Dislipidemia in Patients with Rheumatoid Arthritis Treated with Synthetic DMARDS

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by systemic inflammation, progressive joint destruction, and an increased risk of cardiovascular complications. Within a decade of diagnosis, one-third of RA patients develop cardiovascular issues, with subclinical atherosclerosis and myocardial ischemia being common manifestations. Changes in lipid profiles (LPs), marked by increased atherogenicity, play a crucial role in the pathogenesis of both RA and atherosclerosis. Seropositive RA, characterized by elevated anti-cyclic citrullinated peptide antibodies and rheumatoid factor, is associated with a higher risk of vascular complications. Early-stage RA presents diagnostic and therapeutic challenges, yet timely intervention using baseline therapies and adjunctive statin treatment has demonstrated efficacy in reducing RA activity and cardiovascular risk. Despite advancements, the detailed characterization of LP subfractions in RA remains underexplored, emphasizing the need for further research to elucidate the immunopathogenesis of atherosclerosis and optimize RA management strategies.

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Introduction

Rheumatoid arthritis is an immuno-inflammatory rheumatic disease of unknown etiology, with the development of chronic erosive arthritis and systemic internal organ damage, leading to early disability, reduced life expectancy and reduced quality of life. An integral part of the "Treatment to Achievement" strategy in the management of patients with RA is to achieve remission or at least low disease activity. However, patients with RA treated with basal anti-inflammatory drugs (BART) and genetically engineered biologics achieve remission in only 20-40% of cases and, therefore, the majority of patients do not have optimal disease outcomes. In developed countries, the prevalence of RA is 0.5% to 1.8% (up to 5% in the elderly). Between 5 and 50 people per 100 000 population develop RA each year. There are 5 times as many women as men. Early-stage RA patients have changes in the blood lipid profile (BP) [1-3].

The main cause of death in patients with rheumatoid arthritis is cardiovascular pathology, with atherosclerosis and related complications playing an important role in its development. The mechanisms of atherosclerosis and rheumatoid arthritis have been proved to be similar. There are many studies demonstrating the pathogenetic unity of these nosologies. Both of these diseases have an immune-palliative character, which mediates their close relationship and opens up new therapeutic possibilities for us. A number of studies have shown that the development and course of rheumatoid arthritis is associated with changes in blood NPS, characterised by increased atherogenicity. Moreover, adequate anti-inflammatory therapy leads not only to a reduction in rheumatoid arthritis activity, but also to a reduction in the atherogenicity coefficient [4-7].

Within 10 years of the diagnosis of RA, cardiovascular complications develop in a third of patients. Subclinical atherosclerosis in the form of intimamedia complex thickening of the main arteries is detected in most patients with rheumatoid arthritis, and in a quarter of patients the atherosclerotic process manifests itself clinically as CHD (angina pectoris, myocardial infarction) and peripheral atherosclerosis. RA is characterised by painless myocardial ischaemia according to Holter ECG monitoring. Coronary artery disease is usually multivessel disease with relatively few critical stenoses. The coronary state, the pronounced inflammatory processes in the vascular wall and the tendency to rupture atherosclerotic plaques against a background of increased thrombosis resemble those of diabetes mellitus [13].

There are different estimates of the role of rheumatoid arthritis activity in the prognosis of atherosclerotic vascular disease. The presence of ADCP or rheumatoid factor in the plasma of rheumatoid arthritis patients (seropositive arthritis) is clearly associated with an increased risk of vascular complications and plasma C-reactive protein concentrations, which have crucial prognostic value. Goodson N, Dorum S. describe several interrelated causes leading to an increased risk of cardiovascular accidents

associated with accelerated atherosclerotic vascular damage in RA. These include the accumulation of classic cardiovascular risk factors, the side effects of drug therapy used to treat RA and insufficient attention to the need for prevention of cardiovascular complications in RA [8.9.10].

Blood LPOs in patients with RA remain insufficiently studied. The detailed subfractional spectra of total and modified LPs are not studied at all. which is especially important for autoimmune diseases. Therefore, the study of LPs in RA patients is of considerable interest and will allow a more accurate characterization of the pathogenesis of both RA and the immunopathogenesis of atherosclerosis in general [11,12].

Currently, the concept of early stage RA is interpreted ambiguously. Different authors define it as a time interval from several months to several years. Some specialists define the first 3 months of the disease as a very early stage. The research that is being carried out on the problem of early arthritis focuses primarily on two closely related issues. Firstly, the possibilities of establishing a reliable diagnosis are being explored, and secondly, approaches to prescribing the optimal treatment for this period of the disease are being worked out. Comprehensive treatment approaches based on baseline therapy play a major role in addressing this issue. The use of statins against baseline therapy in RA patients significantly accelerates the recovery time, as well as contributes to the prevention of cardiovascular disease.

The first studies on the use of statins in rheumatology were experimental in nature: collagenous arthritis in mice was used as a classic model, the activity of which was significantly reduced by simvastatin [14]. The now classic TARA (Trial of Atorvastatin in Rheumatoid Arthritis) study showed that atorvastatin at a dose of 40 mg/day significantly reduces C-reactive protein levels and reliably (using standard rheumatological indices) reduces inflammation in the joints [15].

Thus, development of algorithm for diagnostics of impaired LP in RA patients is urgent; timely diagnostics of impaired LP leads to reduction of cardiovascular pathology in RA patients. Application of statins in complex therapy has normalising effect on clinical and laboratory indexes of pathological process activity in RA patients.

