

THERAPEUTIC OUTCOMES ON IL-17 LEVELS WITH CD20 VERSUS TNF-A INHIBITORS IN RHEUMATOID ARTHRITIS

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DOI: <https://doi.org/10.5281/zenodo.17463431>

Abstract

Back ground: Rheumatoid arthritis (RA) is a chronic , systemic , inflammatory disorder that may affect many tissues and organs ,once a diagnosis is made , the main treatment goals are to control disease activity and slow the rate of joint damage ,in addition to minimizing pain, stiffness, inflammation and complications. Important role of IL-17 in the development of disease and can be used as a marker for monitoring of disease activity.

Aim of the Study The aim of the present study to evaluate the effects of CD20 inhibitors therapy in comparison to effects of TNF α inhibitors therapy on IL-17 in patients with active rheumatoid arthritis.

Results:- results obtained in the present study showed that serum level of IL-17 were also decrease significantly in patients treated with Rituximab group 3 (2.28) than those of group 2 Etanercept (anti-TNF α) treated group patients (3.3).

Conclusion:- the role of IL-17 in the development of disease and can be used as a marker for monitoring of disease activity

Keywords: IL-17, TNF- α , CD-20, RA

Introduction

Rheumatoid arthritis (RA) is a chronic , systemic , inflammatory disorder that may affect many tissues and organs ,once a diagnosis is made , the main treatment goals are to control disease activity and slow the rate of joint damage ,in addition to minimizing pain, stiffness, inflammation and complications, Pharmacologic therapies that are used include: a- no biologic and biologic (DMARDs).

B- adjunctive agents such as (Corticosteroids, NSAIDs, Analgesics). (1)

From biologic treatment: - TNF α inhibitors: Tumor necrosis factor alpha (TNF α) is a pro- inflammatory cytokine produce by macrophages and lymphocytes.)²⁾ - Non -TNF α agents: Rituximab (B-Cell Depletion): B-cells are an important inflame-tory cell with multiple functions in the immune response, and these are effected on : - IL- 17: Interleukin - 17 has been implicated in the pathogenesis of a wide range of diseases, IL-17 response can be modulated by multiple cytokines. A combination treatment of Infliximab , an anti TNF- α antibody, and methotrexate, an antimetabolite , is shown to significantly reduce disease along with decrease in the frequency of Th-17 cells and the levels of IL-

17 in RA patients without significant response show that such an agent holds adverse effects, clinical trials aimed at inhibiting IL-17 promise as an efficacious treatment for arthritis.³⁾

II. Subjects and Methods: - 70 patients were enrolled in this study their age range from 20 – 68 years. The

patients were divided into three groups : Group1consist of 20 RA patients received DMARDs(disease modifyinganti rheumatic drugs) , while group 2 and group 3 consists 50 patients received biological treatment : one group of them include25 patients received Etanercept (anti – TNF α) and the other group include 25 patients received Rituximab (anti – CD20) ,with 20 healthy volunteers as control whose their ages and gender were matched with patients group. The assay employs the quantitative sandwich enzyme immunoassay technique. Antibody specific for IL-17 has been pre-coated onto a mice plate. Standards and samples are pipetted into the wells and any IL-17 present is bound by the immobilized antibody. After removing any unbound substances, a biotin-conjugated antibody specific for IL17 is added to the wells. After washing, avidinconjugated Horseradish Peroxidase (HRP) is added to the wells. Following a wash to remove any unbound avidin-enzyme reagent, a substrate solution is added to the wells and color develops in proportion to the amount of IL-17 bound in the initial step. The color development is stopped and the intensity of the color is measured. This measurement was done by ELISA technique.

III. Results

The results in present study showed that there is significant elevation in the median serum level of IL17 in healty control than those of RA patients table 1 and figure 1.

Table 1: Descriptive statistics of IL-17 between RA patients and healthy control group

IL-17	Mean $\pm$ S.E.	P value
Healthy control	26.315 $\pm$ 5.637	0.01
RA patients	3.943 $\pm$ 0.617	

IL-17 (Pg/ml) :Interlukin - 17

S.E. :Standar Error



Figure 1 : Mean serum level of IL-17 in RA patients and ealthv control group

Comparison among RA groups revealed that group 1patients has higher levels of IL-17 than those of patients in group 2 (5.268 $\pm$ 0.69 and 3.811 $\pm$ 0.694 respectively),and group 2 patients has higher levels

of IL-17 than those of patients in group 3, there is statistical significant difference between them every one to other $P=0.01$, table 2 and figure 2.

Table 2: Descriptive statistics of IL-17 in different groups of RA.

IL-17	Mean $\pm$ S.E.	p-value
Group 1	5.268 $\pm$ 0.69	0.01
Group 2	3.811 $\pm$ 0.694	0.01
Group 3	2.75 $\pm$ 0.469	0.01

Group 1 : Not biological treatment :- treated by :

DMARDs – Disease modifying anti- rheumatic drugs- group.

Group 2 : Etanercept(anti-TNF α)treated group.

Group 3 : Rituximab (anti-CD20) treated group.

