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Original Research Article

The impact of anti-tumor necrosis factor alpha drugs on lipid profile of patients with rheumatoid arthritis or seronegative spondyloarthropathy

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ABSTRACT

Background: Inflammatory arthritis is associated with abnormal levels of lipoprotein. The cause is considered to be inflammation. Recently, the use of biologic drugs in the treatment of inflammatory arthritis, especially rheumatoid arthritis (RA) and seronegative spondyloarthropathy, has increased. There are different results of the effect of these drugs on fat profile. Evaluate the impact of anti-tumor necrosis factor (TNF) alpha drugs on lipid profile of patients with RA or seronegative spondyloarthritis.
Methods: In this cross-sectional descriptive study, 50 patients with rheumatoid arthritis or seronegative spondyloarthritis, who were candidates for TNF alpha treatment, were included in the study. After obtaining written consent, a checklist was completed for all patients including demographic information such as age, sex, height, weight, place of residence, level of education, type of disease, and lipid profile test results including total cholesterol, triglycerides (TG), low density lipoprotein (LDL) and high density lipoprotein (HDL) were recorded. Then the patients were treated and evaluated for fat profile after 3, 6, 9 months after receiving the relevant treatment regimen. The test results were recorded in checklists. After completing the study, the data were entered into the statistical package for the social sciences (SPSS) 24 software and analyzed.
Results: The mean age of patients was 46.38±14.33 years. 54% of patients were female. 54% of patients had rheumatoid arthritis. 62% of patients were treated with Sinora. The results of this study showed that serum triglyceride levels increased during the study period and this increase was statistically significant but the trend of changes in serum cholesterol, HDL and LDL levels was not statistically significant. However, serum LDL levels measured in the ninth month increased significantly compared to the initial measurement.
Conclusions: Results showed that there was a significant relationship between lipid profile changes and anti-TNF alpha consumption. Although decreased inflammation appears but other mechanisms may be involved in dyslipidemia.

Keywords: Lipid profile, Rheumatoid arthritis, Seronegative spondyloarthritis

INTRODUCTION

Rheumatoid arthritis (RA) is the most common inflammatory rheumatic disease and has an approximate prevalence of 1% in most societies.[2] In Iran, its prevalence is estimated at 0.19% in urban and 0.33% in rural areas.[3] It usually occurs in teenagers and middle-aged people, in the first, third to fifth decades, and more common in women.[4]

RA is an inflammatory, systemic, chronic, debilitating disease with unknown etiologies which its main symptoms are joint and included morning dryness, swelling of the affected joints, and finally, changes in the shape of the joints. On the other hand, this disease has many extra-articular manifestations, including anemia, fatigue, subcutaneous nodules, neuropathy, vasculitis, and Sjögren's syndrome.[5] The prevalence rate of RA increases

with increasing age and the difference between men and women in older age groups are decreased.[9] The onset of the disease is more common in the fourth and fifth decades of life, in 80% of all patients, appears between the ages of 35 and 50. The components of the disease that have the potential to improve by receiving treatment, which are measured by various methods, for example, the patient's DAS-28 score based on the total number of sensitive and swollen joints (28 joints), the patient's overall assessment of his condition (a number between 0 and 10), the doctor's assessment of the patient's condition (a number between 0 and 10) and CRP are checked (10). Seronegative spondyloarthropathy are a group of relatively common inflammatory polyarthropathies with a prevalence of 1.5% to 2% in the general population and is characterized by sacroiliitis and HLA-B27 positivity.[6] Its most common form is called "ankylosing spondylitis" which damages the joints between the bones that make up the spine (vertebrae). But another form of it called arthritis is a reaction that often occurs after infection in the urinary or digestive tract and tends to damage the joints of the lower limbs.[11] Reactive arthritis occurs as a reaction to an infection in another part of your body, which may include redness, swelling, and joint pain, often in the knees, ankles, and feet.[12] Psoriatic arthritis affects peripheral and axial joints, which usually happens to people who have a skin disease called psoriasis or have a history of psoriasis in family members.[13] Enteropathic spondyloarthropathy is seen in people suffering from gastrointestinal diseases such as Crohn's disease and ulcerative colitis. Almost one out of every 5 people who suffer from Crohn's or ulcerative colitis will have this type of spondyloarthropathy.[14] Anti-TNF alpha drugs are drugs that are made with a special technique of genetic engineering to reduce inflammation and joint damage.[15] These types of drugs act on a molecule called tumor necrosis factor (TNF) and are called TNF blockers or anti TNF drugs that are used to treat rheumatoid arthritis, children's arthritis, psoriatic arthritis and ankylosing spondylitis.[4] Investigations have shown that in patients with active rheumatoid arthritis, the level of lipid profile is at a level that makes the patient susceptible to atherosclerosis, and it also originates from the inflammatory responses in these patients.[16] Among these, inflammatory cytokines and TNF alpha are among the main factors in rheumatic diseases, especially rheumatoid arthritis, as well as in lipid profile disorders.[17] Considering the lack of similar studies in this field at the province and country level and the contradictory results regarding the possibility of atherosclerosis and the risk of coronary diseases following the use of anti-TNF drugs, this study aims to investigate the impact of anti-TNF alpha on lipid profile of patients with evaluate the impact of anti-TNF alpha drugs on lipid profile of patients with rheumatoid arthritis or seronegative spondyloarthritis.

