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**OPTIMIZING STATIN THERAPY IN THE MANAGEMENT OF ISCHEMIC
HEART DISEASE: A CLINICAL ASSESSMENT OF HIGH-INTENSITY REGIMENS
AND ADHERENCE FACTORS**

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Abstract: Ischemic heart disease (IHD) remains the leading cause of mortality in Uzbekistan, necessitating aggressive lipid-lowering strategies. Despite clear international guidelines, the utilization of high-intensity statin therapy remains suboptimal due to concerns regarding side effects and poor patient adherence. This article presents a prospective clinical study conducted at the Department of Cardiology of Andijan State Medical Institute. Using the IMRAD framework, the research evaluates the efficacy and safety of high-intensity Rosuvastatin therapy in patients with stable angina and post-myocardial infarction status. The study involved 200 patients randomized into a standard care group and an intensified education-monitoring group. The results demonstrate that patients receiving intensified support achieved guideline-directed LDL-cholesterol targets significantly more often (65 percent vs 30 percent) without a significant increase in hepatic or muscular adverse events. The study concludes that the primary barrier to effective statin therapy is not biological intolerance but rather psychosocial resistance, which can be overcome through targeted education and monitoring.

Keywords: ischemic heart disease, statins, rosuvastatin, LDL-cholesterol, pleiotropic effects, medication adherence.

**ОПТИМИЗАЦИЯ ТЕРАПИИ СТАТИНАМИ ПРИ ЛЕЧЕНИИ
ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА: КЛИНИЧЕСКАЯ ОЦЕНКА
ВЫСОКОИНТЕНСИВНЫХ РЕЖИМОВ И ФАКТОРОВ ПРИВЕРЖЕННОСТИ**

Аннотация: Ишемическая болезнь сердца (ИБС) остается ведущей причиной смертности в Узбекистане, что требует агрессивных стратегий снижения уровня липидов. Несмотря на четкие международные рекомендации, использование высокоинтенсивной терапии статинами остается неоптимальным из-за опасений по поводу побочных эффектов и низкой приверженности пациентов. В данной статье представлено проспективное клиническое исследование, проведенное на кафедре кардиологии Андijanского государственного медицинского института. Используя структуру IMRAD, исследование оценивает эффективность и безопасность высокоинтенсивной терапии розувастатином у пациентов со стабильной стенокардией и постинфарктным состоянием. В исследовании приняли участие 200 пациентов, рандомизированных в группу стандартного лечения и группу интенсивного обучения и мониторинга. Результаты показывают, что пациенты, получающие интенсивную поддержку, достигали целевых уровней ХС-ЛПНП значительно чаще (65 процентов против 30 процентов) без значительного увеличения печеночных или мышечных побочных эффектов. Исследование делает вывод, что основным барьером для эффективной терапии статинами является не биологическая непереносимость, а психосоциальное сопротивление, которое можно преодолеть с помощью целевого обучения и мониторинга.

Ключевые слова: ишемическая болезнь сердца, статины, розувастатин, холестерин ЛПНП, плейотропные эффекты, приверженность к лечению.

**YURAK ISHEMIK KASALLIGINI DAVOLASHDA STATINLAR TERAPIYASINI
OPTIMALLASHTIRISH: YUQORI INTENSIV REJIMLAR VA KOMPLAYENS
OMILLARINING KLINIK VAHOSI**

Annotatsiya: Yurak ishemik kasalligi (YIK) O'zbekistonda o'limning asosiy sababi bo'lib qolmoqda, bu esa lipidlar darajasini agressiv pasaytirish strategiyalarini talab qiladi. Aniq xalqaro tavsiyalarga qaramay, yuqori intensivli statin terapiyasidan foydalanish nojo'ya ta'sirlar va bemorlarning davolanishga rioya qilmasligi (komplayens pastligi) sababli yetarli darajada emas. Ushbu maqolada Andijon davlat tibbiyot institutining Kardiologiya kafedrasida o'tkazilgan prospektiv klinik tadqiqot natijalari keltirilgan. IMRAD tuzilmasiga asoslangan ushbu ish barqaror stenokardiya va miokard infarktidan keyingi holatdagi bemorlarda yuqori intensivli Rozuvastatin terapiyasining samaradorligi va xavfsizligini baholaydi. Tadqiqotda standart parvarish guruhi va kuchaytirilgan ta'lim-monitoring guruhiga randomizatsiya qilingan 200 nafar bemor ishtirok etdi. Natijalar shuni ko'rsatadiki, kuchaytirilgan yordam olgan bemorlar jigar yoki mushaklardagi nojo'ya ta'sirlarning sezilarli o'sishsiz, tavsiya etilgan PzLP-xolesterin (LDL-C) maqsadlariga sezilarli darajada ko'proq erishdilar (65 foizga qarshi 30 foiz). Tadqiqot samarali statin terapiyasidagi asosiy to'siq biologik o'zlashtira olmaslik emas, balki psixosotsial qarshilik ekanligi va buni maqsadli ta'lim hamda monitoring orqali yengish mumkinligi haqida xulosa qiladi.

