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Which anti-TNF is most effective for my patient? Which one should I choose?

Melih Pamukcu [1], Rabia Aydoğan Baykara [2]

[1] Dışkapı Education and Research Hospital, Health Sciences University, Clinic of Rheumatology, Ankara, Turkey
[2] Department of Physical Therapy and Rehabilitation, Turgut Özal University Medical Faculty, Malatya, Turkey

ORCID ID of the author(s)
MP: 0000-0002-9129-0503
RAB: 0000-0003-0542-266X

Corresponding Author
Melih Pamukcu
Dışkapı Yıldırım Beyazıt Education and Research Hospital, Health Sciences University, Clinic of Rheumatology.
Ziraat, Şehit. Ömer Halisdemir Bulvarı No:1, 06110 Altındağ, Ankara, Turkey
E-mail: melihpamukcu@yahoo.com

Ethics Committee Approval
The approval for the study was obtained from the local ethics committee (Malatya Clinical Research Ethics Committee, İnönü University, 17.02.2021, Approval number: 2021/74).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: Multicenter controlled studies were conducted on the effect of anti-Tumor Necrosis Factor (TNF) agents in rheumatoid arthritis (RA) and varying effectiveness rates were reported. These agents have different advantages over each other. We aimed to compare the disease activation parameters in patients with RA at the beginning and the 52nd week of therapy in patients who were followed up in our center and started on anti-TNF (etanercept, adalimumab, and golimumab), and examine the effects of the drugs that are used by comparing them with each other.

Methods: This retrospective cohort study included 187 patients with RA who were started on anti-TNF therapy because the disease activity could not be controlled by the concomitant use of at least three different conventional Disease-Modifying Anti-Rheumatic drugs, and whose adequate response to anti-TNF were observed at the 12th-week follow-up. RA disease activity was measured using the 28-joint Disease Activity Score incorporating erythrocyte sedimentation rate (DAS-28 ESR) and the patients were evaluated by a Health Assessment Questionnaire (HAQ). For each drug group, disease activation and laboratory parameters were compared before treatment initiation and at 52 weeks of treatment. These values were then compared between the drug groups.

Results: The mean age of 187 patients included in the study was 52.70 (10.17) years, 119 (63.6%) were female and 68 (36.4%) were male. Of the patients, 63 (33.7%) were using adalimumab, 62 (33.2%) were using etanercept and 62 (33.2%) were using golimumab. In all patients, there was a significant improvement in all parameters except mean corpuscular hemoglobin, gamma-glutamyl transferase, and creatinine. There were significant changes in hemoglobin, leukocyte and platelet count, erythrocyte sedimentation rate, C reactive protein, neutrophil count, serum albumin, DAS-28 ESR, and HAQ levels in all three groups ($P<0.05$).

Conclusion: There were no differences in efficacy between adalimumab, etanercept and golimumab therapies, which were planned considering the comorbidities and drug preferences of the patients. In addition to controlled studies, real-life data to be reported by rheumatology centers will help us obtain more accurate information about the therapy results of anti-TNF agents.

Keywords: Arthritis, Rheumatoid; Adalimumab, Etanercept

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Introduction

Rheumatoid arthritis (RA) is the most common chronic inflammatory rheumatic disease which inflicts irreversible damage on the joints. Although it affects the joints and periarticular structures, it can cause comorbid syndromes due to extra-articular involvement, such as rheumatoid nodules, lung involvement, and vasculitis. RA creates a significant burden for both the individual and society [1]. The individual burden consists of physical disability due to musculoskeletal dysfunction, decreased quality of life, and other comorbidities [2]. The socioeconomic burden includes medical costs, loss of workforce, and social isolation [3]. Therefore, early diagnosis and initiation of effective therapy are important to reduce inflammation and subsequent damage and functional loss. Technological developments in recent years revealed new therapeutic targets. The definition of new classification criteria and novel effective therapy strategies provided significant improvements in all outcomes of the disease [4-9].

