

**UNIVERSITY OF MEDICINE AND PHARMACY, TÂRGU MURES
SCHOOL OF DOCTORAL STUDIES**

**CLINICAL AND RADIOLOGICAL EFFICIENCY OF
CONVENTIONAL AND BIOLOGIC DISEASE-
MODIFYING THERAPIES IN RHEUMATOID
ARTHRITIS**

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2012

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KEY WORDS: rheumatoid arthritis, DMARDs, biological therapy, DAS28, HAQ-DI, van der Heijde modified Sharp score, EULAR response, remission, radiological progression, disability

AIM OF THESIS: the evaluation of clinical, biological, functional and radiological efficiency of biologic and conventional therapies in real life, and the outline of correlations comparing clinical, functional and structural parameters.

MATERIAL AND METHODS

This analytical - observational, longitudinal, prospective and retrospective cohort study was conducted on a number of 148 rheumatoid arthritis patients registered at the National Institute of Rheumatology and Physiotherapy, Budapest, Hungary during 2008-2011. Patients were divided into two groups: in the first group (51 patients) were applied mono or combined conventional DMARDs treatment and in the second group (97 patients) were administered biological agents in mono or combined treatment with DMARDs. The biological therapy was administered according to the Therapeutic Protocol for the Treatment of Rheumatoid Arthritis released by the Hungarian Ministry of Health. The patients were evaluated clinically (tender joint count - TJC, swollen joint count - SJC), biologically (ESR, CRP) at the initial visit, marked with V0 and at 3, 6, 9 and 12 months (V1, V2, V3, V4), immunological (antiCCP antibodies, RF) at V0 and V4. DAS28, delta DAS28, delta SJC, delta TJC, delta ESR, delta CPR, delta RF, delta antiCCP antibodies were determined.

The EULAR response to treatment and the achievement of new ACR/EULAR 2011 remission criteria was determined. Clinical, biological and immunological improvements were evaluated and compared within each group and between the two groups. During each visit a HAQ-DI questionnaire was completed for each patient. Delta HAQ was calculated and the decrease of the score evaluated for patients of the same group and between the two groups. In order to establish joint destruction, comparative radiographs of hands and feet were evaluated, using the van der Heijde modified Sharp (vdHmS) score, at V0 and V4. Delta score for hands and feet respectively total vdHmS score and delta erosion and joint space narrowing score were determined separately. Evolution for each joint and the decrease of scores within each group and between groups was also assessed. In order to establish correlations between parameters, delta DAS28, delta HAQ during the four visits, the degree of disease activity defined by DAS28, the EULAR response and the ACR/ EULAR 2011 remission were compared to each other, respectively with the immunological markers (antiCCP antibodies, RF) and radiological progression. The obtained data were statistically analyzed by using MedCalc, statistical software developed for biomedical research and GRAPH Pad Prism 5.

RESULTS

Conventional DMARDs and biological therapies significantly improve disease activity and the degree of disability in patients with rheumatoid arthritis. Delta DAS28 and delta SJC were significantly higher in the group undergoing biological therapy at each visit compared to the group undergoing conventional DMARDs therapy. The achieved results regarding clinical-biological and functional remission after one year of treatment were similar in each group. There were statistically significant differences in EULAR non-responders, the

number of these patients was higher in the group undergoing conventional DMARDs therapy, starting from the third month of treatment. Radiological remission was significantly higher in the group undergoing biological treatment. In the group undergoing conventional DMARDs therapy progression at the level of the hands was statistically significantly greater than in the group undergoing biological therapy. The most important progress was recorded in both groups at the level of the metacarpophalangeal joints, followed by the metatarsophalangeal joints. Statistically significant differences for the two studied groups were registered at the proximal interphalangeal joints and interphalangeal joints for delta erosion and at the metacarpophalangeal joints for both delta erosion and delta joint space narrowing. If progression at the level of the cartilage showed no statistically significant differences between the two groups, delta erosion score was significantly higher in the group undergoing conventional DMARDs therapy, the biological therapy proved to be superior to conventional therapy in reducing joint destructions, by having a protective effect on bone tissue. Delta DAS28 was correlated with delta HAQ-DI at all four visits, the strength of correlations and statistical significance increasing progressively from one visit to another. The final disability score was correlated with the final disease activity score and initial disability index in both groups, without showing correlation with the radiological progression in the bone/ cartilage or with initial activity of the disease. In patients undergoing biological therapy, baseline antiCCP antibody titer was positively correlated with radiological progression. The degree of radiological progression was not correlated with the initial or final activity of the disease, the degree of amelioration of the disease activity, presence/ absence of RF or with its titer or with presence of antiCCP antibodies. The therapeutic response defined by DAS28, EULAR response or ACR / EULAR 2011 criteria did not correlate with the presence/ absence of RF or antiCCP antibodies nor with the titres of these immune markers. At the same time the therapeutic response did not correlate with the radiological progression, which underlines the independent evolution of the two processes (inflammation and destruction). The HAQ-DI of patients who experienced ACR/ EULAR remission primarily depends on the degree of joint destructions and especially on the erosion score, while in patients with active disease depends mainly on the disease activity (DAS28). Regarding these elements, the final HAQ-DI was statistically significantly correlated with TJC and SJC at V4, and the radiological progression with the CRP level at V4.

CONCLUSIONS

Both conventional DMARDs and biological therapies significantly improve disease activity and the degree of disability in patients with rheumatoid arthritis. Biological therapy proved superior to conventional therapy in reducing radiological progression and providing superior bone protection. Clinical remission after one year of biological or conventional treatment was achieved similarly in both groups, but radiological remission is significantly higher in the group treated with biological agents. The disability score of patients in ACR/ EULAR remission depends primarily on the degree of joint destructions, especially on the erosion score, while in patients with still active disease it depends mainly on the degree of disease activity.