

# SYSTEMIC THERAPY OF MODERATE AND SEVERE PSORIASIS WITH METHOTREXATE

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**Abstract:** *The systemic treatment in psoriatic disease is addressed particularly to the severe forms of psoriasis with a PASI > 10. It consists of both conventional therapies (methotrexate, PUVA, cyclosporine, retinoids) and modern therapies with biological preparats. In this study we made a comparative assessment of the effectiveness and tolerance of systemic treatment with methotrexate both as monotherapy and in combination with SUP phototherapy, for patients with psoriasis vulgaris.*

**Key words:** *psoriasis, methotrexate, phototherapy.*

## 1. Introduction

Psoriasis is a chronic disease that affects 2-3% of the population [1]. It is characterized by erythematous plaques, plates and scales, infiltrated disseminated on the trunk, limbs and head hairy skin. The treatment of this disease is not standardized, because there are various therapeutic means and methods used in this disease. These are tailored to the clinical form of the disease and its extension on body surface area and age of patients.

The systemic treatment is used mainly for severe forms of psoriasis, affecting over 10% of body surface area [2]. It has to take into account that systemic treatment has a toxic potential and its use must be well justified. Methotrexate is a systemic citostatic that was introduced in the treatment of psoriasis a few decades ago [3]. This is indicated in the forms of erythrodermic psoriasis, arthropathic psoriasis, pustular psoriasis and forms of

psoriasis that affects over 10% of the skin, PASI above 10 or DLQI above 5.

## 2. Objectives

This study is aimed to make a comparative assessment of the effectiveness and tolerance of the systemic treatment with methotrexate both as monotherapy and in combination with SUP phototherapy for patients who had a PASI above 10.

## 3. Inclusion and exclusion criteria

### 3.1. The study inclusion criteria were:

- patients older than 20 years
- psoriasis vulgaris in plaques and placards,
- PASI above 10
- with normal biological status (CBC, urea, creatinine, SGOT, SGPT, alkaline phosphatase and serum albumin).

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**3.2. The exclusion criteria** were:

- patients with liver or blood illness, which showed changes in CBC, BUN, creatinine, SGOT, SGPT, alkaline phosphatase and / or serum albumin
- pregnancy
- patients younger than 20 years.

**4. Materials and methods**

In this study we followed a group of 101 patients diagnosed with psoriasis, who

had a PASI above 10. The group was composed of 82 men (81.19%) and 19 women (18.81%), and patient age ranged between 20 and 65 years. The time evolution of the disease for 39.60% of patients was over 10 years, for 34.65% the development was between 5 and 10 years, and for 25,75% the development was under 5 years. This data can be seen in table 1.

*Epidemiologic data*

Table 1

|                                       |                     |             |
|---------------------------------------|---------------------|-------------|
| <b>Sex</b>                            | <b>Male</b>         | 81,19%      |
|                                       | <b>Female</b>       | 18,81%      |
| <b>Age</b>                            | <b>Minimal</b>      | 20 years    |
|                                       | <b>Maximal</b>      | 65 years    |
|                                       | <b>Average</b>      | 42,97 years |
| <b>Time of evolution of psoriasis</b> | <b>&lt;5 years</b>  | 25,75%      |
|                                       | <b>5-10 years</b>   | 34,65%      |
|                                       | <b>&gt;10 years</b> | 39,60%      |
| <b>PASI</b>                           | <b>Minimal</b>      | 10,6        |
|                                       | <b>Maximal</b>      | 37,8        |
|                                       | <b>Average</b>      | 22,25       |

These patients were divided into two groups according to the treatment given. So the first group (group I) consisted of 35 patients who received methotrexate alone, and a second group (group II) consisted of 66 patients, receiving methotrexate in combination with phototherapy SUP.

The treatment regimen used was as follows:

- Group I: methotrexate at a dose of 15 mg / week;
- Group II: Methotrexate at a dose of 15 mg / week, which was associated with SUPphototherapy, done into a Saalman cabin, consisting of a column of three lamps of 400 W each. SUP phototherapy is a combination of UVB and UVA, with a wavelength between 300 and 360 nm.

