Efficacy of Etanercept Treatment in Iraqi Patients with Moderate to Severe Psoriasis

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ABSTRACT:

BACKGROUND:

Etanercept is a tumor necrosis factor (TNF) α inhibitor that has been approved for the treatment psoriasis.

OBJECTIVE:

Assessing the efficacy of etanercept therapy in Iraqi patients with moderate to severe psoriasis.

PATIENTS AND METHODS:

This study was a therapeutic interventional study at Medical City; center of dermatology and venereology (Baghdad, Iraq) from January 2017 till June 2018, with 53 patients, 31 (58.49%) males and 22 (41.51%) females, with 51 patients having moderate to severe plaque psoriasis and 2 patients with pustular psoriasis. All patients were given 50 mg subcutaneous injection of etanercept twice weekly for 3 months, followed by single injection of etanercept weekly for the next 9 months. Psoriasis area and severity index calculations were done every 3 months until 1year of treatment.

RESULTS:

The baseline PASI score changed from a mean ± standard deviation of 24.28 ± 14.56 to 1.62 ± 3.11 At the end of 12 months of treatment with a significant difference (P=0.001). Regarding the reduction in the patients' PASI score: At 3 months of treatment, (71.4%) achieved PASI 50, (48.2%) had PASI 75, and (5.35%) had PASI 90, at the 12th month of treatment (75.4%) reached PASI 90, (86.79%) reached PASI 75, &(94.33%) had PASI 50. Side effects were mild and tolerable.

CONCLUSION:

Etanercept is an effective therapy in treating moderate to severe psoriasis with tolerable side effects.

KEYWORDS Psoriasis, Etanercept, Tumor necrosis factorα inhibitors.

INTRODUCTION:

Psoriasis is a chronic, immune-mediated, inflammatory disease which primarily affects the skin and joints.[1] It has a complex, multifactorial nature that is influenced by genetic, environmental factors and immune components, with a worldwide prevalence of approximately 1 to 3%.[2]

An appropriate treatment regimen for a particular patient is selected from available topical and systemic medications as well as phototherapies. In clinical trials, single agents are usually evaluated, but in practice most patients receive combination therapy.[3]

Etanercept: is a receptor antibody fusion protein that combines the human IgG1 Fc region with two TNF type 2 (p75) receptor. In contrast to other TNF-a inhibitors agents which binds to soluble and transmembrane TNF-a, etanercept binds to soluble TNF-α and TNF-b (lymphotoxin-a). Etanercept received FDA approval for treating moderate to severe psoriasis in April 2004 and was also approved for the treatment of rheumatoid arthritis, psoriatic arthritis, juvenile rheumatoid arthritis and ankylosing spondylitis.[4]

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PATIENTS AND METHODS:

This study is a therapeutic interventional study which was conducted at the Medical City; Center of Dermatology and Venereology (Baghdad, Iraq) from January 2017 till June 2018. Ethical approval was granted by the Scientific Council of Dermatology/Iraqi board, and a verbal consent from all patients included in this study was taken; after full explanation about the nature of the study. A total of 56 patients were enrolled, with 53 patients completing the study. The patients included had moderate to severe chronic plaque psoriasis, with 2 patients having pustular psoriasis, that was resistant to other conventional treatments; or these modalities were contraindicated. The exclusion criteria were pregnancy, lactation, patient with severe renal, hepatic, hematological or other systemic disease, patient with immunosuppression, moderate to severe heart failure, lympho-proliferative disease, demyelinating disease, active or latent tuberculosis reactivation, and positive virology screen for hepatitis and HIV.

History, physical examination, determination of the extent and severity of psoriasis and the response to etanercept treatment were done by calculating PASI (Psoriasis Area and Severity Index) score. PASI score assesses the severity and extent of psoriasis giving a score from 0 to 72, moderate to severe psoriasis was defined by having PASI score >10.[1] All the patients who enrolled in the present study were instructed to stop any topical or systemic medications used to treat psoriasis for at least one month, and only bland emollients were allowed as a topical treatment.