The use of anti-tumor necrosis factor (anti-TNF) is a revolutionary therapy. Anti-TNF agents facilitate the achievement of therapy targets with their rapid and powerful effects and significantly increase the rates of controlling disease activation. Etanercept (ETN), Adalimumab (ADA), and Golimumab (GOL) are approved for use in the therapy of RA. ADA and GOL are monoclonal anti-TNF-α full IgG1 antibodies, while ETN is an extracellular domain of TNF receptor 2/IgG1-Fc fusion protein. ETN is administered once a week, ADA once every 2 weeks, and GOL once every 4 weeks by subcutaneous injection.

In the 2021 American College of Rheumatology (ACR) RA therapy guideline, it is stated that anti-TNFs can be used preferably in combination with conventional Disease-Modifying Anti-Rheumatic drugs (cDMARDs) such as methotrexate, or alone [10]**.** Although many studies report that the anti-TNF agents have similar effects, contradictions remain. Structural differences were reported to create differences in both efficacy and toxicity [11, 12]**.** In addition, the rates of primary or secondary therapy resistance that can be seen in these drugs differ [13]**.**

Response to medication delays reaching the therapy goal and requires re-evaluating the treatment alternatives. RA affects a significant part of the population and creates a serious cost burden on the healthcare system. Regular follow-up of the patients and making the necessary interventions improve the prognosis of the disease and reduce all kinds of negative outcomes.

In our daily practice as clinicians, we think it is important to know which of these drugs is the most effective for our patients and whether their effects differ. This study aimed to statistically compare the disease activation parameters in patients with RA at the beginning and in the 52nd week of anti-TNF therapy in patients who were followed up in our center, and comparatively examine the effects of these drugs.

Materials and methods

Study design

This retrospective cohort study included 187 patients who presented to the rheumatology department between August 2017-January 2021 and were diagnosed with RA according to the 2010 College of Rheumatology / European League Against Rheumatism (ACR/EULAR) classification criteria [14]**.** Patients aged 18 years and older, who were started on anti-TNF (ETN, ADA, GOL) therapy because the disease activity could not be controlled by the concomitant use of at least three different cDMARDs and who continued anti-TNF agents with an adequate response to the therapy at the 12th-week follow-ups were enrolled. The 12th-week response criterion consisted of the 28-joint Disease Activity Score, incorporating an erythrocyte sedimentation rate (DAS-28 ESR) decrease of 1.2 units from baseline and DAS-28 ESR <3.2. The patients included in the study were those who did not receive biologic DMARD (bDMARD) therapy before, did not stop or delay their medication after starting the anti-TNF therapy, and did not switch to another drug. We only included patients who received anti-TNF plus 15 mg methotrexate once a week and non-steroidal anti-inflammatory therapy if needed to ensure standard conditions. We did not include patients using cDMARD other than methotrexate and steroids.

In the clinic where the study was conducted, care is taken to use all biological drugs in equal proportions, provided that the co-morbidity and drug preferences of the patients are considered. Although our study is retrospective, the sizes of our study groups are very close.

Participants

Inclusion criteria

The study inclusion criteria were set as follows: Patients aged 18 years and over who were regularly followed up and treated by the anti-TNF agents ADA, ETN, and GOL for RA in the rheumatology clinic, without a history of bDMARD use.

Exclusion criteria

The exclusion criteria were set as follows: Patients aged under 18 years, with a history of alcohol and substance abuse, other uncontrolled medical disorders, and overlap syndromes with RA.

Data collection

All patients' demographic characteristics and clinical data were analyzed. The clinical data included duration of disease, drugs used at the time of admission and before, habits (smoking, alcohol, etc.), and history of other systemic diseases. Laboratory findings, namely, C-reactive protein (CRP, mg/L), albumin (g/dL) levels, ESR (mm/h), and complete blood count parameters were obtained from the hospital records. DAS 28 ESR and Health Assessment Questionnaire (HAQ) values calculated by the rheumatologist during follow-ups were obtained from the patient files.

Measurement tools

Disease Activity Score 28-joint count -erythrocyte sedimentation rate (DAS28-ESR): DAS28-ESR is used to determine the severity of RA using ESR along with the number of sensitive and swollen joints. The number of swollen joints is determined by a visual analog scale and ESR levels. The DAS28-ESR score ranges between 0 and 9.4.

