors) have shown a remarkably greater LDL reduction (-74 ± 10 mg/dl, $p<0.05$).

The lipid reduction profile associated with this medication will induced remarkably higher improvement in cardiovascular disease prevention which is in congruent with previous findings reported by earlier published guidelines supporting the intensive lipid-lowering approaches in patients at high cardiovascular risk [5,9].

The reduction in lipid profile was strong in PCSK9 inhibitors group compared to other groups (-72 ± 12 mg/dl, $p<0.05$) providing a clear insight for application of PCSK9 inhibitors in IHD patients [9]. The mechanism by which PCSK9 inhibitors is helpful could be explained in the context of the role of PCSK9 in increasing the LDL receptor expression and hence increased LDL removal from circulation [15,16]. Moreover, SGLT-2 inhibitors have distinctively reduced TG compared to statins and PCSK9 inhibitors, this finding is also in agreement with Basu et al. (2018) [17] and Bechmann et al. (2024) [18], who have confirmed that SGLT-2 inhibitors reduced TG but at the same time increased LDL, this finding was explained in the context of the capacity of SGLT2 inhibition which reflects that the increased LDL levels demonstrated with this therapy is related to decreased clearance of LDL from the circulation and concurrent increased lipolysis of TG-rich lipoproteins, moreover, SGLT2 inhibition perhaps improved insulin sensitivity and reduced hepatic lipogenesis, while the improved HDL alteration potentially enhanced reverse cholesterol transport mechanisms [19-21].

The comprehensive improvement in lipid parameters (HDL-C, total cholesterol, and triglycerides) associated with combined therapy underscore integrated benefit of blocking of more than one pathway of lipid synthesis, this combined impact harmonized with earlier clinical trials of using these DMMs to provide effective therapy against lipid and hence improve IHD [22-25]. These drugs reprogrammed the fundamental metabolic pathways and boosts lipid homeostasis alongside AMP-activated protein kinase signalling and fatty acid oxidation, overall impact of these drugs provide cardio protection and hinder pathogenesis of cardiac damage [26-29]. The mechanism underlying the improvement in HDL-C, total cholesterol, and triglycerides associated with combination therapy is explained in the context of inhibitory activity of this agent in different master metabolic enzyme (HMG-CoA, PCSK9, and SGLT-2) resulting in more intensive than individual drug alone [30,31], particularly, the combination therapy was useful for hypertriglyceridemia [9,21].

The improved systemic lipid parameters and proper patient-medication adherence in patients on combination therapy provided an additional advantage for the use of these medication together for extensive protection, this adherence also reported in previous research by Al-Maskari et al. (2023) covering the potential importance of adherence to medication to achieve the goal [32].

The subgroup analyses revealing slightly greater LDL-C reductions in females and younger patients within certain treatment groups suggest the potential for personalized treatment strategies based on demographic characteristics. This finding aligns with the research by Kim et al. (2020), who highlighted gender differences in the impact of IHD on heart failure, suggesting that lipid-lowering strategies might also need to consider gender-specific responses [3].

Conclusion.

The combination of DMM medications carry a great values for managing the lipid parameters, potentially reducing risk factors that prone IHD-patients to stroke and MI, providing additional tool with supported evidence for cardiovascular disease managements.

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