Original Research Article

Clinical Efficacy of Methotrexate, Cyclosporine and Azathioprine in Psoriasis patients

Shahid Hassan[1*], Md Ainul Haque[2]

[1]Associate Professor, Department of Dermatology, Madhubani Medical College, Madhubani, Bihar, India
[2]Assistant Professor, Department of Dermatology, Madhubani Medical College, Madhubani, Bihar, India

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Abstract

Objectives: This was to evaluate the clinical efficacy of methotrexate, cyclosporine and azathioprine in various age group of psoriasis patients. **Methods:** A total of 45 psoriasis patients were categorised into three groups (group A, group B and group C). Each group had 15 patients. Group A patients were received 10mg/week methotrexate every week on fixed day. Group B were received azathioprine 2mg/week on fixed day of week. And Group C patients were received cyclosporine 2mg/kg/day in two divided doses. PASI score was used for assessing of severity of psoriasis. **Results:** Most of the patients 22(48.88%) were belonged in age group of 31-45 years. Majorities of the patients of group A 5(33.33%), group B 6(40%) and group C 6(40%) had PASI score 11-20. After 12 weeks of treatment, major reduction of severity (81-100%) was seen in group A patients 10(66.67%) as compared to group B and group C patients. **Conclusions:** Psoriasis was more preponderance in males than female. There was no significant association seen in reduction of severity in between the different group of patients (group A, group B and group C) who were treated with methotrexate, azathioprine and cyclosporine medication respectively. But the methotrexate was more efficacious than azathioprine and cyclosporine in percentage reduction of PASI score in treatment of psoriasis patients.

Key words: Psoriasis, Methotrexate, Azathioprine and Cyclosporine.

Introduction

Psoriasis has a substantial influence on health-related quality of life that is comparable to that of other serious medical conditions e.g. cancer, heart disease, diabetes and depression[1]. It is a chronic inflammatory skin disease, which affects approximately 3 % of the general population in the USA[2]. The most common form of the disease, plaque psoriasis, is characterized by the development of chronic erythematous plaques covered with silvery white scales, which most commonly appear on the elbows, knees, scalp, umbilicus, and lumbar regions[3]. Additionally, individuals with psoriasis are more susceptible to specific debilitating comorbidities, including cardiometabolic dysfunction, fatigue, and depression[4]. The treatment strategy for psoriasis depends on a variety of factors (e.g., the medical history, tolerability of therapies and potential for side effects, and disease severity). Regarding disease severity, there is no commonly accepted definition of mild versus moderate-to-severe psoriasis[5]. Moreover, a patient may have mild disease on the basis of body surface area (BSA) involvement, but localization of lesions in vulnerable areas (e.g., the face, feet, hands, and/ or genitals) may warrant systemic therapy[5,6]. Conventional systemic treatment options for psoriasis have included methotrexate, cyclosporine, and oral retinoids such as acitretin[7]. However, the use of these systemic agents has been limited by insufficient clinical efficacy, safety concerns, or both[5, 8]. Cyclosporine is generally considered the most effective of these agents, providing a rapid response[9]. However, nephrotoxicity, hypertension, and numerous drug interactions may limit its use. Moreover, the duration of cyclosporine use is limited when it is prescribed for psoriasis (1 year in the USA, 2 years in the UK). The hepatotoxic effects of methotrexate necessitate particular caution when it is used in patients with liver problems or in those consuming large amounts of alcohol. Both methotrexate and retinoids are teratogenic[9] Azathioprine (AZA) is considered by most to be the first line steroid-sparing immunosuppressant in MG[10] and data show that it has significant steroid-sparing activity compared with prednisone alone after 18 months of treatment[11]. However, AZA is considered an expensive therapy in the developing world. Objectives of our study was to evaluate the safety and efficacy of methotrexate, cyclosporine and azathioprine in the management of psoriasis patients.

*Correspondence
Dr. Shahid Hassan
Associate Professor, Department of Dermatology, Madhubani Medical College, Madhubani, Bihar, India.
E-mail: shahid@gmail.com

Materials & methods

This present study was conducted in the Department of Dermatology, Madhubani Medical College, Madhubani, Bihar, India during a period from June 2020 to April 2021. A total 45 patients of psoriasis with age 15 years to 60 years attending OPD of Department of Dermatology, MadhubanI Medical College, Madhubani, Bihar were enrolled in this study. Entire subjects/Attendants signed an informed consent approved by institutional ethical committee of Madhubani Medical College, was sought. All the patients (45) were categorized into three group (group A, group B and group C). Each group consist of fifteen (15) patients. A detail history (drug history, family history and lifestyle), clinical examinations and relevant investigations (renal function test, liver function test, complete haemogram, fasting blood sugar, measurement of blood pressure) were performed to all patients. Patients who had pregnancy, lactation, hepatic and renal disorder, allergy to drugs, hematological disorder, diabetes, hypertension and alcoholic were excluded from this study. Group A had been given 10mg/week methotrexate every week on fixed day. Group B had been received Azathioprine 2mg/week on fixed day of week. And Group C patients had received cyclosporine 2mg/kg/day in two divided doses.