Health Assessment Questionnaire (HAQ): HAQ is a comprehensive instrument designed to evaluate a patient's health status. HAQ is one of the measures of the ACR Core Data Set for the assessment of RA disease activity and patient-oriented outcomes, including disability, drug-associated side-effects, discomfort, cost of care, and mortality. It includes 20 items divided into the eight subcategories of dressing, arising, eating, walking, hygiene, reaching, gripping, and usual activities to determine patients' ability to use upper or lower limbs. Each item of HAQ is rated on a 4-point scale ranging from 0 to 3. The final HAQ index ranges from 0 to 3 and is scored by averaging the items from all eight categories. A HAQ score <0.3 is considered normal; however, the average HAQ of the population has been shown to increase with age [15].

Sample size

Since this is a retrospective study, the sample size was not calculated. It has been reported that at least 40 patients should be included in each group with 90% potency to evaluate the efficacy in biological drug studies used in RA [16].

Statistical analysis

Statistical Package for the Social Sciences (SPSS 22.0 for Windows) was used for data analysis. The Kolmogorov-Smirnov test was performed to check the normality of the quantitative variables. Descriptive variables were presented as mean (standard deviation (SD)) for quantitative variables, and as frequencies and percentages (%) for qualitative variables. In-group significant differences were assessed with the dependent sample T-test for quantitative variables. In addition, an ANOVA test with Bonferroni (post-hoc analysis) was utilized to assess the differences between the three groups. The significance of difference for qualitative variables was analyzed using the χ^2 test. *P*-values of <0.05 were considered statistically significant.

Results

The mean age of 187 patients included in the study was 52.70 (10.17) years, 119 (63.6%) were female and 68 (36.4%) were male. Of the patients, 63 (33.7%) were using ADA, 62 (33.2%) were using ETN and 62 (33.2%) were using GOL. Distribution and comparison of demographic characteristics of the patients according to drug groups are presented in Table 1. There was no difference between the drug groups in terms of demographic characteristics (*P*>0.05).

Table 1: Distribution and comparison of demographic characteristics of patients according to groups

	All subject n=187	Etanercept n=62	Adalimumab n=63	Golimumab n=63	*P*-value
Age, mean (SD)	52.70 (10.17)	53.03 (9.42)	52.06 (9.59)	53.00 (11.52)	0.834 *
Sex n(%)					0.940♠
Female	119 (63.6)	40 (64.5)	39 (61.9)	40 (64.5)	
Male	68 (36.4)	22 (35.5)	24 (38.1)	22 (35.5)	
Age of diagnosis (year) mean (SD)	45.61 (10.11)	46.13 (9.24)	44.65 (9.80)	46.08 (11.27)	0.651 *
Presence of additional comorbidities n(%)	29 (15.5)	11 (17.7)	11 (17.5)	7 (11.3)	0.532 ♠

SD: Standard deviation, *: ANOVA test was used; ♠:χ^2 test was used.

One hundred and thirty-nine (74.3%) patients (n=187) had RF positivity and 117 (62.6%) had Anti CCP positivity. The distribution and in-group comparison of laboratory and disease activation parameters measured before and at the 52nd week of therapy are shown in Tables 2 and 3.

In all patients, there was a significant improvement in all parameters except MCH, GGT, and creatinine (0.001<p<0.038). At the end of the first year, there was no increase in the number of additional diseases compared to pre-therapy (n=29, 15.5%). There were significant changes in the hemoglobin, leukocyte and platelet count, ESR, CRP, neutrophil, albumin, DAS-28, and HAQ levels in all three groups (*P*<0.05). A significant decrease was found in lymphocyte counts in the ETN and ADA groups, and in the ALP levels in the GOL group (Table 3).