IL-17 : Interlukin-17

S.E. :standard Error

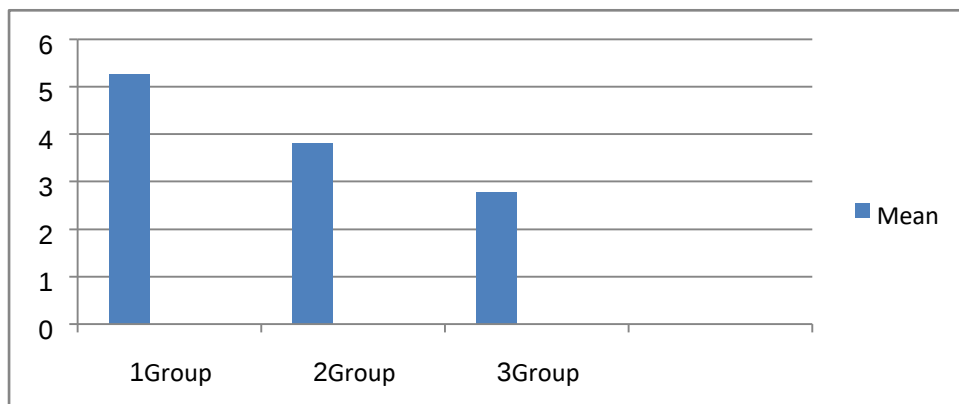


Figure 2: Mean value of IL-17 in different groups of RA.

An anticipated median serum level of IL-17 were also decrease significantly in patients treated with Rituximab group 3 (2.28) than those of group 2 Etanercept (anti-TNF α) treated group patients (3.3)table 3 and figure 3.

Table 3 : Descriptive statistics of IL-17 between group 2 and group 3.

Serum level of IL-17	Group 2	Group 3
Minimum	0.33	0.18
Maximum	16.6	8.52
Median	3.3	2.28
Mean	3.811	2.75
S.D.	3.47	2.345

Group 2 : Etanercept(anti-TNF α)treated group.

Group 3 : Rituximab (anti-CD20) treated group.

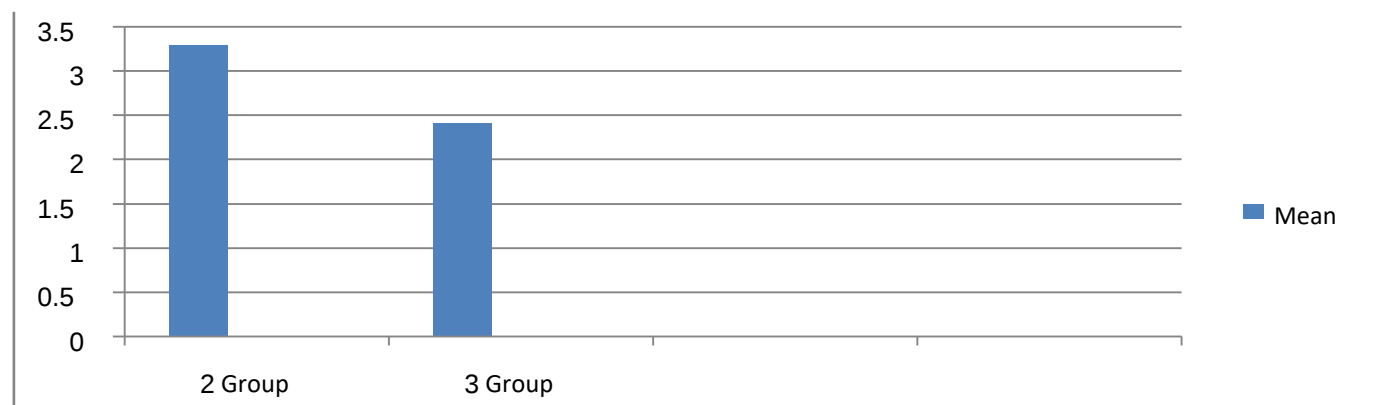


Figure 3 : Median value of Serum IL-17 in group 2 and group 3.

IV. Discussion

Current findings suggest that the management strategy of RA disease status should be improved with an alternative regimen, inversely, patients treated with biologic therapy (Etanercept and Rituximab) showed lower serum IL-17 level when compared with healthy control or when compared with patients received DMARDs, $P < 0.01$, $P < 0.01$ respectively. These results are in agreement with results reported by other studies, who stated that Rituximab reduced the local Th 17 response in RA patients, and the decreased Th17 response was associated with strongly reduced IL-17 as well as reduced inflammation and better clinical outcome.

These results with current findings support that the IL-17 is highly expressed in the inflammatory joints and drives disease activity, implicating it as a key cytokine and potential therapeutic target.

These studies have shown that IL-17 not only drives their inflammatory response but also enhances the effect of TNF- α promoting increased destruction in the RA joint (⁴; ⁵). The current study supports that IL-17 is implicated in the pathology of RA disease especially in active disease rather than remission or milder cases. This statement is argued by several researchers (⁶; ⁷; ⁸) Implication of IL-17 in the RA disease may be explained with different mechanisms, either by promoting matrix turnover and cartilage destruction, especially in the presence of other cytokines, mimicking the joint environment (⁴) mimicking the joint environment (⁹), or stimulate osteoclast increasing or competition of pro-inflammatory network IL-1 and TNF- α inducing joint inflammation and pathology by inducing synovium matrix destruction (¹⁰) and inducing cartilage breakdown (¹¹).

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