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EFFECTIVENESS OF COMPLEX TREATMENT OF PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE IN PSORIATIC ARTHRITIS

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ANNOTATION

A study of the dynamic observation of the effect of treatment with the use of ursodeoxycholic acid in combination with a basic anti-inflammatory agent and genetically engineered agents in patients with psoriatic arthritis and non-alcoholic fatty liver disease was carried out.

Keywords

psoriatic arthritis; psoriasis; non-alcoholic fatty liver disease; basic anti-inflammatory drug (BAID); genetically engineered drugs.

Psoriatic arthritis is considered one type of arthritis that occurs in conjunction with chronic inflammatory psoriasis, which in nearly 20% of cases is associated with psoriasis [1]. According to recent literature, psoriatic arthritis is characterized by low treatment efficiency, and torpidity during treatment, which leads to disability in 30% of cases [2]. A variety of forms of treatment of PsA include the usage of Nonsteroidal anti-inflammatory drugs (NSAID), intra-articular steroid injections (IASI), basic synthetic anti-inflammatory agents, and, in recent years, modern basic anti-inflammatory gene-engineered biological agents. TNF-α plays a central role in the inflammatory process in Nonalcoholic fatty liver disease (NAFLD) the same way it does in chronic inflammatory diseases [8]. Considering the pathogenetic importance of this cytokine, it has been observed that treatment of PsA with anti- TNF-α agents such as infliximab and adalimumab when it is accompanied by liver inflammation showed a positive effect on liver function parameters [6]. When PsA and NAFLD (Non-Alcoholic Fatty Liver Disease) occur together, the use of genetically engineered biological drugs exhibits higher safety when compared to conventional treatment. For instance, when Adalimumab was administered to 32 patients with PsA and liver disease over an average duration of 5 years, no instances of exacerbation or progression of liver disease or liver toxicity were observed. Glucocorticoid inhibitors may have a regulatory effect on certain adipocytokines. Etanercept, Ustekinumab, and Secukinumab do not adversely affect NAFLD (Non-Alcoholic Fatty Liver Disease) and inhibit pro-inflammatory cytokines [5].

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Currently, in patients with psoriasis, the treatment of NAFLD (Non-Alcoholic Fatty Liver Disease) with UDCA (ursodeoxycholic acid) has the most extensive evidence base among other hepatoprotectors [3]. The experience and clinical information gathered to date indicate that UDCA (ursodeoxycholic acid) possesses pleiotropic effects, showing a positive impact on the liver condition [7]. The anti-apoptotic effects include reduced release of mitochondrial cytochrome C, inhibiting the activity of alkaline phosphatase and lactate dehydrogenase. Additionally, choleretic and litholytic effects have been proven, meaning the competition for receptors in the bile duct stimulates the secretion of toxic hydrophobic bile acids, through activation of L-protein kinase C related to Ca in hepatocytes, stimulates exocytosis, lowers the concentration of hydrophobic bile acids, and reduces the lithogenicity of bile. Having been confirmed to have a hypocholesterolemic effect, UDCA reduces cholesterol absorption in the intestines, as well as the synthesis of cholesterol in the liver, and decreases the secretion of cholesterol with bile. Additionally, it exhibits the following anti-inflammatory effects: the reduction of the production of anti-inflammatory cytokines, the effect of phagocytosis, and oxidation processes [4].

In recent years, we have observed growing interest regarding the relationship between NAFLD and PsA. NAFLD is considered a manifestation of metabolic syndrome and is characterized by the disruption of the balance of adipocytokines, along with the presence of low-level inflammation processes [7]. Research studies aimed at investigating the clinical course, outcomes, and impact on therapy when PsA coincides with NAFLD (Non-Alcoholic Fatty Liver Disease) hold significant importance for understanding the underlying disease and its implications.

Scientific research aimed at the comparative study of the combined effect of genetically engineered biological drugs with UDCA (ursodeoxycholic acid) in patients with NAFLD in PsA remains crucial.

Objective. Investigate the effectiveness of comprehensive treatment in patients with psoriatic arthritis (PsA) and non-alcoholic fatty liver disease (NAFLD).

Research materials and methods. The research was conducted at the Multidisciplinary Clinic Republic Rheumatology Center of the Tashkent Medical Academy and the specialized outpatient treatment course in the Rheumatology Departments from 2020 to 2022. The research included a total of 120 patients in both outpatient and inpatient settings. All patients had a confirmed diagnosis of PsA based on CASPAR diagnostic criteria. A comparative assessment of the effectiveness of treatment in PsA patients with NAFLD was studied in 3 groups. Group 1 received standard treatment with Methotrexate 15 mg/week; Group 2 received Etanercept 50 mg/week; Group 3 consisted of patients who received the Interleukin-17 inhibitor Secukinumab at a dose of 150 mg according to the scheme

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and, on the basis of patients who received UDCA (ursodeoxycholic acid) at a dose of 15 mg/kg/day. Efficacy and safety of treatment were conducted before and after treatment in dynamics.

Research results. The study conducted a comparative analysis using the combination of Disease-Modifying Anti-Rheumatic Drugs (DMARDs) such as methotrexate and genetically engineered biological agents (α-TNF inhibitor Etanercept and IL-17 inhibitor Secukinumab) in conjunction with UDCA.

