Effects of Conventional and Biological Drugs Used for the Treatment of Rheumatoid Arthritis on the Quality of Life and Depression

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ABSTRACT

Objective: This study aims to investigate the effects of conventional and biological drugs used for the treatment of rheumatoid arthritis (RA) on patients' quality of life, depression, and anxiety.

Materials and Methods: A total of 80 patients with a diagnosis of RA based on the American College of Rheumatology/Annual European Congress of Rheumatology (ACR/EULAR) 2010 diagnostic criteria were included in the study. Patients were classified into two groups as follows: patients using conventional disease-modifying agents (csDMARDs) alone (Group 1, n=40) and patients using biological disease-modifying agents (bDMARDs) and a csDMARD combination (Group 2, n=40). Demographical patient data were collected. The levels of rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) were measured in both groups. All patients completed the Disease Activity Score (DAS28), Health Assessment Questionnaire (HAQ), Short Form-36 (SF-36), Beck Depression Scale (BDS), and Hospital Anxiety Depression Scale (HADS).

Results: There was no significant difference between the two groups of patients regarding their demographical characteristics, autoantibody positivity, or DAS scores ($p>0.05$). HAQ scores and all parameters and summary scores of the SF-36, BDS, and HADS scores were not significantly different between the two groups ($p>0.05$).

Conclusion: Results of the present study showed that csDMARDs and bDMARDs, which required a more invasive administration and were associated with serious side effects, were not superior to each other in terms of their effects on patients' quality of life. csDMARD and bDMARD were also not superior to each other regarding their effects on anxiety and depression among patients with RA.

Keywords: Rheumatoid arthritis, DMARD, depression, quality of life

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Introduction

Rheumatoid arthritis (RA) is an autoimmune disorder characterized by symmetrical, erosive synovitis and occasionally showing multi-systemic involvement [1]. Being a chronic disease, RA can have significant effects on both physical and psychosocial health, to the detriment of the quality of life of the patient [2]. There are currently no curative therapy options for patients with RA, although conventional disease-modifying agents (csDMARDs) and biological disease-modifying agents (bDMARDs) are essential in its medical treatment [3]. Failure to achieve complete disease control results in physical limitations with the potential of leading to psychological and social problems. In this regard, the main treatment goals should be to increase the quality of life and reduce disability [4]. While the effects of RA itself on patients' quality of life, depression, and anxiety have been investigated in previous studies [5], there are only a limited number of studies in the literature demonstrating the effect of the drugs used in the treatment of RA on the quality of life, depression, and anxiety. Notably, most of the previous studies have compared the effects of two different csDMARDs and/or bDMARDs on the quality of life, depression, and anxiety among patients with RA, while there is a lack of studies involving homogenous patient populations that focus on the Disease Activity Score (DAS28) and the rate of autoantibody positivity (rheumatoid factor [RF] and anti-cyclic citrullinated peptide [CCP]).

Biological disease-modifying agents, have attained an important position in the treatment of RA in recent years and have become associated with the functional status recovery and structural improvement [6]. That said, the more invasive administration route of these therapies and their

serious side effect profiles may have a negative effect on the quality of life and depression among patients with RA [7].

Additionally, there have been no studies to date involving all the csDMARDs and bDMARDs used in the treatment of RA and comparing their effects on the quality of life, anxiety, and depression in patients with RA.

This study may be considered unique, in the sense that it is the first in the literature in which the groups of patients with RA included in the study were homogeneous in terms of the DAS 28 scores and autoantibody positivity and which includes all the csDMARDs and bDMARDs used in the treatment of RA. In this study, we investigate the effects of drugs used in RA treatment on the quality of life, anxiety, and depression.

Materials and Methods

Study Design

This prospective and single-blinded study was conducted between 2016 and 2017 in our University School of Medicine Physical Treatment Clinic. The study sample included 80 patients diagnosed with RA, based on the American College of Rheumatology/Annual European Congress of Rheumatology (ACR/EULAR) 2010 criteria [8], who had been undergoing medical treatment for the preceding 6 months and who consented to take part in the study. The patients with RA were divided into two groups, based on the medications they used: 40 patients using csDMARD alone constituted Group 1, and 40 patients using csDMARD in combination with bDMARD constituted Group 2.