Table 2: Comparison of the laboratory and disease activation parameters of the patients before anti-TNF therapy and in the 52nd week of treatment

	All Subject (n=187)		*P*-value*
	Before (mean (SD))	After (mean (SD))	
Hemoglobin (g/dl)	12.20 (1.62)	13.07 (0.90)	<0.001
Leukocyte (/µl)	7728.07 (1767.73)	6290.96 (1518.49)	<0.001
Thrombocyte (10^3/µl)	245.68 (63.84)	226.81 (52.77)	<0.001
MCV (fL)	86.02 (3.24)	86.44 (2.49)	0.027
MCH (pg)	26.23 (2.31)	26.06 (1.74)	0.301
ESR (mm/h)	40.30 (9.76)	12.67 (4.37)	<0.001
CRP (mg/L)	21.37 (8.68)	2.80 (1.47)	<0.001
Neutrophil (/µl)	5612.57 (1848.81)	3577.81 (1350.51)	<0.001
Lymphocyte (/µl)	1855.56 (382.33)	1617.38 (382.33)	<0.001
Albumin (g/L)	4.24 (0.18)	4.45 (0.16)	<0.001
ALT (U/L)	17.27 (7.48)	16.13 (3.09)	0.006
AST (U/L)	16.98 (4.66)	15.99 (3.11)	0.038
ALP (U/L)	84.49 (19.07)	81.14 (12.88)	0.024
GGT (U/L)	24.73 (10.45)	23.32 (7.90)	0.078
Creatinine (mg/dL)	0.73 (0.15)	0.71 (0.11)	0.115
DAS 28-ESR	5.89 (0.19)	2.60 (0.42)	<0.001
HAQ	1.30 (0.24)	0.33 (0.11)	<0.001

MCV: mean corpuscular volüme, MCH: mean corpuscular hemoglobin, ESR: erythrocyte sedimentation rate, CRP: C reactive protein, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma glutamyl transferase, DAS 28-ESR: 28-joint Disease Activity Score incorporating erythrocyte sedimentation rate, HAQ: Health assessment questionnaire, SD: Standard deviation, *: Dependent T test was used.

Table 3: Distribution and comparison of laboratory and disease activation parameters of patients before anti-TNF treatment and in the 52nd week of treatment according to drugs

	Etanercept (n=62)		*P*-value*	Adalimumab (n=63)		*P*-value*	Golimumab (n=62)		*P*-value*
	Before Mean (SD)	After Mean (SD)		Before Mean (SD)	After Mean (SD)		Before Mean (SD)	After Mean (SD)	
Hemoglobin (g/dL)	12.29 (1.70)	13.21 (0.86)	<0.001	12.06 (1.63)	12.89 (1.04)	<0.001	12.24 (1.53)	13.11 (0.74)	<0.001