The emergence of DMARDs (α-TNF and IL-17 inhibitors) marked a significant new stage in treating Psoriatic Arthritis (PsA). The effectiveness of DMARDs has been demonstrated in various clinical presentations of PsA. Currently, there is no standard treatment for NAFLD. According to some studies, TNF-α has been considered an independent predictor in the progression of liver fibrogenesis and the development of the disease. The treatment methods used were assessed for effectiveness before and after treatment, and the following indicators were taken into consideration: evaluating the dynamics of psoriasis activity using the PASI index before and after treatment. The dynamics of the joint syndrome were assessed through tender/swollen joint count, visual analog scale (VAS), and DAS28 index; the dynamics of adiponectin, leptin, TNF-α levels, and the degree of steatosis were monitored. The PASI index of psoriasis can trace the disruption of joint function to the dynamics of the inflammatory process. Consequently, based on the dynamics of the above-mentioned indicators, the functional parameters of the skin and joints, as well as the joint activity measured by the DAS28 index, have changed. By the 6th month of the study, more improvement in joint activity in the 2nd and 3rd groups was clearly observed compared to the 1st group. The comparative effectiveness of the impact of this treatment on the skin-joint syndrome was investigated when using Methotrexate with UDCA, and genetically engineered basis drugs with UDCA in patients with PsA and NAFLD concurrently (Figure 1).

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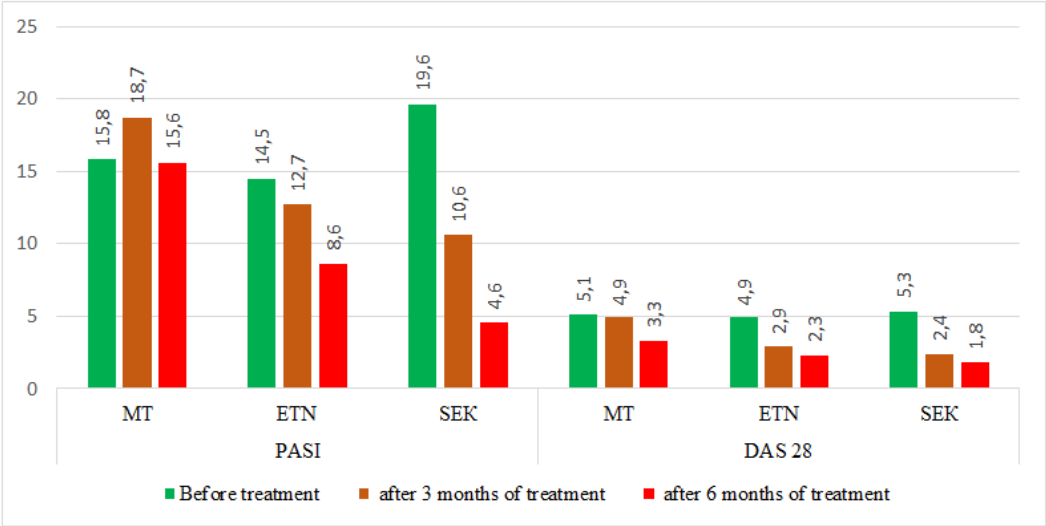

Figure 1. The comparative effectiveness of complex therapy in patients with psoriatic arthritis and liver non-alcoholic fatty disease

In the group of patients with Psoriatic Arthritis (PsA) with NAFLD, the complex therapy with Secukinumab and Etanercept, administered with UDCA, proved to be more effective on skin and joint syndromes compared to therapy involving Methotrexate with UDCA (PASI and DAS 28).

The effect of complex treatment on the amount of cytokines was studied (Figure 2).

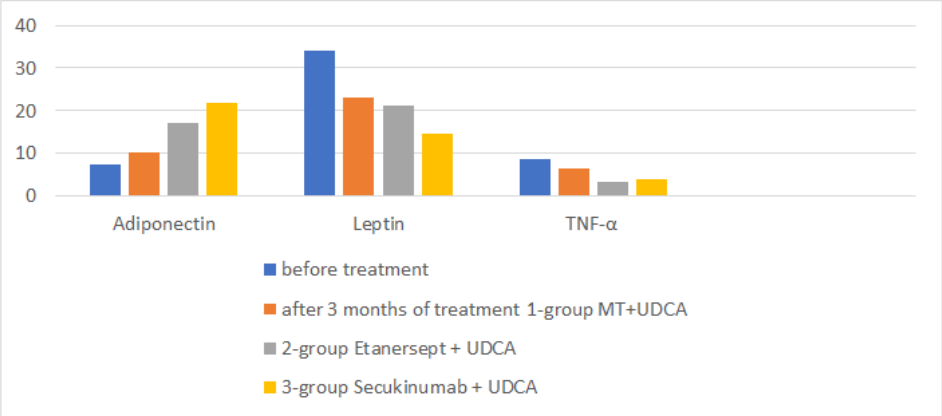

Figure 2. Cytokine levels in patients with nonalcoholic fatty liver disease in psoriatic arthritis

According to the results of the complex therapy with Secukinumab and UDCA, an increase in adiponectin levels after 6 months of treatment was observed ($p>0.05$), while a significant decrease in leptin levels was noted. However, a complete normalization was not observed in comparison to the indicators of the control group ($p<0,05$). The analysis of cytokine levels during the dynamics showed that, under the treatment with Etanercept and UDCA, the quantity of TNF-α decreased by 2.5 times, which in turn indicated the effectiveness of the treatment.

Summary. According to literary information, there is a different perception regarding the risk of hepatotoxicity when using methotrexate. Treatment with gene-engineered base drugs is considered safe for the liver, and it does not have an adverse effect on liver enzymes. The frequency of adverse effects and the transition from long-term treatment to remission is lower in patients receiving gene-engineered base drugs compared to those undergoing standard basic therapy. Clinical monitoring results indicate that the use of the IL-17 inhibitor Secukinumab in treatment does not show signs of an increase in liver enzymes or indications of liver damage.

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