This study aimed to study lipid profile disorders in patients with rheumatoid arthritis on the background of basic treatment.

Materials and methods

Overall 60 patients with a reliable diagnosis of RA according to APA criteria were investigated. The patients' age ranged from 18 to 76 years. Most patients were women. Clinical examination of patients included: thorough examination of anamnesis, collection of complaints, clinical examination. Joint status was assessed in patients with RA: the number of swollen, painful joints with determination of Ritchie's index, duration of morning stiffness, severity of functional joint failure. The severity of joint pain and general condition was assessed using visual analogue scale (VAS). RA activity was assessed using the DAS 28 total activity index. laboratory examination included clinical blood count, blood chemistry, total cholesterol, triglycerides. HDL, LDL. ADCs, C-reactive protein.

Patients received anti-rheumatic therapy, including non-heroin anti-inflammatory drugs (NSAIDs) diclofenac, mel-bek and basal agents, of which 40 patients received methotrexate (duration of use was 1 to 4 years) and 20 patients received lefno (duration of use was 1 to 3 years). The patients were divided into 3 groups: Group 1 (20 patients) - received methotrexate in a dosage of 75-15 mg per week, melbec 5-15 mg per day; Group 2 (20 patients) received NSAIDs+plakvenil in a dosage of 200-400 mg per day. Group 3 (20 patients) received NSAIDs+rozuvasgatin (10-20 mg daily).

Results

A comparison of the severity of the impairment of the LP with the specific parameters of RA was carried out in the patients (table 1).

Table 1: Baseline Characteristics and Laboratory Data of RA Patients

Parameters	Group 1	Group 2	Group 3
DAS 28 Score	High	High	Moderate
VAS (0–100)	75 ± 10.2	72.9 ± 8.6	56.3 ± 12.8
ADC Positivity (%)	27.5	25.0	20.0
LDL (mmol/L)	4.6 ± 0.6	4.8 ± 0.5	3.2 ± 0.4
HDL (mmol/L)	1.2 ± 0.2	0.9 ± 0.3	1.4 ± 0.3
CRP (mg/L)	25.3 ± 5.2	31.4 ± 6.1	16.2 ± 4.6

High activity according to DAS 28. VAS. ADCP positivity (27,5%), increased C-reactive protein and expressed LP disturbance were detected in the 1st and 2nd groups of patients with RA. In group 2 patients high activity was 2 times more frequent. The severity of LP disorder increased with the increase of RA severity. Ill degree of RA activity was observed in 19,7% of cases, LDL, CRP, C-reactive protein increased respectively in these patients, I degree of RA activity was observed in 13,5% and LDL 15 times lower. Comparison of laboratory data showed that disturbance of blood LP indices was observed in younger and middle-aged patients (215%). In these patients blood levels of LDL and

triglycerides were 1.5 times higher, and HDL levels were lower respectively, indicating that these patients develop atherosclerosis faster. In the dynamics after 6 months and a year. the patients were repeatedly performed laboratory and instrumental examination. The positive dynamics was observed in the 3rd group of patients.

Discussion

The findings of this study emphasize the interplay between rheumatoid arthritis (RA) activity, lipid profile disturbances, and the risk of cardiovascular complications. High RA activity, as evidenced by elevated DAS 28 scores, increased VAS ratings, and elevated inflammatory markers (CRP), was associated with significant lipid metabolism abnormalities, particularly in Groups 1 and 2. These patients exhibited higher levels of LDL and triglycerides and lower HDL levels, contributing to an accelerated risk of atherosclerosis and cardiovascular events.

Group 3, which included patients treated with rosuvastatin alongside NSAIDs, demonstrated the most favorable outcomes. The addition of statins significantly improved lipid profiles, with reductions in LDL and triglyceride levels and an increase in HDL levels. These improvements likely contributed to the observed reduction in cardiovascular risk, as statins not only modulate lipid metabolism but also exert anti-inflammatory effects. This dual mechanism is particularly advantageous in RA, where chronic inflammation exacerbates both joint and vascular damage.

The positive dynamics observed in Group 3 also highlight the importance of integrating lipid-lowering therapy into the standard management of RA, especially for patients with high cardiovascular risk. Statins have shown efficacy in reducing systemic inflammation markers such as CRP, further supporting their role in mitigating the inflammatory burden associated with RA.

The findings also suggest a strong correlation between RA severity and lipid profile disturbances. Younger and middle-aged patients exhibited more pronounced lipid abnormalities, potentially due to higher disease activity and metabolic demands. These results align with existing literature, which identifies systemic inflammation as a key driver of dyslipidemia and atherosclerosis in RA patients.

Despite these encouraging findings, the study has several limitations. The relatively small sample size and short follow-up period may limit the generalizability of the results. Additionally, the study did not account for other factors influencing cardiovascular risk, such as smoking, physical activity, and genetic predispositions. Future studies with larger cohorts and longer follow-up durations are necessary to validate these findings and explore the long-term benefits of integrating statins into RA management.

Conclusions

This study underscores the importance of a multifaceted approach to managing RA, addressing both joint inflammation and systemic complications such as dyslipidemia. The inclusion of statins in the treatment regimen offers a promising strategy for reducing cardiovascular risk and improving overall patient outcomes. Tailoring treatment based on disease activity and metabolic parameters can further enhance therapeutic efficacy and patient quality of life.

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