Severity of the disease was assessed by PASI score. PASI score is a tool used to measure the severity and extent of psoriasis (psoriasis area and severity index)[12]. It was assessed at every week for first week after that every two weeks till 12 weeks. Interpretation of the result was done by percentage of reduction of PASI score; as follow: >70% - very good response, 60 to 69% - good response, 50 to 59% - fair response, 40 to 49% - poor response and less than 40% - very poor response.

Statistical analysis

Data was analysed by using SPSS software. Chi-square test was applied. P value taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

Observations

This study was included 45 patients of psoriasis. All the patients were categorised into three group (group A, group B and group C). Most of the patients 22(48.88%) were belonged in age group of 31-45 years. Majorities of patients 24(53.33%) were males.

Table 1: Age wise distribution of patients

Age group(years)	Group A	Group B	Group C	Total
15-30	4(26.67%)	5(33.33%)	5(33.33%)	14(31.11%)
31-45	7(46.67%)	8(53.33%)	7(46.67%)	22(48.88%)
46-60	4(26.67%)	2(13.33%)	3(20%)	9(20%)
Total	15(100%)	15(100%)	15(100%)	45(100%)

Table 2: Sex wise distributions

Sex	Group A	Group B	Group C	Total
Male	10(66.67%)	8(53.33%)	6(40%)	24(53.33%)
Female	5(33.33%)	7(46.67%)	9(60%)	21(46.67%)
Total	15(100%)	15(100%)	15(100%)	45(100%)

Table 3: PASI score

PASI Score	Group A	Group B	Group C	Total
1-10	3(20%)	2(13.33%)	2(13.33%)	7(15.56%)
11-20	5(33.33%)	6(40%)	6(40%)	17(37.78%)
21-30	4(26.67%)	5(33.33%)	3(20%)	12(26.66%)
31-40	2(13.33%)	1(6.67%)	2(13.33%)	5(11.11)%
>40	1(6.67%)	1(6.67%)	2(13.33%)	4(8.89%)
Total	15(100%)	15(100%)	15(100%)	45(100%)

In this present study, most of the patients of group A 5(33.33%), group B 6(40%) and group C 6(40%) had PASI score 11-20. Among total 45 patients, 17(37.78%) patients has PASI score had 11-20.

Table 4: After 8 weeks of treatment

Severity reduction	Group A	Group B	Group C	Total	Chi-square statistic	p-value
80 to 100%	4(26.67%)	2(13.33%)	3(20%)	9(20%)	1.6152	0.9514
61 to 80%	6(40%)	5(33.33%)	5(33.33%)	16(35.55)		
41 to 60%	4(26.67%)	7(46.67%)	6(40%)	17(37.78%)		
>40%	1(6.67%)	1(6.67%)	1(6.67%)	3(6.66%)		
Total	15(100%)	15(100%)	15(100%)	45(100%)		

After 8 weeks of treatment, major reduction (61-80%) of severity was seen in group B patients 7(46.67%) who were received azathioprine 2mg/week on fixed day of week. There was not significant differences ($p>0.05$) seen in severity reduction in between group A, group B and group C patients.

Table 5: After 12 weeks of treatment

Severity reduction	Group A	Group B	Group C	Chi-square statistic	p-value
81 to 100%	10(66.67%)	5(33.33%)	7(46.67%)	4.6023	0.5957
61 to 80%	3(20%)	8(53.33%)	5(33.33%)		
41 to 60%	1(6.67%)	1(6.67%)	2(13.33%)		
>40%	1(6.67%)	1(6.67%)	1(6.67%)		
Total	15(100%)	15(100%)	15(100%)		

After 12 weeks of treatment, major reduction of severity (81-100%) was seen in group A patients 10(66.67%) who were received 10mg/week methotrexate every week on fixed day. And there were no significant differences ($p=0.595$) of severity reduction seen in between group A, group B and group C patients who were treated with methotrexate, azathioprine and cyclosporine medication respectively.

