


## Comparison of Psoriasis Area and Severity Index (PASI) Scores in Patients Treated with Oral Methotrexate and A Combination of Oral Methotrexate and Narrow Band-Ultraviolet B (NB-UVB) Phototherapy

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### ABSTRACT

**Background:** Psoriasis Vulgaris is an autoimmune disease characterized by chronic skin inflammation and epidermal hyperplasia. Psoriasis Area Severity Index (PASI) score is one of the assessments to measure the psoriasis severity. Oral methotrexate is one of the effective therapies for psoriasis patients. Narrow Band-Ultraviolet B (NB-UVB) phototherapy is an adjunctive psoriasis therapy given concurrently with oral methotrexate. **Purpose:** Determine the difference in Psoriasis Area Severity Index (PASI) scores between Psoriasis Vulgaris patients treated with oral methotrexate and a combination of oral methotrexate and NB-UVB phototherapy. **Methods:** This observational analytic study was conducted at the Dermatology and Venereology Clinic, Dr. Moewardi General Hospital Surakarta. The patients received oral methotrexate and a combination of oral methotrexate and and Narrow Band-Ultraviolet B (NB-UVB) phototherapy. A retrospective study of medical records was conducted to determine the patient's PASI score before the therapies and 3 months after. All data were analyzed with the Shapiro Wilk normality test and the independent T-test. A p-value was <0.05, and it was considered significant. **Result:** The mean of decreased PASI scores in the oral methotrexate group was (6.00 +2.47) and (6.08 +2.17) in the combination therapy group. Based on the statistical test results from the 24 subjects, it was found that the PASI score decreased (p=0.931). **Conclusion:** There was no significant difference in the decrease in PASI between the oral methotrexate group and the combination therapy group. The mean reduction of PASI scores was more significant in the combination therapy than in the methotrexate group.

**Keywords:** phototherapy, methotrexate, psoriasis vulgaris, PASI score, NB-UVB.

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### BACKGROUND

Psoriasis vulgaris is a chronic inflammatory autoimmune disease characterized by skin inflammation and epidermal hyperplasia. The chronic course of this disease can lead to lower quality of life and more stress. The etiology of psoriasis vulgaris is multifactorial with the ratio of male and female sufferers being almost the same worldwide.<sup>1</sup>

Research by Springate et al. in 2017 reported that the prevalence of psoriasis vulgaris worldwide is

estimated at 2–3% of the entire world population.<sup>1,2</sup> Lonnerberg et al. in 2016 reported that the highest prevalence of psoriasis vulgaris was found in European countries such as the UK (2.2. %) and Norway (4.5%), while the prevalence of psoriasis in the Asian continent is low at <0.05%.<sup>2,3</sup> Psoriasis is reported to be lower in Asia, with a prevalence of 0.14% in East Asia.<sup>3</sup> Research by Pratiwi et al. at Dr. Soetomo Hospital Surabaya in 2017 reported that the incidence of psoriasis vulgaris was 8.12% of all patients in the

Dermatology and Venereology Section of RSUD Dr. Soetomo Surabaya.<sup>4</sup> The prevalence of psoriasis throughout Indonesia has not yet been reported.

Clinical symptoms of psoriasis vulgaris include erythematous plaques accompanied by thick, layered scales. This disease has a predilection for the elbow, knee, scalp, lumbosacral, and intra-gluteal areas. Psoriasis symptoms vary from person to person and can worsen with age. One way to measure the severity of psoriasis is using the PASI (Psoriasis Area and Severity Index) score. PASI grade classification is divided into 3, namely mild psoriasis (PASI score <5), moderate psoriasis (PASI score 5–10), and severe psoriasis (PASI score >10). The decrease in the PASI score is one of the benchmarks for psoriasis improvement.<sup>5</sup>

Methotrexate is one of the therapies for psoriasis. Methotrexate has an immunosuppressant and anti-proliferative effect, which is quite effective in reducing the severity of psoriasis. However, it has several immunosuppression-related side effects.<sup>5</sup> Psoriasis vulgaris therapy is often combined with Narrowband Ultraviolet B (NB-UVB) phototherapy. NB-UVB phototherapy is an adjuvant therapy considered quite effective with minimal side effects. A psoriasis vulgaris combination therapy of oral methotrexate and NB-UVB phototherapy is often given to patients with moderate to severe PASI scores.<sup>6</sup>