Kalit so'zlar: yurak ishemik kasalligi, statinlar, rozuvastatin, PzLP-xolesterin, pleyotrop ta'sirlar, davolanishga sodiqlik.

INTRODUCTION

Ischemic heart disease (IHD) constitutes the single largest contributor to the global burden of disease and is particularly prevalent in Central Asia due to dietary habits and lifestyle factors. The pathophysiology of IHD is intrinsically linked to atherosclerosis, a process driven by the accumulation of low-density lipoprotein cholesterol (LDL-C) within the arterial intima. Consequently, the reduction of LDL-C is a cornerstone of secondary prevention. Statins, or HMG-CoA reductase inhibitors, have revolutionized cardiology not only by lowering cholesterol but also through their pleiotropic effects, which include plaque stabilization, reduction of vascular inflammation, and improvement of endothelial function.

Current guidelines from the European Society of Cardiology (ESC) and the American Heart Association (AHA) strongly recommend "high-intensity" statin therapy for all patients with established IHD, aiming for LDL-C reduction of at least 50 percent from baseline and a target level below 1.4 mmol/L. However, a significant gap exists between these evidence-based guidelines and real-world clinical practice in Uzbekistan. Many practitioners prescribe suboptimal doses of statins due to an exaggerated fear of hepatotoxicity or myopathy. Furthermore, patients often discontinue therapy due to the "nocebo" effect, where negative expectations lead to perceived side effects, or due to misinformation from social circles regarding the safety of long-term medication.

At the Department of Cardiology of Andijan State Medical Institute, it was hypothesized that the widespread underutilization of statins is a modifiable behavioral issue rather than a pharmacological limitation. We proposed that a structured intervention involving patient education on the safety of statins, combined with rigorous lipid monitoring, would significantly improve adherence and clinical outcomes. This article aims to evaluate the efficacy of high-

intensity Rosuvastatin therapy in a local cohort of IHD patients and to analyze the impact of psychosocial support on treatment adherence.

METHODS

This randomized, open-label, prospective study was conducted at the Andijan State Medical Institute Clinic over a period of 12 months. The study protocol adhered to the Helsinki Declaration and was approved by the institutional ethics board.

Study Population - The study recruited 200 patients aged 40 to 75 years with a confirmed diagnosis of Ischemic Heart Disease (stable angina pectoris functional class II-III or history of myocardial infarction >6 months prior). Inclusion criteria required a baseline LDL-C level greater than 1.8 mmol/L. Patients with active liver disease (ALT/AST >3 times the upper limit of normal), severe renal insufficiency, or known hypersensitivity to statins were excluded.

Study Design - The research methodology utilized a randomized allocation process to divide the participants into two distinct and equal cohorts for comparative analysis. The first cohort, designated as Group A or the Standard Care group, consisted of one hundred patients who were prescribed high-intensity statin therapy, specifically Rosuvastatin at doses of 20 to 40 mg or Atorvastatin at 40 to 80 mg. The management protocol for this group adhered to conventional clinical practice, involving routine follow-up visits scheduled every three months without the inclusion of any specific or structured educational interventions. The second cohort, identified as Group B or the Intensified Care group, also comprised one hundred patients who received identical statin prescriptions to the control group. However, the management strategy for this group was augmented by a comprehensive support program. This included mandatory participation in monthly educational sessions focused on explaining the physiological benefits of plaque stabilization and clarifying the rarity of severe side effects. Furthermore, patients in this group received proactive monthly telephone calls from the research team to monitor medication adherence and immediately address any emerging concerns or misconceptions.

Endpoints and Assessment - The primary efficacy endpoint was the percentage of patients achieving the LDL-C target of <1.4 mmol/L at 12 months. Secondary endpoints included the percentage change in high-sensitivity C-reactive protein (hs-CRP) as a marker of inflammation, and the incidence of adverse events (myalgia, elevation of liver enzymes, new-onset diabetes). Adherence was measured using the Morisky Medication Adherence Scale (MMAS-8).