Baseline investigations: All the patients were requested to do the following investigations before starting the treatment: Complete blood count, Liver function test, Renal function test, Virology screen for hepatitis B & C viruses and HIV, Tuberculin skin test, Chest X ray with report, Pregnancy test for female of child bearing age.

Treatment protocol

All patients enrolled in the current study were given 50 mg subcutaneous injection of etanercept twice weekly for 3 months, followed by single injection of etanercept weekly for the next 9 months. Measuring PASI score of the patients every 3 months until completing one year of treatment was done, with careful follow-up using the routine investigations and reporting any adverse effect was done at each visit.

RESULTS:

In the present study, 56 patients were initially included, 53 patients completed the study with 31 (58.49%) were males and 22 (41.51%) were females, 3 patients defaulted due to poor response within the first 3 months of treatment.

Regarding the male patients, their ages ranged from 15 to 68 years with a mean ± SD of 41.53± 13.877, and the disease duration ranged from 2 to 45 years with a mean ± SD of 13.81± 8.785.

Female patients' ages ranged from 18 to 54 with a mean ± SD of 31.5 ±11.788, with disease duration from 1 to 25 years with a mean ± SD of 9.1± 7.241. The above data are illustrated in table (1).

Regarding previous drug history, 45 patients (80. 35%) were previously treated with methotrexate, 22 patients (39.28%) were on acitretin, and 13 patients (23.21%) received cyclosporine. 25 (44.64%) of the patients received previous phototherapy (whether PUVA or NB-UVB), and none of them included in this study previously received other biologic agents. A positive family history of psoriasis was seen in 8 (14.28%) of patients and 46 (82.14%) had received BCG vaccination during childhood, none of these patients had history of active tuberculosis or close contact with infected patients.

- **Psoriasis Area and Severity Index score:**

The baseline PASI score of the patients with chronic plaque psoriasis ranged from 8.8 to 59.4 with a mean ± SD of 24.28 ± 14.56. After 3 months of treatment, the PASI score changed to a mean ± SD of 9.53 ± 7.93 from the baseline visit, with a significant difference (P=0.001). At 6 months of treatment, the score became 5.63 ± 6.48 with a significant difference from the baseline readings of (P=0.001). After 9 months, the patients reached 2.55 ± 4.44 with a significant difference of (P=0.001) as compared to the first visit.

After completing 1 year of etanercept treatment, the patients' mean PASI score became 1.62 ± 3.11 with a significant difference (P=0.001), as shown in table (2). Patients with pustular psoriasis had complete clearance of their disease.

Regarding the reduction in the patients' PASI score is shown in figure (1).

The following adverse effects were reported during the treatment period:

- 3 patients (5.66%) recorded recurrent appearance of skin infections (boils) during the course of treatment, which responded to conventional therapy.
- 3 patients (5.66%) reported mild to moderate injection site reaction in the form of mild to moderately painful erythema which resolved spontaneously within few days.
- And 2 patients (3.77%) had mild elevation in their liver enzymes which was transient and did not need further intervention.

No serious side effects were reported during the course of treatment.

Figure (2) and figure (3) show the improvement of patients on etanercept treatment.

Table (1): baseline data of the patients.

	Male patients				Female patients			
	minimum	maximum	mean	Std. deviation	minimum	maximum	mean	Std. deviation
Age	15	68	41.53	13.87	18	54	31.5	11.78
Duration of illness	2	45	13.81	8.785	1	25	9.1	7.24
Baseline PASI	8.8	55.2	26.24	13.79	10.1	59.4	21.67	15.44
Baseline BSA	7	93	35.93	24.53	10	91	29.95	22.46

Table (2): PASI score at different months of treatment with mean ± SD with minimum and maximum values.