Leukocyte (/µl)	7890.48 (1798.87)	6395.97 (1557.13)	<0.001	7768.40 (1854.06)	6524.44 (1506.05)	<0.001	7524.68 (1651.54)	5948.71 (1454.04)	<0.001
Thrombocyte (10^3/µl)	238.17 (70.59)	223.80 (61.69)	<0.001	255.90 (54.73)	235.28 (44.11)	<0.001	242.80 (65.01)	221.20 (50.91)	<0.001
MCV (fL)	85.63 (2.43)	86.11 (2.36)	0.092	86.20 (4.11)	86.44 (3.03)	0.461	86.23 (2.95)	86.75 (1.97)	0.151
MCH (pg)	25.79 (2.54)	25.82 (1.83)	0.908	26.47 (2.24)	26.39 (1.75)	0.771	26.42 (2.10)	25.98 (1.62)	0.116
ESR (mm/h)	41.74 (8.84)	12.87 (4.71)	<0.001	39.56 (10.45)	12.51 (4.08)	<0.001	39.63 (9.91)	12.65 (4.37)	<0.001
CRP (mg/L)	21.59 (8.85)	2.85 (1.42)	<0.001	21.80 (4.43)	2.76 (1.50)	<0.001	20.71 (8.86)	2.79 (1.51)	<0.001
Neutrophil (/µl)	5666.29 (1773.44)	3682.90 (1433.82)	<0.001	5676.98 (2001.01)	3589.84 (1225.98)	<0.001	5493.39 (1784.92)	3460.48 (1397.30)	<0.001
Lymphocyte (/µl)	1841.77 (719.72)	1586.13 (328.07)	0.003	2078.10 (825.22)	1720.95 (421.60)	<0.001	1643.23 (489.93)	1543.39 (373.90)	0.093
Albumin (g/L)	4.26 (0.16)	4.46 (0.15)	<0.001	4.24 (0.23)	4.50 (0.17)	<0.001	4.24 (0.15)	4.41 (0.13)	<0.001
ALT (U/L)	16.36 (5.15)	16.15 (3.07)	0.766	18.15 (9.76)	16.04 (3.42)	0.064	17.30 (6.75)	16.22 (2.78)	0.238
AST (U/L)	17.10 (4.44)	16.25 (3.13)	0.152	17.46 (5.81)	16.10 (3.43)	0.071	16.38 (3.38)	15.63 (2.74)	0.160
ALP (U/L)	79.76 (17.94)	81.42 (12.05)	0.464	85.41 (20.66)	80.11 (15.83)	0.054	88.29 (17.74)	81.90 (10.21)	0.016
GGT (U/L)	24.35 (9.18)	21.65 (7.07)	0.055	27.87 (13.52)	25.57 (8.29)	0.157	21.92 (6.68)	22.71 (7.87)	0.460
Creatinine (mg/dL)	0.74 (0.17)	0.71 (0.13)	0.136	0.70 (0.15)	0.69 (0.11)	0.885	0.75 (0.12)	0.73 (0.10)	0.216
DAS 28-ESR	5.90 (0.20)	2.56 (0.49)	<0.001	5.93 (0.18)	2.61 (0.44)	<0.001	5.85 (0.17)	2.62 (0.47)	<0.001
HAQ	1.31 (0.25)	0.35 (0.14)	<0.001	1.30 (0.23)	0.32 (0.14)	<0.001	1.31 (0.23)	0.32 (0.13)	<0.001