The treatment was initiated at a dose of 300 mJ/cm<sup>2</sup>, the dose was increased until it reached the minimum dose eritematogene, but the maximum dose did not exceed 3900 mJ/cm<sup>2</sup> per meeting. The total number of phototherapy sessions was 40 sessions for 16 weeks, administered as follows:

- 5 sessions / week for 2 weeks;
- 4 sessions / week for 2 weeks;
- 3 sessions / week for 4 weeks;
- 2 sessions / week for 2 weeks;
- 1 session / week for 6 weeks.

Before starting the treatment with methotrexate each patient was evaluated biological (CBC, urea, creatinine, SGOT, SGPT, alkaline phosphatase, serum albumin). During the treatment, the

patients were well monitored, aiming in particular the following laboratory tests:

- Complete blood count each 2-4 weeks (CBC);
- Each 3-4 weeks investigation of renal function (urea, serum creatinine);
- Each 4-8 weeks investigation of liver function (SGOT, SGPT, alkaline phosphatase, serum albumin).

## 5. Results and discussions

The results were evaluated at 16 weeks after the starting of the treatment. **PASI  $\geq 75\%$**  was considered a very good result, PASI 50-75% was considered a good result and PASI below 50% was considered a poor result. The tables below present the study results:

*PASI 75% after 16 weeks*

Table 2

| Group | PASI $\geq 75\%$ | PASI 50-75% | PASI < 50% |
|-------|------------------|-------------|------------|
| I     | 57,69%           | 30,77%      | 11,54%     |
| II    | 66,67%           | 28,89%      | 4,44%      |
| Total | 63,38%           | 29,58%      | 7,04%      |

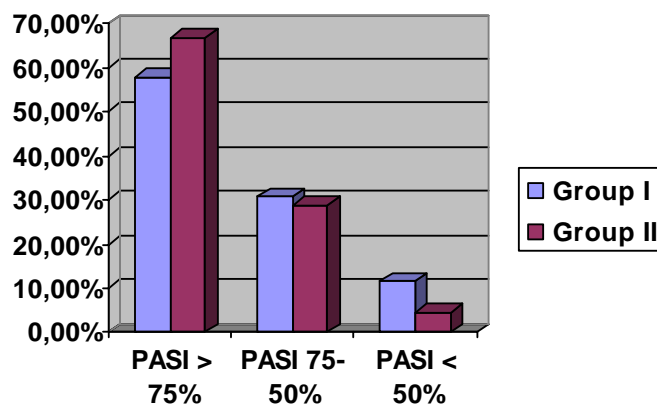


Fig. 1. Graphic of results at 16 weeks (PASI 75%)

*PASI 90% after 16 weeks*

Table 3

| Group | PASI $\geq 90\%$ | PASI 90-75% | PASI 75% |
|-------|------------------|-------------|----------|
| I     | 34,61%           | 23,08%      | 57,69%   |
| II    | 46,67%           | 20%         | 66,67%   |
| Total | 42,25%           | 21,13%      | 63,38%   |

The side effects seen in patients treated with methotrexate were:

- Itching skin from a patient in the first group (2.86%)
- Nausea in 3 patients, all in the first group (8.57%)
- Headache in a patient in the second group (1.51%)
- Fever in a patient also of the second group (1.51%). (Table 4)

*Adverse events after methotrexate therapy*

Table 4

| Side effect  | Group I | Group II |
|--------------|---------|----------|
| Skin itching | 2,86%   | 0        |
| Nausea       | 8,57%   | 0        |
| Headache     | 0       | 1,51%    |
| Fever        | 0       | 1,51%    |

*Advers events after phototherapy*

Table 5

| Side effect      | Group II |
|------------------|----------|
| Solar erythema   | 7,58%    |
| No advers events | 92.43%   |

After phototherapy, 5 patients (7.58%) of the second group showed a pronounced erythema similar to solar erythema. Its appearance did not lead to discontinuation of phototherapy. (Table 5)

After completing the therapy, the patients were monitored for a period of one year to observe the occurrence or the recurrence of psoriasis. So in the first group the recurrences occurred in 14 patients (40%) in less than a year, and in the second group in 8 patients (12.12%)

The efficacy of methotrexate treatment in psoriasis is well known. It is used since the 50s, (1,3,4). Lately, the methotrexate was combined with PUVA, UVB, aromatic retinoids and cyclosporine, improving its efficiency, reducing the doses and limiting the toxic effects (4-8). The Methotrexate doses recommended in the literature are of 15-30 mg / week in psoriasis vulgaris.