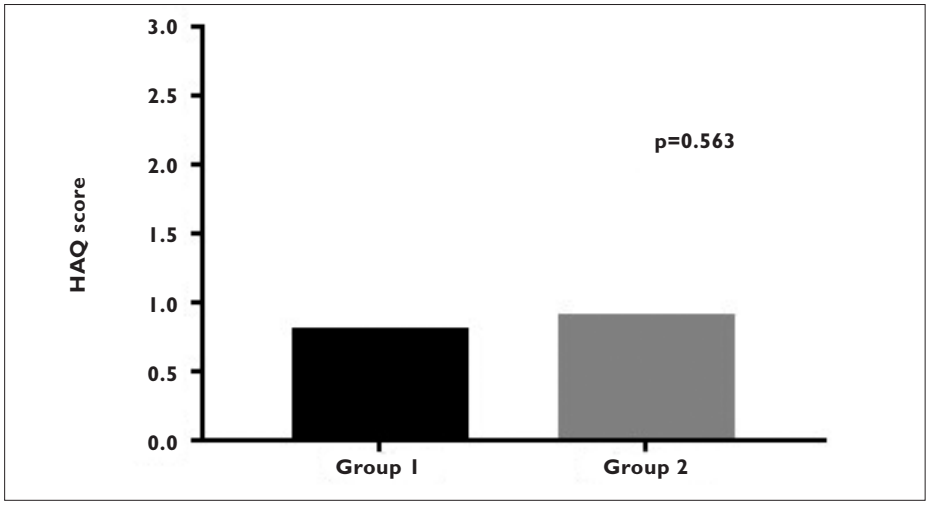

Figure 1. Mean Health Assessment Questionnaire (HAQ) score in Group 1 and 2.

Table 1. Sociodemographic Characteristics of Patients

Characteristic		Group 1 (n=40)	Group 2 (n=40)	p
		Mean±SD	Mean±SD	
Age		53.73±10.79	53.88±12.33	0.954
		n (%)	n (%)	
Gender	Female	33 (82.5)	34 (85)	0.762
	Male	7 (17.5)	6 (15)	
Marital status	Married	33 (82.5)	33 (82.5)	
	Unmarried	4 (10)	3 (7.5)	0.867
	Widow	3 (7.5)	4 (10)	
Level of education	Illiterate	10 (25)	12 (30)	
	Primary school	17 (42.5)	20 (50)	
	Secondary school	1 (2.5)	1 (2.5)	0.775
	High school	8 (20)	5 (12.5)	
	University	4 (10)	2 (5)	
Concomitant diseases	Hypertension	6 (15)	8 (20)	0.925
	Others	3 (7.5)	4 (10)	

Patients with a history of psychiatric disorders and those using antipsychotic medications, those with a concomitant inflammatory rheumatoid disease, those with a history of treatment with a biological agent who were not actively using this medication at the time of screening, pregnant or lactating women, and those younger than 18 years of age were excluded from the study.

Sociodemographic data of the patients (i.e., age, gender, marital status, the level of education, smoking history, body mass index, disease duration, dose and duration of treatment with drugs used for RA) were recorded, and the serum RF and anti-CCP levels of patients in both groups were measured. Anti-CCP and RF values within normal ranges according to ACR/EULAR 2010 criteria [8] or three times higher than the upper limits were classified as low positivity, and values more than three times higher than the upper limits were classified as high positivity. All patients completed a DAS28, Health Assessment Questionnaire (HAQ), a Short Form-36 (SF-36), a Beck Depression Scale (BDS), and a Hospital Anxiety Depression Scale (HADS). The questionnaires of all patients and the DAS 28 scores were assessed through a blind evaluation by the same physician.

The study was approved by the Ethics Committee of Cumhuriyet University (2016-09/04) and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from each of the study participants.

Disease Activity Score 28 (DAS28): The DAS 28 score was used to assess disease activity and was calculated using the following formula: 0.56×√Number of tender joints (NTJ28)+0.28×√Number of swollen joints (NSJ28)+0.014×General health assessment (GHA)+0.70×Estimated sedimentation rate (ESH) [9].

Health Assessment Questionnaire (HAQ): The HAQ consists of 20 items and assesses eight activities, including dressing, standing up, eating, walking, hygiene, cognition, and daily activities. Each answer is graded on a scale of 0–3. The HAQ scale reflects functional status, and its scores are shown to be correlated with the markers of disease activity [10]. A reliability and validity study of the Turkish HAQ was carried out by Kucukdeveci et al. [11].

Short Form (SF) 36: The SF has been developed to assess the quality of life in clinical practice and research studies. The SF-36 consists of 36 questions relating to eight sub-scales: physical

functioning, physical role limitations, body pain, overall health, vitality, social functioning, emotional role limitations, and mental health [12]. A Turkish validation study of the SF-36 was carried out by Kocyigit et al. [13].

