Bulletin of the *Transilvania* University of Braşov
Series VI: Medical Sciences • Vol. 5 (54) No. 2 - 2012

THE THERAPY OF THE REBEL SEVERE PSORIAZIS WITH BIOLOGICAL PREPARATS

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Abstract: *Biological therapy consists in the use of substances which are a top medical technology and research, which are based on clinical trials on thousands of patients, proofing their efficacy and safety. The study was conducted on 18 patients diagnosed with severe psoriasis who have not responded to conventional treatments. Eleven patients received adalimumab 80 mg in the first week, then 40 mg every two weeks throughout and 7 patients received etanercept at a dose of 50 mg/week.* ***Conclusion:*** *Both adalimumab and etanercept is an effective therapeutic alternative for the treatment of rebel severe psoriasis.*

Key words: *psoriasis vulgaris, adalimumab, etanercept, biologic therapy.*

1. Introduction

In recent years, following the acquisition of modern research on immunological implications in the etiopathogenesis of psoriasis, it appears some new therapeutic modalities directed by this mechanism. These are the biological treatments used successfully in the treatment of rheumatoid arthritis, psoriatic arthritis and recently used with beneficial effects in treatment of skin psoriasis.

Biological therapy consists in the use of substances which are a top medical technology and research, which are based on clinical trials on thousands of patients, proofing their efficacy and safety.

2. Objective

To highlight the effectiveness of treatment with biological preparations, especially with etanercept and adalimumab, and the evaluation of side effects after treatment with these drugs.

3. Inclusion and exclusion criteria

For the patient to be included in the study and treated with biologics, he/she has to meet the following criteria:

- Be diagnosed with severe psoriasis with a PASI above 10.
- Failure to previously received standard treatment (methotrexate, PUVA, etc.) or to submit intolerance or contraindications to these therapies.

From the study were excluded the patients with the following:

- Active severe infections, such as sepsis, abscesses, tuberculosis, opportunistic infections;
- Failure to previously received standard treatment (methotrexate, PUVA, etc.)

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or to submit intolerance or contraindications to these therapies.
- Severe congestive heart failure (NYHA class III / IV);
- History of hypersensitivity to etanercept or adalimumab;
- Pregnancy / lactation;
- Children aged 0 to 17 years;
- Malignant and premalignant disease;
- Demyelination.

4. Material and methods

Given the above, in this study we followed the evolution of a group of 18 patients diagnosed with psoriasis who have not responded to other therapeutic methods (starting with local treatments, phototherapy or systemic treatments such as methotrexate) or who had frequent relapses at short intervals of time.

Group was composed of 10 men (55.56%) and 8 women (44,44%). The patients were aged between 30 and 65 years. The development duration of psoriasis of 13 studied patients (72.22%) was 10 years.

All patients were clinically diagnosed with severe psoriasis with a PASI score ranging from 27.1 to 41.5, and an average score of 31.85.

It has been investigated the biological status of all patients (ESR, CBC, creatinine, SGOT, SGPT, cholesterol, triglycerides, urinalysis), IDR of PPD before treatment. The tests were repeated at 4, 8 and 16 weeks, less PPD's IDR.

The histopathology exam, mandatory for these patients, confirmed the clinical diagnosis. At this examination, the following observations were made: increased hyperkeratosis and parakeratosis, interpapilla increases deepened by hyperplasia and interpapilla acanthosis, frequent mitoses in the deeper layers of the epidermis, Mounraud-Saboureaud microabscess at the corneum stratum, and dermal, at papillae and perivascular level, an infiltrate consisting of lymphocytes and histiocytes.

These 18 patients were divided into two subgroups depending on the chosen regimen, as follows: a first subset of seven patients who received Etanercept (Enbrel ®) at a dose of 50 mg / week subcutaneously and a second subset of 11 patients who received adalimumab (Humira ®) in subcutaneous dose of 80 mg in the first week, followed by 40 mg in the second week, then 40 mg every two weeks interval.