*: Dependent T test was used.

While the pre-therapy values were similar in all three groups, the lymphocyte count, albumin, and GGT levels measured after the therapy were significantly different (*P*=0.024, *P*=0.005, and *P*=0.015, respectively). Subgroup analysis revealed that in the ADA group, lymphocyte count (*P*=0.027) and albumin (*P*=0.003) levels were higher than in the GOL group, and GGT levels were higher compared to the ETN group (*P*=0.016) (Table 4).

The distribution and comparison of the changes in therapy and evaluation parameters according to the groups are presented in Table 5. A significant difference was found in the

change in ALP and albumin levels (P=0.005 and P=0.043, respectively). In subgroup analysis, the change in albumin level was significantly higher in the ADA group compared to the GOL group (P=0.005). The decrease in ALP level was significantly higher in the GOL group compared to the ETN group (P=0.047).

No serious side effects were observed in any of the patients included in the study.

Table 4: Comparison of pre-treatment and end-of-first year values of patients receiving Etanercept, Adalimumab and Golimumab treatment

	Etanercept (n=62) Mean (SD), n(%)	Adalimumab (n=63) Mean (SD), n(%)	Golimumab (n=62) Mean (SD), n(%)	*P*-value
Before treatment				
Hemoglobin (g/dL)	12.29 (1.70)	12.06 (1.63)	12.24 (1.53)	0.710*
Leukocyte (/µl)	7890.48 (1798.87)	7768.40 (1854.06)	7524.68 (1651.54)	0.505*
Thrombocyte (10^3/µl)	238.17 (70.59)	255.90 (54.73)	242.80 (65.01)	0.274*
MCV (fL)	85.63 (2.43)	86.20 (4.11))	86.23 (2.95)	0.507*
MCH (pg)	25.79 (2.54)	26.47 (2.24)	26.42 (2.10)	0.193*
ESR (mm/h)	41.74 (8.84)	39.56 (10.45)	39.63 (9.91)	0.368*
CRP (mg/L)	21.59 (8.85)	21.80 (4.43)	20.71 (8.86)	0.790*
Neutrophil (/µl)	5666.29 (1773.44)	5676.98 (2001.01)	5493.39 (1784.92)	0.826*
Lymphocyte (/µl)	1841.77 (719.72)	2078.10 (825.22)	1643.23 (489.93)	0.053*
Albumin (g/L)	4.26 (0.16)	4.24 (0.23)	4.24 (0.15)	0.807*
ALT (U/L)	16.36 (5.15)	18.15 (9.76)	17.30 (6.75)	0.441*
AST (U/L)	17.10 (4.44)	17.46 (5.81)	16.38 (3.38)	0.423*
ALP (U/L)	79.76 (17.94)	85.41 (20.66)	88.29 (17.74)	0.059*
GGT (U/L)	24.35 (9.18)	27.87 (13.52)	21.92 (6.68)	0.052*
Creatinine (mg/dL)	0.74 (0.17)	0.70 (0.15)	0.75 (0.12)	0.133*
RF positivity	47 (75.8)	42 (66.7)	50 (80.6)	0.194♠
Anti-CCP positivity	43 (69.4)	32 (50.8)	42 (67.7)	0.059♠
DAS28-ESR	5.90 (0.20)	5.93 (0.18)	5.85 (0.17)	0.058*
HAQ	1.31 (0.25)	1.30 (0.23)	1.31 (0.23)	0.990*
After treatment				
Hemoglobin (g/dL)	13.21 (0.86)	12.89 (1.04)	13.11 (0.74)	0.125*
Leukocyte (/µl)	6395.97 (1557.13)	6524.44 (1506.05)	5948.71 (1454.04)	0.084*
Thrombocyte (10^3/µl)	223.80 (61.69)	235.28 (44.11)	221.20 (50.91)	0.285*
MCV (fL)	86.11 (2.36)	86.44 (3.03)	86.75 (1.97)	0.367*
MCH (pg)	25.82 (1.83)	26.39 (1.75)	25.98 (1.62)	0.176*
ESR (mm/h)	12.87 (4.71)	12.51 (4.08)	12.65 (4.37)	0.897*
CRP (mg/L)	2.85 (1.42)	2.76 (1.50)	2.79 (1.51)	0.941*
Neutrophil (/µl)	3682.90 (1433.82)	3589.84 (1225.98)	3460.48 (1397.30)	0.657*
Lymphocyte (/µl)	1586.13 (328.07)	1720.95 (421.60)	1543.39 (373.90)	0.024*
Albumin (g/L)	4.46 (0.15)	4.50 (0.17)	4.41 (0.13)	0.005*
ALT (U/L)	16.15 (3.07)	16.04 (3.42)	16.22 (2.78)	0.907*
AST (U/L)	16.25 (3.13)	16.10 (3.43)	15.63 (2.74)	0.518*
ALP (U/L)	81.42 (12.05)	80.11 (15.83)	81.90 (10.21)	0.725*
GGT (U/L)	21.65 (7.07)	25.57 (8.29)	22.71 (7.87)	0.015*
Creatinine (mg/dL)	0.71 (0.13)	0.69 (0.11)	0.73 (0.10)	0.228*
DAS28-ESR	2.56 (0.49)	2.61 (0.44)	2.62 (0.47)	0.752*
HAQ	0.35 (0.14)	0.32 (0.14)	0.32 (0.13)	0.444*

RF: Rheumatoid factor, Anti CCP: Cyclic Citrullinated Peptide Antibody, SD: Standard deviation, *: ANOVA test was used; ♠:χ^2 test was used.

Table 5: Comparison of the changes in Etanercept, Adalimumab and Golimumab treatments before and after the first year of treatment