METHODS

This cross-sectional descriptive study was conducted from 2018 to 2019 on 50 patients with rheumatoid arthritis or seronegative spondyloarthropathy (psoriatic arthritis, ankylosing spondylitis and enteropathic arthritis) referred to the rheumatology clinic of Ardabil city hospital who were candidates for anti-TNF alpha treatment. Patients with a definitive diagnosis of rheumatoid arthritis or seronegative spondyloarthropathy and age over 18 years and having the condition of receiving anti-TNF alpha and consenting to the study were included in the study. Patients with chronic diseases such as cancer or contraindications to receive anti-TNF alpha and unwillingness to take anti-TNF alpha and receive anti-lipid profiling drugs (having a history of hyperlipidemia under treatment) were excluded from the study. The results of lipid profile tests including total cholesterol, TG, LDL and HDL were recorded for all patients. Then the patients were treated and their fat profile was evaluated 3, 6 and 9 months after receiving the respective treatment regimen. The required information was recorded in a checklist and the resulting data were analyzed in statistical package for the social sciences (SPSS) software version 21 using descriptive statistical methods in the form of tables and graphs and repeated measures analysis of variance (ANOVA) statistical test to evaluate changes in fat profile. This study was approved by the ethics committee of Ardabil University of Medical Sciences and registered with the code IR.ARUMS.REC.1399.325. A significance level of less than 0.05 was selected for all tests as significant.

RESULTS

This study was conducted on 50 patients with rheumatoid arthritis or seronegative spondyloarthropathy with an average age of 46.38±14.33 years with the aim of investigating the effect of treatment with anti-TNF alpha drugs on lipid profile. Cinno RA drug was the most used drug in patients with a frequency of 31 (62%). 23 patients (46%) were male and 27 (54%) patients were female. Triglyceride serum level at the beginning was 126.12±6.91, three months later it was 127.02±6.74, six months later it was 133.57±7.94, and nine months later it was 135.43±7.05 mg/dl and increased during the study period and this increase was statistically significant (p=0.008). The changes in serum levels of cholesterol, HDL and LDL in the measured times were not statistically significant (p=0.001) (Figure 1).

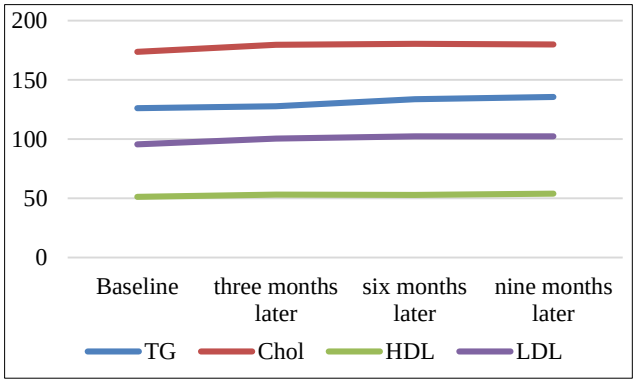

Figure 1: The serum level of lipid profile indices in measurement times by mg/dl.

In this study, only triglyceride had significant changes in patients taking Sinura and Altebra, and changes in cholesterol, HDL and LDL were not significant based on the drugs used (Figure 2).

