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EVALUATION OF TREATMENT WITH RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Abstract: The aim of this study was to evaluate the treatment and adverse effects of rituximab in patients with rheumatoid arthritis refractory by disease-modifying antirheumatic drugs therapies. This is a prospective study involving 50 patients with high activity of rheumatoid arthritis. All patients fulfill the criteria of American College of Rheumatology and the European League Against Rheumatism for the diagnosis of rheumatoid arthritis. These patients were hospitalized in the clinic of Rheumatology and followed as outpatients. Rituximab was administered as a 1000-mg intravenous infusion on days 1 and 15. Before treatment, all patients were with high disease activity, DAS 28 > 5.1, while after treatment with rituximab at 24 weeks, 5 (10%) patients had no improvement, where DAS 28 was > 5.1; 11 (22%) patients had partial improvement, where DAS 28 was < 5.1 to > 3.2; 34 (68%) patients had significant improvement where DAS 28 was < 3.2. Treatment with rituximab in patients with rheumatoid arthritis refractory by Disease-modifying antirheumatic drugs therapies is effective, tolerabe and stable by controlling the symptoms of the disease and prevent progression of articular damage. Some patients have required repetition of the treatment with rituximab after 6 or 12 months, according to the activity of the disease.

Keywords: Rheumatoid arthritis, Rituximab, Disease-modifying antirheumatic drugs

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INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory disease characterized by joint swelling, joint tenderness, and destruction of synovial joints, leading to severe disability and premature mortality [1,2]. Early diagnosis and prompt initiation of treatment are needed to reduce or prevent structural damage of joints in rheumatoid arthritis. Uncontrolled active rheumatoid arthritis causes joint damage, decreased quality of life and other comorbidities. Several guidelines for management of rheumatoid arthritis exist, including recommendations from American College of Rheumatology and European League of Arthritis and Rheumatism[3,4]. The key therapeutic drugs that reduce synovitis and systemic inflammation and improve function are Disease-modifying antirheumatic drugs [5]. Biological agents are used when arthritis is uncontrolled with Disease-modifying antirheumatic drugs. Recent research indicates that B cell may act at multiple levels of the inflammatory cascade by disrupting antigen presentation by T cells as well as inducing an increased expression of proinflammatory damage observed in rheumatoid arthritis [6]. Since 2006, B cell-targeted therapy using the anti-CD20 monoclonal antibody rituximab is an effective treatment for rheumatoid arthritis and has also been approved for use in patients with moderate-to-severe rheumatoid arthritis refractory to Disease-modifying antirheumatic drugs and anti-tumor necrosis factor therapy[7, 8].

The aim of this study was to evaluate the treatment and adverse effects of rituximab in patients with rheumatoid arthritis refractory by Disease-modifying antirheumatic drugs therapies.

MATERIALS AND METHODS

This is a prospective study involving 50 patients with high activity of rheumatoid arthritis.

All patients fulfill the criteria of American College of Rheumatology and the European League against Rheumatism for the diagnosis of rheumatoid arthritis[9].

The patients in this study were recruited from outpatient consultations in the Rheumatology clinic at the University Hospital Center Mother Teresa in Tirana.

Pregnancy patients and patients with recent infection, were excluded from the study. All patients had been treated with Disease-modifying anti-rheumatic drugs for at least 16 weeks. These patients were hospitalized in the clinic of Rheumatology and followed as outpatients

Rituximab was administered as a 1000-mg intravenous infusion on days 1 and 15.

Rheumatoid arthritis activity was evaluated according to" Disease Activity Score" of 28 joints (DAS 28) with 3 variables (tender and swollen joint counts plus value of erythrocyte sedimentation rate) [10]. We used the European League Against Rheumatism activity criteria, based on the " Disease Activity Score" of 28 joints (clinical remission values below 2.6, low activity between 2.6 to 3.2, moderate activity from 3.2 to 5.1 and high activity values over

5.1 [11]. Erythrocyte sedimentation rate was measured using the Westergren method. The efficacy of treatment with rituximab and clinical assessments were performed at 24 weeks according to" Disease Activity Score" of 28 joints [10,11].

Statistical analysis

Continuous variables were expressed as mean values and their respective standard deviations. Categorical variables were presented in absolute values and their respective percentages.

Differences between the categorical variables were assessed with Chi square test. The P value ≤ 0.05 was considered a statistically significant. Data were analyzed using the Statistical Package for the Social Sciences software, version 19.0

RESULTS

The mean (±SD) age of the patients was 46.17 (±8.75) years. The mean (±SD) duration of disease was 9.21 (±3.54) years. Female patients are 76 (70.4%) and male patients are 32 (29.6 %). Before treatment, all patients were with high disease activity DAS 28 > 5.1, while after treatment with rituximab at 24 weeks, 5 (10%) patients had no improvement, where DAS 28 was > 5.1; 11 (22%) patients had partial improvement where DAS 28 was < 5.1 to > 3.2; 34 (68%) patients had significant improvement where DAS 28 was < 3.2 (table 1). During the 24-weeks period, adverse effects were reported in 2 patients. The severe adverse effects observed were respiratory tract infection in one patient and cystitis in one patient, adverse effects occurred during or within 24 hours after the first infusion of rituximab were: transient hypertension in two patients, pruritus and rash in one patient (table 2).

Table 1 Disease activity score of rheumatoid arthritis after treatment with rituximab

Variable	Total	BeforeTreatment	After Treatment			
		DAS 28 >5.1	DAS 28 > 5.1	DAS 28< 5.1 to3.2	DAS 28 < 3.2 to 2.6	P-value
Patients	50(100.0)*	50 (100.0)*	5 (10.0)	11(22.0)	34(68.0)	0.0005

*Absolute numbers and row percentage (in parentheses).

Table 2 Adverse effects of treatment with rituximab

Advers effects	Number of patients
Respiratory tract infections	1 (2.0)*
Cystitis	1 (2.0)
Hypertension	2 (4.0)
Pruritus and rash	1 (2.0)

*Absolute numbers and column percentage (in parentheses).4

DISCUSSION

In 24-weeks study, we evaluated the treatment with rituximab and adverse effects in patients with highly active rheumatoid arthritis, who experienced an inadequate response to conventional Disease-modifying antirheumatic drugs therapies. At 24 weeks, patients receiving rituximab demonstrated statistically significant improvement of disease activity. Both rituximab dosages were effective, with 22 % of patients achieving an DAS 28< 5.2 to 3.2 response by week 24, and a high proportion 68 % achieving DAS 28< 3.2 to 2.6 responses. These patients had improvement of all investigated parameters such as; tender joint, swollen joint and value of erythrocyte sedimentation rate. Various studies demonstrate the efficacy, safety and prevention of structural joint damage of rituximab in refractory rheumatoid arthritis [12,13,14]. The efficacy of B cell depletion in rheumatoid arthritis confirms the role of B cells in the pathogenesis of rheumatoid arthritis [13, 15]

Both dosages of rituximab were generally well tolerated, with a low incidence of serious adverse events, including serious infections. The nature of the infections reported and their clinical course were consistent with serious infection events typical of patients with rheumatoid arthritis treated with Disease-modifying antirheumatic drugs or other biological therapies [16, 17].

CONCLUSIONS

Treatment with rituximab in patients with rheumatoid arthritis refractory by disease-modifying antirheumatic drugs therapies is effective, tolerable and stable by controlling the symptoms of the disease and prevent progression of articular damage. Some patients have required repetition of the treatment with rituximab after 6 or 12 months, according to the activity of the disease.

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