	Etanercept (n=62) Mean (SD)	Adalimumab (n=63) Mean (SD)	Golimumab (n=62) Mean (SD)	*P*-value*
Hemoglobin (g/dL)	0.92 (1.38)	0.83 (1.29)	0.86 (1.57)	0.935
Leukocyte (/µl)	-1494.51 (1968.50)	-1243.95 (1981.13)	-1575.96 (1739.40)	0.596
Thrombocyte (10^3/µl)	-14.37 (162.61)	-20.61 (236.81)	-21.59 (276.52)	0.172
MCV (fL)	0.48 (2.24)	0.23 (2.56)	0.52 (2.83)	0.796
MCH (pg)	-0.03 (2.06)	-0.08 (2.24)	-0.44 (2.18)	0.444
ESR (mm/h)	-28.87 (8.95)	-27.04 (11.24)	-26.98 (9.67)	0.492
CRP (mg/L)	-18.74 (8.43)	-19.03 (7.96)	-17.92 (8.49)	0.740
Neutrophil (/µl)	-1983.38 (1649.38)	-2087.14 (2084.66)	-2032.90 (1693.54)	0.951
Lymphocyte (/µl)	-255.64 (647.99)	-357.14 (770.09)	-99.83 (460.24)	0.080
Albumin (g/L)	0.19 (0.15)	0.26 (0.19)	0.16 (0.10)	0.005
ALT (U/L)	-0.21 (5.61)	-2.10 (9.12)	-1.08 (7.15)	0.365
AST (U/L)	-0.84 (4.59)	-1.35 (5.72)	-0.74 (4.14)	0.754
ALP (U/L)	1.66 (17.75)	-5.30 (21.40)	-6.38 (20.30)	0.043
GGT (U/L)	-2.70 (10.91)	-2.30 (12.76)	0.79 (8.36)	0.147
Creatinine (mg/dL)	-0.03 (0.18)	-0.01 (0.18)	-0.01 (0.13)	0.564
DAS28-ESR	-3.33 (0.49)	-3.32 (0.41)	-3.23 (0.46)	0.362
HAQ	-0.96 (0.24)	-0.98 (0.20)	0.98 (0.20)	0.770

SD: Standard deviation, *: ANOVA test was used.

Discussion

In our study, we aimed to statistically compare the disease activation parameters at the beginning and the 52nd week of anti-TNF therapy in patients who were followed up in our center, and comparatively examine the effects of the drugs used. We showed that there was a significant decrease in DAS28-ESR, CRP, ESR, and HAQ scores at the 52nd week of therapy in patients who were started on ADA, ETN, and GOL due to RA. In addition, the effects of ADA, ETN, and GOL therapies at the end of 52 weeks were similar.

Well-defined mediators of inflammation such as interleukin 6 (IL-6), interleukin 1 (IL-1), interferon-gamma, especially the pro-inflammatory cytokine TNF secreted from B and T lymphocytes stimulated as a result of inappropriate activation of the immune system, play role in the pathogenesis of RA [17]. Among these cytokines, TNF has been shown to have the most critical role [18]. After this was discovered, controlling the inflammation pathway that starts with TNF and blocking the effects of TNF became one of the main goals of treatment in reducing the chronic effects of RA. For this purpose, anti-TNF agents with different molecular structures targeting TNF began to be used. ETN, which blocks the membrane and soluble form of TNF [19], ADA, which prevents TNF from binding to its specific receptor [20], and GOL, which blocks the soluble and transmembrane form of TNF, are three of these drugs [21].

Many studies investigated the effectiveness of ADA, ETN, and GOL therapies, albeit not comparatively. It was reported that the combination of anti-TNF agents with MTX provides permanent clinical improvement and reduces radiographic progression in patients with RA. Evaluation of the patients according to the ACR response criteria revealed that the efficacy of anti-TNF agents in patients using this combination was similar [22].

Studies report that patients using ADA plus MTX had a better clinical course and radiographic progression than patients using MTX alone [23-25]. Also, patients using ETN plus MTX had better clinical course compared to patients using ETN or MTX alone [26]. The efficacy of GOL was demonstrated by multicenter studies conducted with different patient groups investigating the efficacy and safety of the drug [27-29]. Unlike all these multicenter studies, we compared the laboratory and disease activation scores for each anti-TNF agent at therapy initiation and the end of 52 weeks and found a significant difference in inflammation parameters and disease activation scores at the 52nd week of therapy in all three anti-TNF agents. However, the effects of the three agents did not significantly differ when compared to each other. Another result of our study is that the serum ALP level was higher in patients using ETN than in patients using the other two agents, while the GGT level decreased with therapy in patients using ETN and ADA but increased with GOL therapy. Larger and controlled studies are needed to evaluate this finding more accurately.

Limitations

Its single-center and retrospective design, and the sparse number of patients are the two main limitations of this study.

Conclusion

In this retrospective study, we found that there were no significant differences in the efficacy between ADA, ETN and GOL therapies, which were planned considering the comorbidities and drug preferences of the patients. In addition to controlled studies, real-life data to be reported by rheumatology centers will help us to obtain more accurate information about the therapy results of anti-TNF agents. Larger studies with larger patient groups are needed for the reliability of these data.

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