PASI	*No.*	*minimum*	*maximum*	*mean*	*Std. deviation*
Baseline	53	8.8	59.4	24.28	14.56
At 3 months	53	2	38.1	9.53	7.93
At 6 months	53	0	26.6	5.63	6.48
At 9 months	53	0	22.7	2.55	4.44
At 12 months	53	0	16.2	1.62	3.11

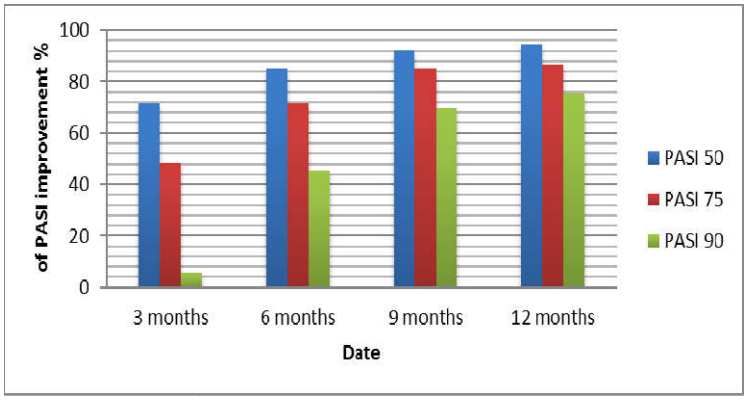

Figure (1): Percentage of patients' improvement in PASI score at different months of treatment.