Hospital Anxiety and Depression Scale (HADS): HADS is a self-assessment scale used to determine a patient's risk of anxiety and depression, and to measure the level and change in the intensity of anxiety and depression [14]. A validity and reliability study of the Turkish version of HADS was carried out by Aydemir O. [15].

Beck Depression Scale (BDS): The BDS is useful for screening the frequency of depression among patients, and it is used to determine the risk of depression and measure the level and change in the intensity of depressive symptoms [16]. The validity and reliability study of the Turkish version of BDS was carried out by Hisli [17]. We used the BDS to support the reliability of the study, as HADS does not fully cover the depressive symptoms specified in the DSM-IV anxiety and depression scale.

Table 2. Disease Durations, DAS 28 Scores, Anti-CCP, and RF Levels

		Group (n=40) Mean±SD	Group (n=40) Mean±SD	p
DAS28		3.52±1.60	3.23±0.996	0.348
Disease duration, months		117.60±65.79	146.1±92.02	0.115
		n (%)	n (%)	
Anti-CCP	Negative	4 (10)	6 (15)	
	Low-positive	5 (12.5)	9 (22.5)	0.335
	High-positive	31 (77.5)	25 (62.5)	
RF	Negative	10 (25)	14 (35)	
	Low-positive	15 (37.5)	10 (25)	0.428
High-positive		15 (37.5)	16 (40)	

DAS28: disease activity scores; Anti-CCP: anti-cyclic citrullinated peptide; RF: rheumatoid factor.

Table 3. SF-36 Sub-scale Scores and Summary Health Scores in Both Groups

SF-36 Sub-scales		Mean±SD	p
Physical functioning	Group 1	58.00±26.64	0.900
	Group 2	57.25±26.45	
Physical role limitation	Group 1	48.75±41.58	0.225
	Group 2	60.00±40.74	
Emotional role limitation	Group 1	60.83±38.40	0.471
	Group 2	67.50±43.68	
Vitality	Group 1	41.12±23.54	0.843
	Group 2	40.12±21.46	
Pain	Group 1	51.81±28.17	0.921
	Group 2	52.43±28.11	
General health perception	Group 1	40.37±19.75	0.510
	Group 2	37.25±22.41	
Social functioning	Group 1	62.06±26.45	0.218
	Group 2	69.50±27.11	
Mental health	Group 1	66.20±21.73	0.511
	Group 2	63.00±21.64	
SF-36 summary scores			
Physical health score	Group 1	36.33±10.54	0.683
	Group 2	37.32±11.06	
Mental health score	Group 1	46.19±11.90	0.844
	Group 2	45.67±11.68	

SF-36: Short Form-36.

Statistical Analysis

All statistical analyses were performed using the Statistical Packages for the Social Sciences (IBM, SPSS Corp.; Armonk, NY, USA) version 22 software. As appropriate to the nature of the parameters in the dataset, analyses were made using frequency tables, descriptive statistics, difference tests, and chi-squared tests. Since the non-categorical variables of the study were not found to be significant in a Kolmogorov–Smirnov Z test ($p>0.05$), the analyses continued with parametric tests. Accordingly, an independent samples t-test was used to calculate the differences between bi-categorical variables, and an F-test was used to calculate the differences between multi-categorical variables. In cases where the F-test indicated a significant difference, the least significant difference method was used post-hoc to determine which pair resulted in a significant difference. The level of statistical significance was considered to be 95 percent. In the study, when $\alpha=0.05$, $\beta=0.10$ $(1-\beta)=0.90$, it was decided to include 40 individuals in each group, and the power of the test was found to be p=0.9017. The statistical analysis was performed by a statistician who was completely blind to the groups.

Results

A total of 80 patients with RA, including 40 patients with RA who used csDMARD alone (Group 1) and 40 patients with RA who used a csDMARD and bDMARD combination (Group 2) took part in the study. The age, gender, educational status, marital status, and concomitant diseases of the groups were similar ($p>0.05$). Table 1 presents the sociodemographic characteristics of the groups.

There was no significant difference in the disease duration between the groups ($p>0.05$) and the DAS28 scores, as well as the mean Anti-CCP and RF levels were not significantly different between the two groups ($p>0.05$). Table 2 presents the mean DAS 28 scores, the disease duration Anti-CCP and the RF levels of both groups.

The mean HAQ scores of Groups 1 and 2 were 0.81±0.73 and 0.91±0.73, respectively, revealing no significant difference between the two groups ($p>0.05$). Figure 1 shows the mean HAQ scores of both groups.

