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EFFECTIVENESS AND SAFETY OF ETANERCEPT IN RHEUMATOID ARTHRITIS

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ABSTRACT

Background: A chronic autoimmune illness that causes progressive joint degeneration, rheumatoid arthritis (RA) is a major source of pain and functional impairment. The United States Food and Drug Administration (FDA) authorized etanercept (ETN) as the first biologic response modifier for use in RA. Etanercept has been shown in several clinical trials to be both safe and effective in treating active RA. **Objective:** To assess the effectiveness and safety of etanercept in rheumatoid arthritis (RA) in a sample of Iraqi patients. **Patients and methods:** Over the course of 12 months, 100 Iraqi patients with RA who were referred from rheumatology seniors in Nineveh province to the biologics committee in the rheumatology sector at IBN_SINA Teaching Hospital between April 2019 and April 2020 participated in this open-labeled single group retrospective study. From the beginning of the trial until its conclusion, all of the enrolled patients received etanercept at a dose of 50 mg by subcutaneous injection every week, either with or without methotrexate. After three and six months, the patients' safety and effectiveness of the medication were assessed. Every patient's side effects were examined and documented on each doctor's appointment, and data was gathered. **Results:** The usage of etanercept resulted in a substantial decrease in platelet count ($P \leq 0.05$) and a significant improvement in disease activity score (DAS28) ($P \leq 0.05$) after 6 months of therapy. Aspartate aminotransferase, alanine aminotransferase, urea, creatinine, hemoglobin level, and white blood cell count, however, did not alter significantly. **Conclusion:** For individuals with RA, etanercept 50 mg once weekly for 24 weeks was a reasonably safe and successful medication.

KEYWORDS: Effectiveness, Etanercept, Rheumatoid Arthritis, Safety.

INTRODUCTION

A chronic autoimmune inflammatory illness, rheumatoid arthritis (RA) affects 0.5–1% of people worldwide and is characterized by joint involvement, substantial morbidity, increasing disability, and an elevated risk of mortality. Although the exact origin of RA is uncertain, higher susceptibility and the severity of the disease have been associated with a number of genetic polymorphisms and environmental factors. Bone erosion and cartilage loss are the main effects of RA's inflammatory development of synovial tissue on peripheral joints.[1] Chronic systemic inflammation in RA can lead to extra-articular symptoms such malignancy, type-2 diabetes mellitus, infections, osteoporosis, tiredness, chronic anemia, interstitial lung disease, increased cardiovascular disease, and psychological impairment.[2]

According to the American College of Rheumatology's treatment guidelines, the goals of RA pharmacotherapy are to prevent additional joint damage, reduce disease activity, establish remission, and maintain strict control via medical care. RA has been treated with glucocorticoids, nonsteroidal anti-inflammatory medications, and disease-modifying anti-rheumatic medications. medicines known as disease-modifying anti-rheumatic medicines (DMARDs) can reduce RA symptoms and indicators while delaying the advancement of damage.[3]

Biologics are drugs that are created from living things or contain parts of living things and are intended to stop or change the function of cytokines. Examples of these include methotrexate and tumor necrosis factor blockers.

In 2002, etanercept—the first biopharmaceutical specifically designed to treat RA—was authorized to help individuals with psoriatic arthritis manage their arthritis symptoms. Etanercept is a soluble fusion protein that is attached to the Fc region of human IgG1 and consists of two 75 kD TNFR II proteins.[4,5]

The most frequent adverse effect perceived after using anti-TNF therapy is injection site reaction, raised hazard of serious long-term infections, particularly respiratory ones, and reactivation of latent tuberculosis (TB) remains a major problem.[6] Common infections include histoplasmosis, influenza, adenovirus, Pneumocystis pneumonia, latent viral infections (varicella-zoster, herpes-zoster), infections of the skin and soft tissues, and urinary tract infections. Legionella outbreaks have also been reported. The less frequent adverse effects include leucopenia, hypersensitivity responses, nervous system disorders, and severe hepatic reactions.

There is now no proof of an increase in any malignancy, despite certain meta-analyses examining the elevated risk of malignancies due to anti-TNF medication. A higher incidence of non-melanoma skin cancer has been associated with TNF-blocker treatment.[7,8] It has been discovered that certain patients have higher levels of antibodies against double-stranded DNA.[9]

OBJECTIVE: To evaluate etanercept's safety and efficacy in treating rheumatoid arthritis (RA) in a group of Iraqi patients.

PATIENTS AND METHODS

Over the course of a 12-month period, 100 Iraqi patients who diagnosed to have RA were recommended by rheumatology seniors to the biologics committee in the rheumatology sector at Ibn-Sina Teaching Hospital between April 2019 and April 2020 participated in an open-labeled single group retrospective study. All of the patients were sent to the biologic medicine distribution committee at Ibn-Sina Teaching Hospital after receiving a RA diagnosis from their physicians. Five expert rheumatologists make up this committee, which makes the ultimate determination on a patient's appropriateness for biologic treatment, including etanercept. The committee adheres to national RA treatment standards that were approved by the Ministry of Health but not yet publicly published.

From the beginning of the trial to its conclusion, all enrolled patients received weekly subcutaneous injections of etanercept (Enbrel) at a dose of 50 mg. Patients were evaluated for the drug's safety and efficacy at three and six months.