Epidemiologic data Table 1

Sex	**Male**	55,56%
	Female	44,44%
Age	**Minimal**	30 years
	Maximal	65 years
	Average	42,97 years
Time of evolution of psoriasis	**<5 years**	0%
	5-10 years	27,78%
	>10 years	72,22%
PASI	**Minimal**	27,1
	Maximal	41,5
	Average	31,85

Results PASI ≥ 75% after 16 weeks Table 2

SET	PASI ≥75%	PASI 50-75%	PASI <50%
Adalimumab	77,77%	22,22 %	0
Etanercept	50%	33,33%	16,67%
TOTAL	66,67%	26,66%	6,67%

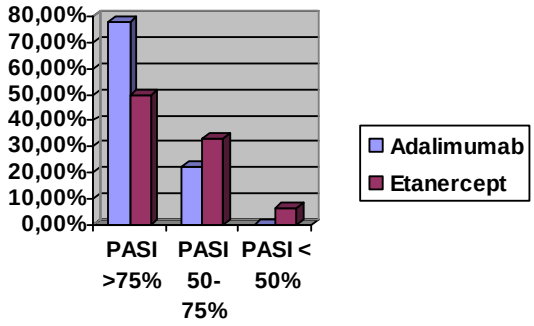

Fig 1. *Grafic of the results PASI ≥ 75%*

Results PASI ≥ 90% after 16 weeks Table 3

SET	PASI ≥ 90%	PASI 90-75%	PASI ≥ 75%
Adalimumab	55,55%	22,22%	77,77%
Etanercept	16,67%	33,33%	50%
Total	40%	26,67%	66,67%%

5. Results and discussions

The evaluation of the results was performed at 16 weeks after the starting of the treatment. 2 patients were excluded from the study (one from each subset due to the infectious side effects, exacerbated by biological therapy), and one never presented to the second dose of treatment or evaluation visits. This patient was member of the subgroup who received treatment with adalimumab.

In the studied group the side effects were minimal. Thus, to those who had been treated with etanercept only one patient experienced furunculosis therefore was excluded from the study. To those who had been treated with adalimumab, one patient also presented a broad tinea corporis. Also this patient discontinued the treatment.

In the last period, the therapeutic strategy in psoriatic disease, moderate or severe, requires increasingly more the use biological preparations. In help of this affirmation there are a number of randomized trials that assessed their effectiveness. Preparations commonly used in the treatment of systemic psoriasis are: adalimumab, etanercept, infliximab and ustekinumab. The use of these medications should follow a well-established algorithm, because some may have side effects or contraindications.

The indication of such preparations is well established, and they are used for dealing with severe psoriasis where the conventional treatments have failed, are

contraindicated, or cannot be used because of the association of comorbidities or the patient is intolerant to standard therapies [1].

The patients chosen in the study group presented a form of severe psoriasis who have not responded to standard treatment with methotrexate, phototherapy with UVB and local treatments. The number of patients enrolled was 18. In the end, the final number was 15 patients, 3 of them left the study for the following reasons: 2 patients experienced side effects, and one patient left the study voluntarily.

The 15 remaining patients in the study were divided into two subgroups depending on the chosen biological preparation, so a first subset of six patients received treatment with etanercept, and the second subset of 9 patients received treatment with adalimumab.

The biological treatments efficiency, as mentioned above, has been well documented in several randomized studies. Thus, for the efficiency of adalimumab the following studies are cited:

- CHAMPION (2), a study of 108 patients, in which PASI ≥ 75% was achieved in 79.5% after 16 weeks of treatment
- REVEAL (3), a study of 814 patients, in which PASI ≥ 75% is found in 71%;
- BELIEVE (4) on 364 patients, in which PASI ≥ 75% was achieved in 70.9%.

In this study, PASI ≥ 75% following treatment with adalimumab, was obtained in 77.77% of patients. It is a percentage that falls within the data range presented in the literature.

Regarding the effectiveness of etanercept, in the literature there are cited studies by:

- Leonardi et al (5) (n = 164, PASI ≥ 75% to 49%),
- Papp et al (6) (n = 194, PASI ≥ 75% to 49%),
- Gottlieb et al (7) (n = 57, PASI ≥ 75% to 30%).

In the study presented above PASI ≥ 75% was achieved in 50% of patients after treatment with etanercept.

Regarding the side effects, it is known that these biological preparations may have many side effects, ranging from simple reactions at the place of the injection to some of the most serious, such as liver and kidney toxicity, inhibition of the immune system which can lead to serious infection and the development of tumors (cancers). It is very important to balance the benefits and disadvantages of any treatment to avoid such unwanted side effects.

Adalimumab has the following more common side effects: respiratory tract infection, leukopenia, anemia, increased serum lipids, headache, abdominal pain, nausea, vomiting, SGOT, SGPT increased redness at injection, musculoskeletal pain. [8]

Side effects of etanercept are: injection site reactions, infections (IACRS, lung, bladder and skin), pruritus cutaneous, thrombocytopenia, urticaria, angioedema, severe infections (pneumonia, cellulitis), anemia, leukopenia, vascular, LEC, demyelinating disorders, tuberculosis [9].