To this date, the most effective therapy for psoriasis vulgaris is still under research. Methotrexate therapy as one of the effective therapeutic agents for psoriasis vulgaris is considered to have many side effects.<sup>7</sup> This study aims to determine the PASI scores difference between psoriasis vulgaris patients treated with oral methotrexate and a combination of oral methotrexate and NB-UVB phototherapy. The study result is expected to contribute as a reference in selecting effective therapy for psoriasis vulgaris to minimize the side effects of methotrexate.

## METHODS

This was an observational analytic study conducted at the Dermatology and Venereology Polyclinic, RSUD Dr. Moewardi Surakarta from November 2020 to February 2021. This study involved 24 patients diagnosed with psoriasis vulgaris where 16 of them were males, and 8 of them were females. The study participants were within the age range of 20 and 70 years. The inclusion criteria were patients diagnosed with psoriasis vulgaris aged between 20 and 70 years old who received oral methotrexate therapy or combination therapy of oral methotrexate with NB-UVB phototherapy for at least 3 months. They would receive an explanation of the study procedure and have signed the consent sheet. The exclusion criteria were

patients diagnosed with erythroderma, generalized pustular psoriasis, and guttate psoriasis. Enforcement of patient diagnosis is only based on history and clinical manifestations and not by histopathological examinations because not all patients undergo histopathological examinations. After the diagnosis of psoriasis was established, the patients were categorized by severity using the PASI score. Patients who dropped out of therapy with oral methotrexate or combined oral methotrexate with NB-UVB phototherapy before at least 3 months of therapy were also excluded from this study.

A retrospective study of medical records and clinical photographs was conducted to determine the patient's PASI score before and after 3 months of oral methotrexate therapy and combination therapy of oral methotrexate and NB-UVB phototherapy. The subject characteristic of sex is nominal, and the data were presented in a frequency distribution. This was then followed using the chi-square test to determine the difference between the oral methotrexate therapy group and the combined therapy group. The age data were presented numerically in mean value + standard deviation. The collected data were then processed for statistical analysis using the Shapiro Wilk test to determine the data distribution. The comparison test was carried out using the Independent T-test only if the data were normally distributed. If not, the data were then analyzed using the Mann-Whitney test. The data were analyzed using SPSS version 21 (IBM, Chicago, IL, USA) with a  $p < 0.05$ . This study has received ethical approval from the Health Research Ethics Committee of RSUD Dr Moewardi/Faculty of Medicine, Sebelas Maret University, Surakarta, under number: 1,155/XII/HREC/2021. All obtained data are treated confidential and only used for research and scientific purposes.

## RESULT

The results showed that the demographic data of male subjects at 66.70% and female subjects at 33.30% (Table 1). The mean age of all subjects was  $50.79 \pm 12.76$  years. The results of the statistical test showed that sex ( $p = 1.000$ ) and age ( $p = 0.309$ ) got  $p > 0.05$ , which means that there was no significant difference in patient characteristics based on sex and age between the oral methotrexate therapy group and the combined therapy group of oral methotrexate and NB-UVB phototherapy.

Based on Table 2, it is known that the decrease in PASI scores in the oral methotrexate group had an average of  $6.00 + 2.47$ , while in the combination group, it was  $6.08 + 2.17$ . Based on the statistical test results from the 24 subjects, it was found that the PASI score

decreased ( $p=0.931$ ), getting  $p>0.05$ , which means that there was no significant difference in the decreased PASI score between the oral methotrexate group and the combined oral methotrexate and NB-UVB phototherapy group.

Notes: The PASI Score grading sheets and results are available in the appendix section.