In all subcomponents of SF-36, no statistically significant difference was found in either group

in terms of the physical and mental health summary scores (physical functioning, physical role weakness, emotional role weakness, vitality, body pain, general health perception, social functioning, mental health). The mean SF-36, sub-scale scores, and summary health scores of both groups are presented in Table 3.

The mean HADS anxiety scores in Groups 1 and 2 were 6.50±3.93 and 7.08±4.27, respectively, indicating that the difference in the HADS anxiety scores between the two groups was not significant ($p>0.05$). The HADS depression scores in Groups 1 and 2 were 7.03±4.46 and 5.95±3.54, respectively, indicating that the mean HADS depression scores were not significantly different between the two groups ($p>0.05$).

The mean BDS scores in Groups 1 and 2 were 12.35±8.71 and 11.70±7.16, respectively, meaning that the BDS scores were not significantly different between the two groups ($p>0.05$).

Discussion

The present study found that the csDMARD and bDMARD therapies used in the treatment of RA did not differ in terms of their effects on the quality of life and depression. These findings are consistent with the findings of previously reported studies [18-20].

Rheumatiod arthritis is associated with pain, weakness, functional limitation, and mood disorders, and it may result in irreversible structural and functional damage if treatment is delayed [21]. It has previously been shown that RA has a significant effect on the quality of life and that it may result in unemployment, disability, increased medical and social costs, and a significant rate of morbidity and mortality [22-24].

In a study carried out by Direskeneli et al. [25], using a self-developed scale, the authors found no significant difference between the quality of life of RA in patients treated with bDMARD or csDMARD. In another study including patients with RA, Joensuu et al. [26] could find no significant difference between the DAS28 and HAQ scores of patients with RA treated with or without bDMARDs. In line with these studies, we were unable to find any significant difference in the HAQ scores or the quality of life between the RA patient groups in the present study [25, 26].

Gerhold et al. [27] reported that patients with RA treated with csDMARDs had higher physical and mental health scores and a better quality of life than patients treated with bDMARDs. In contrast, Inotai et al. [28] and Giacomelli et al. [29] demonstrated that patients with RA treated with bDMARDs had a better quality of life, based on all parameters of the SF-36 and HAQ scores, than patients using csDMARDs. In all three studies, it can be seen that the group with a lower quality of life score had a higher DAS28 score, and we conclude that the inconsistencies between the results of these studies and the findings of the present study can be attributed to differences in the DAS28 scores of the study populations.

Rheumatiod arthritis affects every aspect of a patient's life and has a deep effect on social, economic, and psychological well-being [30, 31]. Psychological factors, such as anxiety and depression, represent significant health problems among patients with RA [32-34].

The BDS was used to assess patients with RA in a previous study conducted by Alkan et al. [19], in which the correlation analyses performed to compare the patients using csDMARD and bDMARD identified no significant relationship between the drugs and BDS. A study by Kekow et al. [20] reported no significant differences in the HADS depression and anxiety scores of groups treated with etanercept (Enbrel, Pfizer PFE) and methotrexate (MTX) (methotrexate sodium, Rheumatrex) in combination or with MTX alone. In line with the previous studies reported above, the depression and anxiety scores in the present study were not found to be significantly different between the two groups.

In their study of patients with RA treated with anti-tumor necrosis factor (anti-TNF) or csDMARD, Bae et al. [35] found depression and anxiety to be less common among those receiving anti-TNF (etanercept), although, unlike the present study, the one by Bae et al. [35] included patients with RA with high disease activity, and only one anti-TNF treatment was considered.

Despite the significant improvements in RA treatment, pain, long-term drug use, drug side effects, fatigue, incapacity to work, and mood disorders still lead to serious psychosocial outcomes in patients with RA [4, 36], and physicians should take these factors into consideration when treating patients with RA. There are several limitations to our study, including a limited number of patients, lack of an RA-related deformity evaluation and radiological scores, evaluation of anxiety and depression by a non-psychiatrist, and the non-cross-sectional nature of the study.

In conclusion, there is no superiority between csDMARD and bDMARD in terms of the effect on the quality of life of patients with RA. That said, csDMARDs are easier and more comfortable to use as a treatment for RA, as bDMARDs require invasive administration in a hospital environment, have a serious side effect profile, and are more difficult to use. Furthermore, there is no superiority between csDMARD and bDMARD in terms of the anxiety and depression in patients with RA. We believe that these results may assist physicians in the selection of medications for the treatment of patients with RA, although further clinical trials are needed to investigate the effects of drugs used in RA treatment on the quality of life, depression, and anxiety of patients with RA.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Cumhuriyet University (2016-09/04)

Informed Consent: Informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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