In the studied group the side effects were minimal. Thus, to those who had been treated with etanercept only one patient experienced furunculosis therefore was excluded from the study. To those who had been treated with adalimumab, one patient also presented a broad tinea corporis. Also this patient discontinued the treatment.

Note that each patient reacts differently to treatment. Thus a treatment that has proven effective for a certain period of time may not have the desired effect at some point and so forth a treatment that did not work at first may improve the symptoms when used again after a period of time.

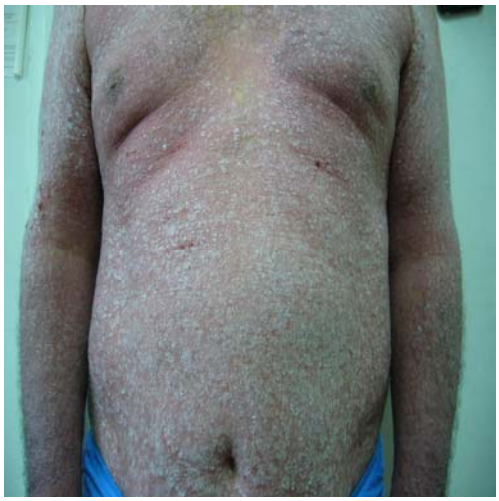

Fig. 2. *Before treatment*

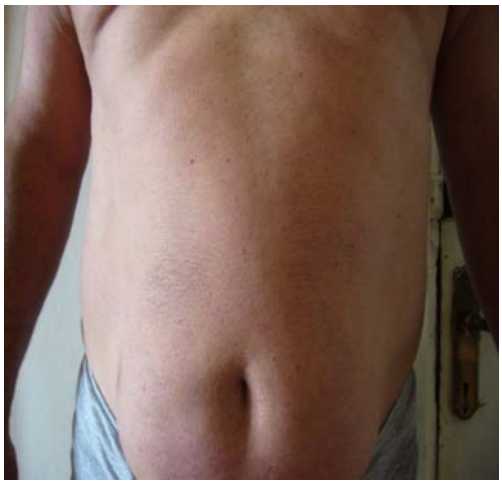

Fig. 3. *After the treatment with adalimumab*

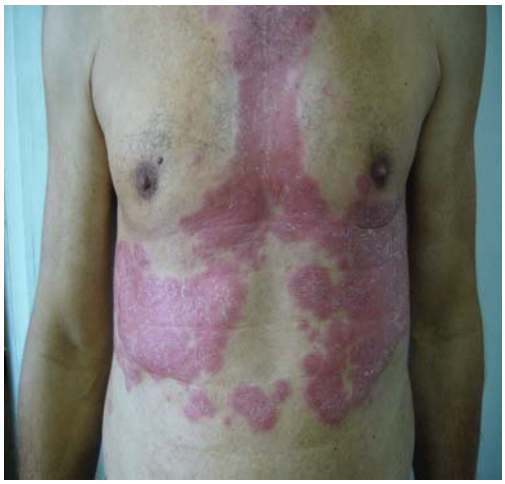

Fig. 4. *Before treatment*

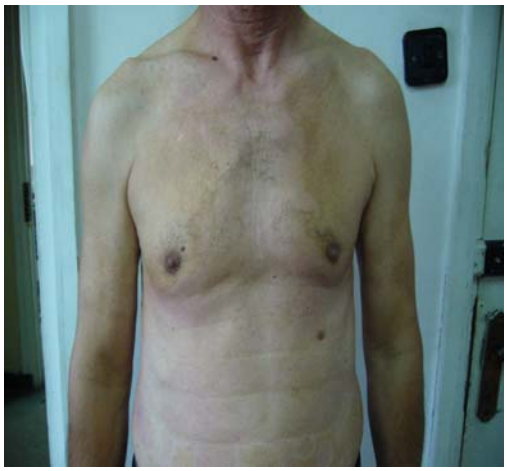

Fig. 5. *After the treatement with etanercept*

6. Conclusion

The biological therapy in psoriatic disease is an effective therapeutic modality regardless of the used preparation, thus following treatment with adalimumab PASI ≥ 75% was obtained in 77.77% of the cases and with etanercept in 50% of the cases.

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