**Table 1.** Characteristics of research subjects

Variable	Number	Group		p-Value
		Oral Methotrexate	Oral Methotrexate + Phototherapy	
Sex <sup>a</sup>				1.000
Male	16 (66.67%)	8 (33.33%)	8 (33.33%)	
Female	8 (33.33%)	4 (33.33%)	4 (33.33%)	
Age (years) <sup>b</sup>	50.79 ±12.76	48.08 ±13.68	53.50 ±11.71	0.309

Notes: a nominal categorical data (Chi-square test), b normal distributed numerical data presented in the mean value + standard deviation (Independent t-test)

**Table 2.** Differences in PASI scores between the oral methotrexate therapy group and the combined therapy group of oral methotrexate and NB-UVB phototherapy.

Variable	PASI Score Decrease mean ± standard deviation	p-value
Oral Methotrexate	6.00 ± 2.47	0.931
Oral Methotrexate + Phototherapy	6.08 ± 2.17	

PASI, Psoriasis Area Severity Index; NB-UVB, Narrow Band Ultraviolet B

## DISCUSSION

The characteristics of the study subjects that they were within the age range of 20–70 years (Table 1), with a higher percentage of psoriasis vulgaris in males, which is 66.67% compared to 33.33% in females. Research by Mitran et al. in 2017 in Romania reported that psoriasis vulgaris could occur at any age, with the highest incidence in the age group of 15–30 years, and it rarely occurs before the age of 10 years.<sup>12</sup> The genetic role of human leukocyte antigen (HLA) class I, especially HLA-Cw6, is associated with earlier age onset and a family history of the positive ones.<sup>13</sup> In this study, the PASI score was found to be higher for females with an average of 18.40, compared to males with an average of 15.76. The results of this study differ from a previous study by Hagg et al. in Sweden in 2017 with a sample of 5,438. The study stated that the severity of psoriasis vulgaris, which was assessed using the PASI score, was higher in men compared to women. It was associated with women taking more care of their skin and hair and more discipline in taking medicine.<sup>14</sup> The difference in the results of the two studies can potentially be due to the smaller number of samples in this study, and the size is not representative enough.

Psoriasis treatment aims at relieving the symptoms of the disease. Psoriasis therapy administration is adjusted individually by considering

the type and severity of psoriasis. Psoriasis therapy is said to be successful if a PASI score of 75 is achieved, which is a 75% decrease from the initial PASI score. Psoriasis therapy is said to have failed if the PASI score of 50 is not achieved, that is, a 50% decrease from the initial PASI score is not achieved. Inappropriate psoriasis therapy can affect the remission period and the success of treatment. Therefore, prescribing the most appropriate therapy is strongly necessary.<sup>9</sup>

Methotrexate is an effective therapy for moderate and severe psoriasis vulgaris. Methotrexate has the effect of inhibiting DNA synthesis, immunosuppressive, and anti-inflammatory effects. Methotrexate can be given as an initial oral dose of 2.5–5 mg at 12-hour intervals over a 24-hour period.<sup>15,16</sup> The dose can be increased gradually until it produces an optimal response to treatment, with the maximum dose not exceeding 25 mg/week. The toxic effects of methotrexate need to be considered during psoriasis therapy.<sup>17</sup> Methotrexate toxicity that can occur includes increased liver function values, aplastic anemia, leukopenia, thrombocytopenia, interstitial pneumonitis, ulcerative stomatitis, nausea, vomiting, diarrhea, weakness, fatigue, chills, fever, dizziness, decreased resistance to infection, gastric ulceration and bleeding, photosensitivity, and alopecia. The risk of methotrexate toxicity may also increase due to interactions with barbiturates, sulfamethoxazole,

NSAIDs, penicillin, and trimethoprim.<sup>17,18</sup> Table 2 shows that the treatment of psoriasis vulgaris using oral methotrexate reduced the PASI score quite well by  $6.00 \pm 2.47$ . The results of this study follow previous research by Haider et al. in 2014 in Pakistan. The study proved the effectiveness of oral methotrexate in reducing PASI scores in patients with moderate and severe psoriasis vulgaris.<sup>18</sup> Oral methotrexate was considered effective in lowering PASI scores through inhibition of DNA synthesis through competitive inhibition of the dihydrofolate enzyme reductase modulates the immune system through the induction of apoptosis of immune cells, inhibition of the T cell activation, and has a strong anti-proliferative effect, thereby repairing plaque lesions in psoriasis.<sup>19</sup>