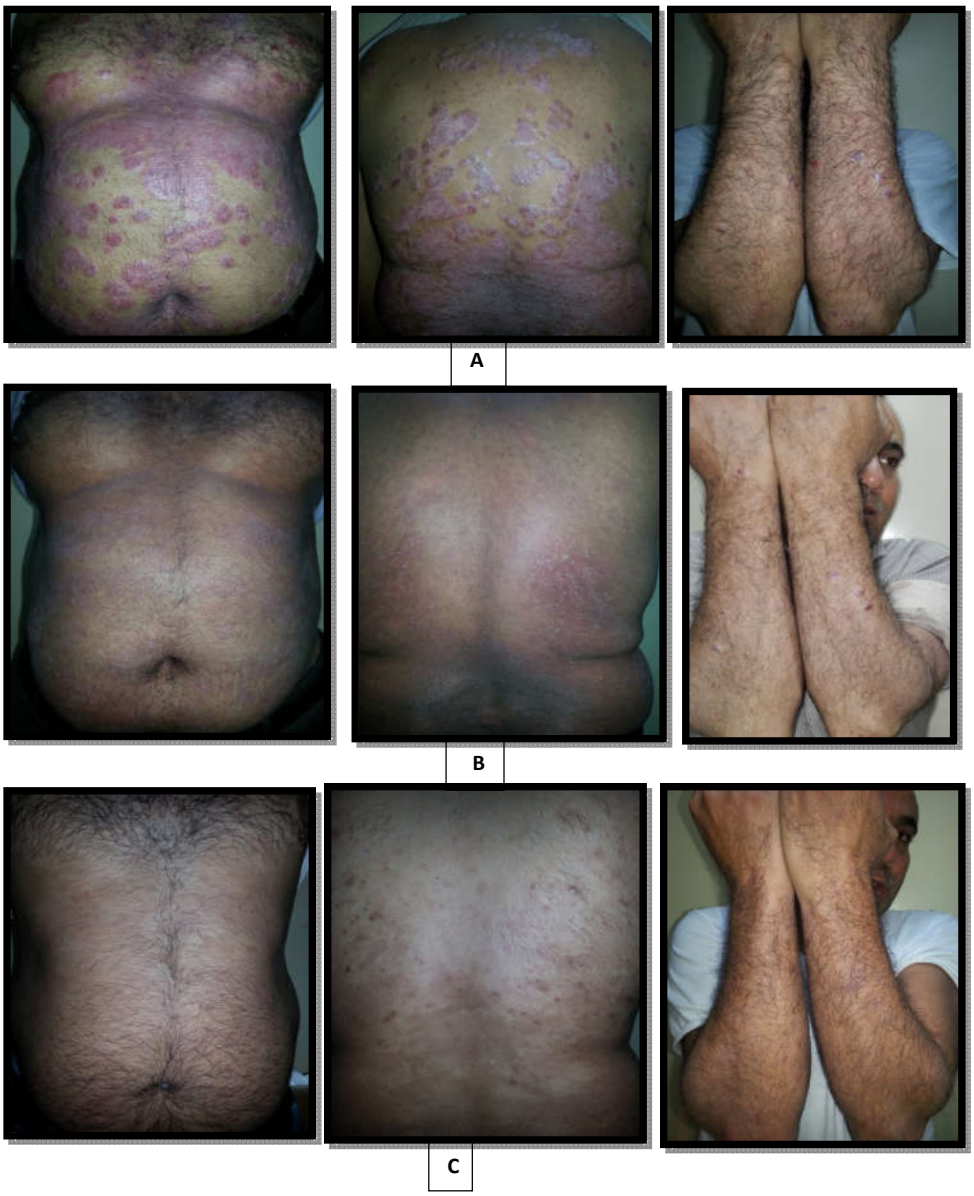

Figure (2): A 38 years old patient with 6 years duration of chronic plaque psoriasis