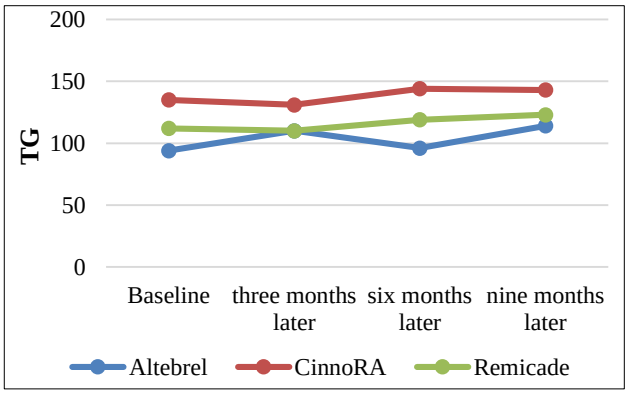

Figure 2. Compare the serum level of TG by type of used drugs in measurement times by mg/dl.

Changes in serum cholesterol levels among men at different measurement times was significant, but the rest of the indicators were not significant based on gender. In this study, RA was the most common disease in the study subjects with a frequency of 27 cases (54%).

DISCUSSION

In this study, the average age of patients was 46.38±14.33 years. 54% of the patients were female, 54% had rheumatoid arthritis and 62% were treated with Synora drug. The results of this study showed that the serum level of triglyceride increased during the study period and this increase was statistically significant, but the trend of changes in the serum level of cholesterol, LDL and HDL was not statistically significant. Hassan et al.'s study showed that treatment with anti-TNF alpha inhibitors caused a significant increase in the TG level of patients, which was consistent with the results of the present study.[18] Filho et al in a similar study showed that the use of anti-TNF alpha with an increase in triglycerides has been observed in patients, which is consistent with the results of our study.[19] França et al showed in a study that good control over the chronic inflammatory condition present in the body of RA patients can be effective on the lipid profile and the risk of cardiovascular diseases. Lower cholesterol levels may be associated with a better response to anti-TNF alpha drugs.[20] Wang et al showed in a study that anti-TNF-α agents can play an important role in regulating the effects of lipid profile disorders and glucose levels in RA patients. Inhibition of TNF alpha can be a powerful strategy to prevent metabolic syndrome and can play a role in reducing cardiovascular risk in patients with RA, which was consistent with the results of our study, although the glucose level of the patients was not checked in this study. Lipid disorder is one of the effective factors in increasing the risk of cardiovascular disease.[21] Hassan et al showed in a study that TNF-α inhibitor is significantly associated with an increase in total cholesterol, triglycerides and AI. Adding statins showed a significant decrease in LDL levels.[22] In the study conducted by Corrado et al, it was seen that anti-TNF-α agents can play an important role in regulating the effects of lipid profile disorders and glucose levels in rheumatoid arthritis patients. TNF alpha inhibition can be a powerful strategy to prevent metabolic syndrome and can play a role in reducing cardiovascular risk in patients with rheumatoid arthritis.[23] In the study conducted by Cacciapaglia et al, lipid profiles in rheumatoid arthritis patients treated with anti-TNF-α and their changes in relation to disease activity and prediction of clinical response were investigated. In this study, rheumatoid arthritis patients confirmed according to the criteria of ACR/EULAR 2010 who did not respond to other treatments were included in the study, and the patients were examined after 24 and 52 weeks in terms of DAS-28 and lipid profile. It was observed that good control of the chronic inflammatory condition in the body of these patients can be effective on the fat profile and the risk of cardiovascular diseases. Probably, low cholesterol level with better response to anti-TNF alpha drugs is effective, but more studies are needed in this field.[24] In another study by Bergström et al, the results showed that all of the total cholesterol, LDL cholesterol, HDL cholesterol, apolipoprotein B and ApoA1 P are increased, but there was no major change in LDL and HDL. Also, no changes were observed in triglyceride levels. Disease activity was significantly reduced from baseline to the 3-month assessment, and there was no major change in intima-media thickness of the common carotid artery. Although these results suggest that the control of inflammation can have a beneficial effect on the lipid profile by increasing the level of HDL cholesterol, the observed protective effect on cardiovascular disease events by tumor necrosis factor blockers may be due to mechanisms other than changes in lipid levels or effects. Short term on carotid artery atherosclerosis is explained.[25] The most important limitations of the present study were the small sample size and the short intervention time.

CONCLUSION

In this study, a significant relationship was observed between lipid changes and anti-TNF alpha consumption. It seems that although anti-TNF alpha medication is expected to reduce the level of inflammation and lipid profile, but according to the studies conducted, dyslipidemia may have been caused by anti-TNF alpha medication by another mechanism. To verify the results of this study as much as possible, it is suggested to conduct similar research with a larger sample size. Also, prospective clinical trials in the future are necessary to confirm the effect of early fat-reducing treatment.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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