Statistical Analysis - Data were analyzed using SPSS 26.0 software. Continuous variables were compared using Student's t-test, and categorical variables were analyzed using the Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

The study revealed a stark contrast in outcomes driven by adherence levels rather than drug efficacy, as the prescribed molecules were identical in both groups.

Lipid Lowering Efficacy At the 12-month follow-up, patients in Group B (Intensified Care) achieved significantly lower mean LDL-C levels compared to Group A (1.35 mmol/L vs 1.9 mmol/L). Crucially, 65 percent of patients in Group B successfully reached the stringent target of <1.4 mmol/L, whereas only 30 percent of patients in Group A achieved this goal. This disparity was largely attributed to dose de-escalation or discontinuation in Group A; 40 percent of patients in the standard care group had either stopped the drug or reduced the dose on their own advice or that of a non-specialist, citing vague symptoms or fear of liver damage.

Anti-inflammatory Effects - The pleiotropic effect of statins was evident in the reduction of systemic inflammation. Group B showed a statistically significant reduction in hs-CRP levels (-45 percent from baseline) compared to Group A (-20 percent). This suggests that consistent high-

intensity therapy effectively dampens the vascular inflammation that precipitates acute coronary syndromes.

Safety and Tolerability - Contrary to common fears, the incidence of true pharmacological intolerance was low and similar in both groups. Asymptomatic elevation of liver transaminases ($>3x$ ULN) occurred in only 1.5 percent of the total population. Muscle symptoms (myalgia) were reported by 12 percent of Group A but only 4 percent of Group B. Since the drug regimen was the same, the higher rate of muscle complaints in the standard group suggests a "nocebo" effect driven by anxiety and lack of reassurance. No cases of rhabdomyolysis were observed.

Adherence Metrics - The MMAS-8 scores indicated "high adherence" in 82 percent of Group B participants versus only 45 percent in Group A. The structured education successfully debunked myths about statin toxicity, empowering patients to continue therapy.

DISCUSSION

The findings from Andijan State Medical Institute highlight that the management of Ischemic Heart Disease is as much a sociological challenge as it is a biological one.

The Reality of Statin Intolerance - Our data supports the international consensus that true statin intolerance is rare. The significantly higher reporting of side effects in the unmonitored group points to psychological factors. However, the management of these patients requires careful consideration of biological markers as well. As highlighted by Juraboyev and Tashtemirova [9], the assessment of lipid peroxidation processes and lipid metabolism disorders in patients with ischemic heart disease undergoing hypolipidemic therapy is crucial. Understanding these underlying metabolic processes can help differentiate between true pharmacological intolerance and nocebo effects, ensuring that essential therapy is not prematurely discontinued.

Systemic Metabolic Context - The necessity of strict lipid control must be viewed within the broader context of systemic metabolic health. Tashtemirova [8] has extensively studied the functional activity of the sympathetic-adrenal system and free radical processes in metabolic syndrome. These oxidative and neurohormonal pathways overlap significantly with those in IHD, reinforcing the value of the pleiotropic anti-oxidant effects of high-intensity statins. Furthermore, the complexity of diagnosing and treating angina-like syndromes requires precision; as reviewed by Tashtemirova [10] regarding Cardiac X Syndrome, attentive reviews and diagnostic criteria are essential to tailor treatments effectively. This aligns with our finding that personalized monitoring leads to superior clinical outcomes.

Clinical Inertia - The study also addresses "clinical inertia" among physicians. The safety data from our cohort confirms that high-intensity Rosuvastatin is safe for the Uzbek population. Physicians should not preemptively reduce doses based on unfounded fears but should treat to target.

CONCLUSION

The clinical investigation conducted at Andijan State Medical Institute leads to several definitive conclusions regarding the use of statins in Ischemic Heart Disease.

Firstly, high-intensity statin therapy (e.g., Rosuvastatin 20-40 mg) is highly effective in achieving modern LDL-C targets and reducing vascular inflammation in the local population.

Secondly, the primary barrier to effective treatment is poor adherence driven by societal myths and psychological resistance (the nocebo effect), rather than genuine pharmacological toxicity.

Thirdly, an intensified management strategy that includes patient education and regular monitoring significantly improves adherence, reduces perceived side effects, and doubles the rate of target lipid achievement.

Therefore, we recommend that the standard of care for IHD patients must evolve from simple prescription writing to a holistic management model that actively addresses patient concerns and counters negative societal narratives regarding long-term medication.

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