A- before treatment

B- 3 months of treatment

C- 1 year of treatment

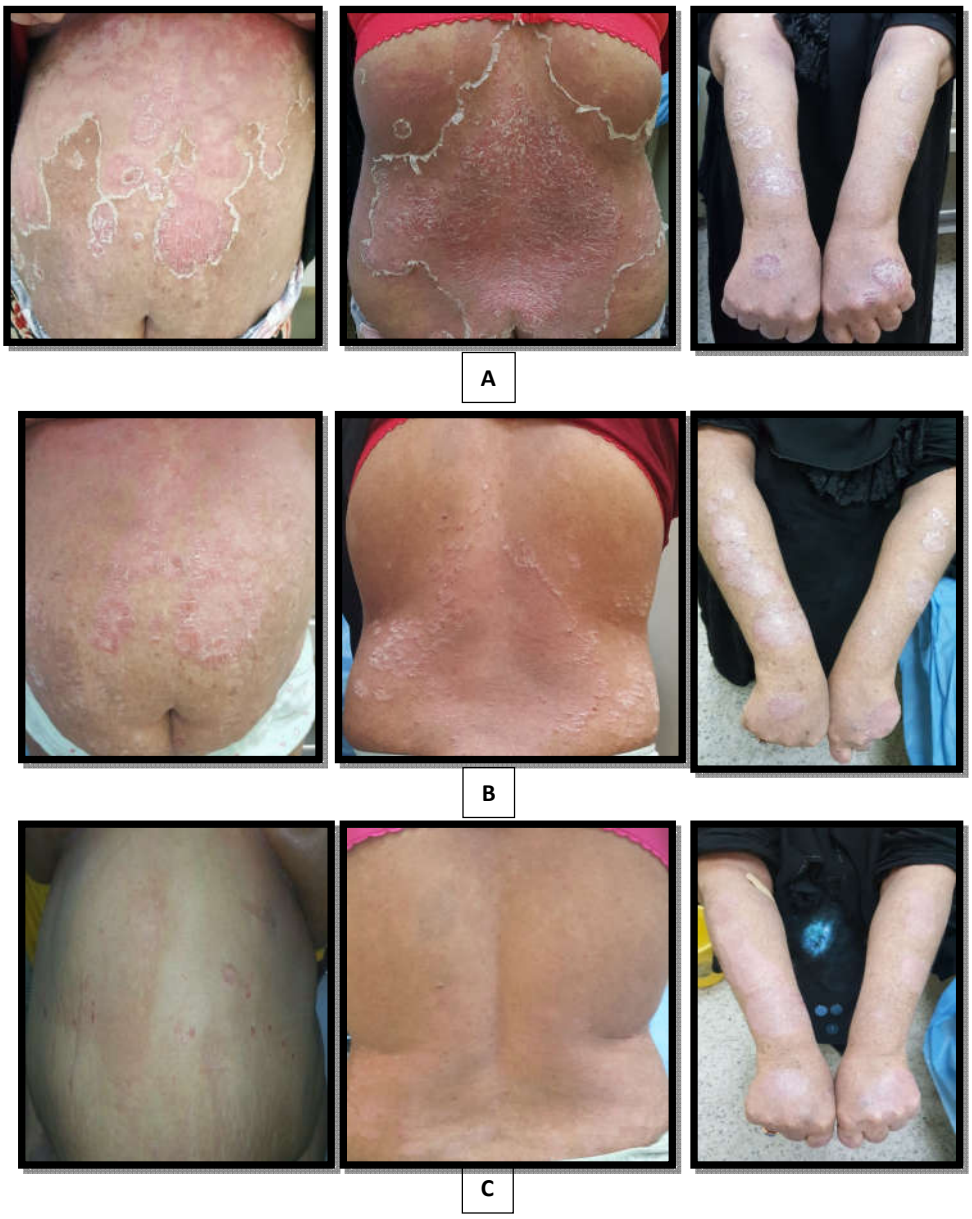

Figure (3): A 41 years old patient with 20 years duration of chronic plaque psoriasis

A- before treatment

B- 3 months of treatment

C- 1 year of treatment

DISCUSSION:

Psoriasis is a chronic inflammatory disease with a significant impact on the quality of life.[1] Until the year 2000, methotrexate, acitretin, cyclosporine and oral methoxsalen with UVA phototherapy were the only FDA approved systemic medications for psoriasis. Although these drugs are effective in treating psoriasis, they have multiple undesirable side effects which limit their use. [1] Etanercept had been FDA approved for the treatment of moderate to severe plaque-type psoriasis in adults since 2004. [8]

Etanercept was not available in Iraq until 2012, when it was first introduced at the rheumatology department of Baghdad teaching hospital at the Medical City, and for the last 2 years it has remained the only biologic agent available in the dermatology center of the same hospital. In the current study, PASI scores improved significantly with etanercept treatment.

Two previous two studies from Iraq have reported on etanercept treatment for psoriasis; both studies used the same treatment regimen as that used in the present study. Etanercept monotherapy was tested over a period of six months in one study while in the other study it was compared to methotrexate. Abass (2018) results agree with the results of the present study at 6 months of treatment regarding PASI scores reduction. The results were comparable to our study, except for PASI 75 which was (60%) versus (71.69%) in the present study.[9]

While Obeed (2018) compared the efficacy of etanercept and methotrexate treatment for psoriasis in Iraqi patients. After 6 months of treatment, there was no statistical differences between the two groups.[10]

Etanercept treatment for 1 year was also studied in Italy by Di Lernia et al. (2017). The results of patients achieving PASI 75 in their study at both the 6th and 12th month of treatment was inconsistent with the results in the present study.[11] This inconsistency may be due to the difference in the age group included.

Zweegers et al. (2017) study, compared between 3 biologic drugs (etanercept, ustekinumab & adalimumab), and showed a similar effectiveness in the mean PASI between the 3 drugs at 1 year, with a higher chance of attaining PASI 75 with adalimumab and ustekinumab than with etanercept at 1 year of treatment.[12]

In the same field, etanercept (50 mg twice weekly) versus infliximab (5 mg/ kg infusions were given at week 0, 2, 6, 14 and 22) were studied by de Vries et al. (2013). Etanercept was inferior to infliximab based on PASI 75, at week 24, (35%) of patients on etanercept group reached PASI 75 versus (72%) of patients from infliximab. Our results disagree with de Vries et al results, as PASI 75 at week 24 was (71.69%), which is comparable with the result on infliximab group. [13]

In the present study, etanercept was effective with tolerable, non-serious side effects.

CONCLUSIONS:

From this study we conclude that etanercept is an effective therapy in treating moderate to severe psoriasis with tolerable side effects.

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