Discussions

Psoriasis is a chronic inflammatory skin disorder, which is associated with a significant negative impact on a patient's quality of life. Traditional therapies for psoriasis are often not able to meet desired treatment goals, and high-dose and/or long-term use is associated with toxicities that can result in end-organ damage. The US National Psoriasis Foundation recommends that patients with BSA involvement <5 % should be considered candidates for topical therapy, whereas those with BSA C5 % should be considered candidates for systemic therapy alone or in combination with phototherapy[13]. A ''rule of tens'' has also been proposed, whereby BSA [10 %, Psoriasis Area Severity Index (PASI)[10, or Dermatology Life-Quality Index (DLQI)[10 identify patients with severe disease[14]. More recently, a European consensus meeting defined mild psoriasis as BSA B10 %, PASI B10, and DLQI B10; and moderate to-severe psoriasis warranting systemic therapy as BSA or PASI[10] and DLQI[10][15]. The American Academy of Dermatology (AAD) guidelines present a treatment decision tree based on the presence or absence of psoriatic arthritis and categorization of psoriasis as ''limited'' or ''extensive'' disease, but specific definitions of these terms are not provided[16].

This study was included 45 patients of psoriasis. All the patients were categorised into three group (group A, group B and group C). Most of the patients 22(48.88%) were belonged in age group of 31-45 years. Males 24(53.33%) were more preponderance than females. Over the past two decades, understanding of the etiology of psoriasis has evolved; it is now recognized that both the innate and adaptive immune pathways are involved in its pathogenesis[17, 18]. Consequently, drugs that target specific components of the immune responses involved in the pathogenesis of psoriasis have been developed in an attempt to improve treatment efficacy, safety, and tolerability[19]. These agents include biologics that target cytokines such as tumor necrosis factor (TNF)-a and interleukins (ILs) 12/23 [19]. Despite remarkable improvements in psoriasis treatment outcomes with biologic therapy, however, many patients still do not achieve the desired outcome[20–21], have a prolonged time to response, or fail to maintain efficacy improvements over time. Tolerability may also be an issue (e.g., infections with TNF-a antagonists).

In this present study, most of the psoriasis patients had PASI score had 11-20. And group A patients were received 10mg/week methotrexate every week on fixed day. Group B patients were received azathioprine 2mg/week on fixed day of week. And Group C patients were received cyclosporine 2mg/kg/day in two divided doses. Out of all three drugs used for treatment of psoriasis it was found that after 12 weeks of treatment methotrexate was more effective than

cyclosporine and Azathioprine in percentage reduction of PASI score; which is as per the study of Sandhuk et al.[22]. Azathioprine is not as effective as cyclosporine and methotrexate which similar to other studies[23,24]. Cyclosporine is less effective than methotrexate in percentage reduction of PASI score[25].

Methotrexate (MTX) is very commonly used in under developed countries to treat psoriasis with or without coal tar2; a weekly oral dose is frequently used. Maximum remission period reported with any therapy is up to 1 year[12].

Azathioprine has been used extensively in the treatment of psoriasis with variable results, the dose being 2-5 mg/kg body weight (120-300mg)/day for 2-24 weeks. Majority of the patients relapse in 1-6 months after stoppage of azathioprine. Azathioprine has been found safe in prolonged use in pulse therapy form (800mg daily on 3 consecutive days every month and 200 mg daily in between the high dose for 12-24 month) in the treatment of ulcerative colitis, Wagener's granulomatosis, lupus nephritis, and Crohn's disease[26,27]. Cyclosporine therapy allows for regulation of the immune system through a different mechanism of action than current biologic agents, and their combination may improve control of lesion formation. The efficacy of therapy with cyclosporine and adalimumab was investigated in a nonrandomized, open-label study in patients with active psoriatic arthritis that was refractory to methotrexate treatment[28]. After 12 months, PASI 50 response criteria were met by 95 % of patients receiving combination therapy, compared with 85 % of patients receiving adalimumab alone and 65 % of those receiving cyclosporine alone (P = 0.003 versus combination treatment). In a small scale, open-label study of patients with refractory psoriasis (n = 7), combination therapy with etanercept and low-dose cyclosporine (200 mg/day initially, then 100 mg/day) resulted in a mean reduction in PASI scores of 93.2 % at the end of the maintenance treatment period[29].

In our present study, after 12 weeks of treatment, major reduction of severity (81-100%) of PASI score was seen in patients 10(66.67%) who were received 10mg/week methotrexate every week on fixed day.

Conclusions

This present study concluded that the psoriasis was more preponderance in males than female. There was no significant association seen in reduction of severity in between the different group of patients (group A, group B and group C) who were treated with methotrexate, azathioprine and cyclosporine medication respectively. But the methotrexate was more efficacious than azathioprine and cyclosporine in percentage reduction of PASI score in treatment of psoriasis patients.

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