The Ibn-Sina Teaching Hospital's rheumatology registry provided the data. A prospective longitudinal cohort, the rheumatology patient registry was started in 2019. All cases with rheumatic disorders who have established biological agent treatment at the rheumatology department are included. In order to be eligible for the study, patients had to meet the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for RA, which include low disease activity (DAS28 equal to or greater than 3.2) or failure to achieve remission within three months of starting MTX at maximally tolerated doses within the standard therapeutic range.

RESULTS

Table (1) displayed the incidence of etanercept therapy side effects among 100 rheumatoid arthritis patients. Elevated liver enzyme, itching, injection site response, and a significant chest infection were the most frequent adverse effects.

Table 1: Adverse reaction in rheumatoid patient.

Adverse effect	No.	%
Elevated Liver transaminases	4	4%
leucopoenia (<3000)	2	2%
Headache	1	1%
Itching	4	4%
Serious chest infection	3	3%
Injection site reactions	4	4%

After three and six months of therapy, etanercept dramatically decreased DAS28 ($p<0.001$). Additionally, as seen in table (2), there were notable variations in the number of swollen and sensitive joints as well as the ESR.

Table 2: DAS28 change and ESR.

	Baseline	3 Month	6 Month	P value*
DAS28	6.18 + 1.29 a	5.07 + 1.35 b	5.25 + 1.48 b	0.050
ESR	44.57 + 22.86 a	34.68 + 24.19 b	30.40 + 1.89 b	0.050
SWJ	6.99 + 6.2 a	3.59 + 3.5 b	3.40 + 4.2 b	0.050
TJ	15.65 + 8.2 a	10.06 + 7.7 b	10.92 + 8.3 b	0.050

*One-way ANOVA with post hoc test; different letters means significance while similar letters means no significance

DISCUSSION

In this research, individuals with extremely active RA in Mosul, Iraq, had their safety and efficacy with Etanercept evaluated. It demonstrated a statistically significant and clinically meaningful decrease in disease activity. Furthermore, etanercept was comparatively safe, with just a few side effects, such as a brief increase in liver transaminases, itching, and injection site response (4%), as well as a 3% risk of chest infections, a 2% risk of leukopenia, and a 4% risk of non-serious infections. Other research revealed similar results. In open-label extension studies after initial double-blind trials of etanercept, Weinblatt et al.[10] assessed the safety and effectiveness of etanercept beyond 10 years of therapy in North American patients with early and longstanding rheumatoid arthritis. They concluded that etanercept was well-tolerated and effective as long-term, continuous therapy for the treatment of RA, with a favorable risk/benefit ratio. Another Japanese study, which is one of the biggest observational trials that have been carried out so far in RA patients treated with biologics, assessed the safety and efficacy of etanercept in a 6-month postmarketing surveillance study that included all Japanese RA patients who were treated with etanercept over a two-year period. When data for 13,894 patients (1334 locations) were gathered between March 2005 and April 2007, it was shown that etanercept was safe and effective for Japanese patients.[11] Furthermore, Koike et al.[5] found that in Japanese patients with RA, combination treatments including etanercept and methotrexate or another DMARD were somewhat well-tolerated and that etanercept plus methotrexate at higher dosages was more efficacious than etanercept monotherapy. Adding etanercept to methotrexate showed well effectiveness than adding one other conventional DMARD to methotrexate, according to Machado et al.[12], who conducted an observational study comparing the addition of etanercept versus conformist DMARDs in subjects with active RA in spite of methotrexate treatment in the Latin American region. There were no new safety concerns noted. For RA patients, etanercept and methotrexate together offered a good benefit-risk profile. Another research by Pedro Santos-Moreno et al.[13] comparing the safety and efficacy of anti-TNF medications in rheumatoid arthritis patients in Colombia reveals a significant response to 50 mg of etanercept compared to 25 mg and other anti-TNF members. In Ilić et al.'s trial[14], individuals with active RA receiving DMARD therapy were treated with etanercept at weekly dosages of 50 mg while still receiving DMARD. In the twelfth week, the effectiveness of this type of treatment was assessed. Eighty percent of patients saw an ACR20 response after 12 weeks of etanercept therapy, and eighty-five percent had a clinically meaningful drop in the DAS28 index. The medication's safety profile was adequate. Mochizuki et al.[15] performed a research to compare the effectiveness of twice-weekly administration of 25 mg ETN (ETN25) with that of once-weekly administration of 50 mg ETN (ETN50). At 24 weeks, they discovered that 76.9% of ETN50 patients had minimal disease activity and 42.3% had DAS28-ESR remission (<2.6). Additionally, linked to cases in the ETN25 group, cases in the ETN50 group had lower disease activity rates, higher DAS28-ESR remission rates, and a more notable enhancement in DAS28-ESR at 4 weeks. The safety analysis set did not suffer any significant adverse occurrences. Lack of immunogenicity or negligible immunogenicity to etanercept therapy in comparison to other TNF blockers may be the reason for the explanation of the reply to etanercept management.[16]

CONCLUSION

Etanercept was shown to be a successful treatment for RA patients in the present trial, which examined the safety and effectiveness of giving patients 50 mg of the medication once weekly for six months. The disease activity significantly and quickly improved. Etanercept was a rather well-tolerated and safe medication. The majority of side effects were minor and prevented therapy from being stopped.

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