In this study the dose of methotrexate was 15 mg / week for 16 weeks in all 101 patients. PASI score of 75% was achieved in 63.83% of them.

Also, the effectiveness of phototherapy is very well known. This is the reason why I wanted to join the two therapeutic modalities.

Methotrexate was administered alone to 35 patients, achieving a PASI score  $\geq 75\%$  in 57.69% of patients. For the remaining 66 patients, methotrexate was associated

with SUP phototherapy. After 16 weeks, PASI score  $\geq 75\%$  was obtained in 66.67% of them. We see an increased efficiency in patients who used combination therapy than methotrexate monotherapy. We can see the good results of the treatment in Fig. 2 and Fig. 3.

We don't have to forget that side effects may occur after both treatment with methotrexate and phototherapy.

After methotrexate therapy the following side effects may occur (9):

- General: fatigue, headache, chills, fever;
- Skin: itching, pain, phototoxicity, urticaria;
- Digestive: nausea, vomiting, stomatitis, stomach ulcer, and rarely diarrhea, hepatotoxicity;
- Blood: thrombocytopenia, megaloblastic anemia, leukopenia
- Urogenital: azotemia, microscopic haematuria, oligospermia;
- CNS depression, vertigo.

The most severe short-term side effect that can occur after methotrexate therapy is the bone marrow toxicity, and the most severe long-term side effect is hepatotoxicity.

After following a long time treatment with methotrexate in high doses it may occur cirrhosis. It may occur at a cumulative dose of 2200 mg of

methotrexate [10]. For patients following a long-term methotrexate therapy, the liver changes should be highlighted through a liver biopsy.



Fig. 2. *Before treatment*

The biopsy was not necessary for the patients of the studied groups, because treatment was done for short periods of time with low doses of methotrexate.



Fig. 3. *After 16 weeks with Methotrexate and SUP*

After treatment with methotrexate, the biological test results showed no changes in CBC, BUN, creatinine, transaminases (SGOT, SGPT), alkaline phosphatase and serum albumin.

The side effects seen in patients treated with methotrexate study were minor, occurring in 6 patients 5.94%. They consisted of nausea, skin itching, headache and fever.

Acute side effects of fototerpaiei consist of erythema, which occurs in 4-6 hours after exposure, phototoxicity, keratitis, if the eyes are not protected. Long term side effects of phototherapy consists of photoaging, carcinogenic risk (basal and squamous cell carcinomas appearance) or melanogenetic (occurrence of malignant melanoma) [9].

For 5 of the 66 patients (7.57%) that followed SUP phototherapy we could notice the emergence of a pronounced erythema but it did not require the discontinuation of therapy.

After completing the therapy, the patients were monitored for a period of one year to

observe the occurrence or the recurrence of psoriasis. So in the first group the recurrences occurred in 14 patients (40%) in less than a year, and in the second group in 8 patients (12.12%).

The results of the present study are comparable with data from the literature. I believe that the combination of methotrexate and phototherapy has a positive role as methotrexate doses are reduced, the administration time is reduced and the risk of occurrence of severe side effects, both blood and the liver, is low.

Also after the combination methotrexate - phototherapy, the one year recurrence rate was lower in the group that followed this regimen than in the group of patients who had been treated only with methotrexate.

A drawback of treatment with phototherapy was that the patient had to come almost every day to perform clinical cure with UV, with a duration of at least an hour a day.

## 6. Conclusion

Systemic treatment with methotrexate, both as monotherapy and in combination with phototherapy, remains a major therapeutic modality in psoriatic disease.

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