NB-UVB phototherapy is an important treatment for moderate and severe psoriasis vulgaris. Dermatologists initially opted for broadband UVB (BB-UVB) to treat psoriasis in the late 1970s. However, the next two decades later, they discovered that narrowband UVB (NB-UVB) is potentially safer and more effective with faster skin cleansing and longer-lasting wound 'healing'. NB-UVB phototherapy has a mechanism of signaling inhibition of interferon types 1 and 2, modulating the decrease in T-helper 17 cells, modulating genes involved in epidermal proliferation, and differentiation in epidermal hyperplasia to improve PASI scores in psoriasis. The initial dose of phototherapy with NB-UVB according to skin type is 130–400 mJ/cm<sup>2</sup> or 50% minimum erythemal dose (MED). The dose may be increased by 15–65 mJ/cm<sup>2</sup> or 10% of the initial MED. Phototherapy is performed 3 to 5 times per week.

The initial healing effect with NB-UVB can be seen after 8 to 10 treatments. Maintenance therapy can prolong remission.<sup>20</sup> Table 2 shows that psoriasis vulgaris therapy using a combination of oral methotrexate and NB-UVB phototherapy had a more significant decrease in PASI scores, which is  $6.08 \pm 2.17$  than the oral methotrexate therapy. However, the decline was not significant, with a p-value of 0.931 ( $p > 0.05$ ). The results of this study agree with a previous study in 2020 by El-Hamd et al. in Egypt. They reported that a combination of oral methotrexate and NB-UVB phototherapy was more effective in treating moderate and severe psoriasis compared to NB-UVB phototherapy alone. The combination of methotrexate and NB-UVB phototherapy has a synergistic effect where both have potent anti-proliferative and anti-inflammatory effects and increase lymphocyte apoptosis as well as other inflammatory cells in psoriasis vulgaris, resulting in improvements in thickness, scale, and inflammation.<sup>21</sup>

Table 2 shows that the combination of oral methotrexate and NB-UVB had a greater reduction in PASI scores than oral methotrexate alone, but the scores were not statistically significant. The results of this study are in accordance with the study of Khadka et al. in 2015 in Nepal, which stated that there was no significant difference in psoriasis vulgaris between patients who have received a combination therapy of oral methotrexate and NB-UVB and a single therapy in 20 weeks. Conversely, Khadka et al. (2015) found a significant result in 24 weeks. The result could be due to the difference in duration of NB-UVB exposure.<sup>22</sup> This finding applies to this study, too, since patients who receive NB-UVB therapy for a minimum of 12 weeks can be included. Thus, there is a variance in the duration of NB-UVB exposure found in this study. These results differ from other studies by El-Hamd et al. in Egypt in 2020, who reported that a combination of oral methotrexate and NB-UVB phototherapy was more effective in treating moderate and severe psoriasis compared to NB-UVB phototherapy alone or oral methotrexate alone. The difference outcome of this study possible due to several factors such as the number of samples, the level of homogeneity of the research sample, the subjectivity factor of the assessor of the PASI score, and several other external factors. A combination of methotrexate combination and NB-UVB phototherapy is still better because it demonstrates a higher improvement in PASI scores and in reducing the side effects and toxicity from single oral methotrexate therapy.<sup>21</sup>

In Indonesia, it is still rare to find comparison research on the effectiveness of various therapeutic modalities in psoriasis vulgaris treatment, which is the strength of this study. The study results, which were not statistically significant, could be due to the small sample size as a result of the COVID-19 pandemic, the lack of homogeneity of the PASI degree before therapy was given, and the subjectivity factor in assessing the PASI score.

This study result showed no significant difference in the decreased PASI scores between the single oral methotrexate therapy and combination therapy of oral methotrexate and NB-UVB phototherapy. The combination therapy group of oral methotrexate and NB-UVB phototherapy had a more significant decrease in the mean PASI score. The combination therapy of methotrexate and NB-UVB phototherapy is still better because it improves PASI scores and reduces the side effects and toxicity of single oral methotrexate therapy. Further research on the effective treatment for psoriasis vulgaris is still required.

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