IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 5 Ver. IX (May. 2016), PP 109-116
www.iosrjournals.org

Methotrexate versus Azathioprine in Chronic Plaque Type Psoriasis: A Comparative Study

Atishay Bukharia[1], Nidhi Jain[2], Shyam Sundar Chaudhary[3]
[1]*M.D.(Derm) Resident, Rajendra Institute Of Medical Sciences, Ranchi, Jharkhand, India*
[2]*Psychiatry Senior Resident, Central Institute Of Psychiatry, Ranchi, Jharkhand, India*
[3]*Prof & Head, Department Of Dermatology, Venereology And Leprosy, Rajendra Institute Of Medical Sciences, Ranchi, Jharkhand, India*

Abstract
Introduction: *Psoriasis is chronic disease where treatments are often needed throughout life. Since 1806, when Thomas girdlestone used potassium arsenate for Psoriasis to present era, we are still in search of drug which can cure this disease. Azathioprine is a relatively safe drug which has not been tested vigourously for chronic plaque type Psoriasis.*
Aims and objectives: *To evaluate and compare the effect of Methotrexate and Azathioprine in chronic plaque type Psoriasis.*
Material and methods: *this study was a randomized, double blind control hospital based study, conducted over 100 Psoriasis patients, divided into two groups of 50 each. Group A which received Methotrexate in a dose of 15 mg weekly for 12 weeks. Group B received Azathioprine in a dose of 2 -3 mg/kg/day for 12 weeks. Severity of Psoriasis was assessed by PASI on 0,4,8 and 12 weeks and relapse was seen within 8 weeks of stopping the medication.*
Results: *Statistically significant difference found after 8 and 12 weeks of treatment, with significantly higher PASI Clearnace by Methotrexate in comparison to Azathioprine.*
Conclusion: *Although azthioprine is effective but Methotrexate is more effective than Azathioprine in chronic plaque type Psoriasis.*

I. Introduction

Psoriasis is a common, chronic, disfiguring, inflammatory and proliferative condition of unknown etiology. The disease is enormously variable in duration, periodicity of flares and extent. It has a bimodal age of onset affecting both males and females equally.[1] Although rarely fatal but it has significant impact on quality of life because of its chronicity and relapsing tendency. Its prevalence is about 2%.[2] At some places prevalence of 4.8% has also been reported.[3] Various studies have shown a serious impairment in quality of life[47,48] and patients also feel that current available treatment do not provide long term relief [4,5,6.] Psoriasis patients have a higher financial burden due to absenteeism in addition to the cost of treating their disease [7,8.] We are still unable to comment over the prognosis of disease, how long the disease will last, whether a relapse will occur, or for what period of time the patient will remain free from Psoriasis[1]

All forms of therapies have their own merits and demerits, often no single treatment is ideal. Treatment of Psoriasis remains a challenging and often frustrating experience for dermatologists where cure is not ensured. The management includes relevant investigations and treatment of the disease. The treatment depends upon age, sex, occupation, general health, intelligence of the patient, clinical type, extent and duration of the disease. Reassurance and emotional support are valuable. In general, therapy should be simpler, potentially less toxic and more effective.

The therapeutic tools available to combat this disease are numerous, as are their untoward effects.[12] Local therapy include Tar, Dithranol, Topical corticosteroid, topical calcineurin inhibitors, intralesional corticosteroids, calcitriols, retinoid.[1] Systemic therapies for Psoriasis which are in common use include psoralen photochemotherapy , biologicals, retinoids, Methotrexate and cyclosporine.[13] Of these the equipment required for psoralen photochemotherapy is not easily available, also there is always a risk of basal cell carcinoma and squamous cell carcinoma.[14] This carcinogenic property is further compounded by its use with immunosuppressive like cyclosporine.[9] Hydroxycarbamide (hydroxyurea) carries significant side effect of bone marrow suppression and leucopenia in most treated patients.[10] Systemic retinoids can not be used in females of child bearing age, children below 12 years of age, in patients with existing hyperlipidemia.[15,1.]

Cyclosporine is effective but nephrotoxicity, hypertension, and malignancy potential raises a concern about its use.[11,32] Biologicals like infliximab and Adalimumab is FDA approved for chronic plaque type Psoriasis[16,17,18.] but the cost, side effects like infusion reactions, anti-drug antibodies and inadequate experience

in using these limits its use in developing countries like ours.[19] Methotrexate is quite effective but is toxic to liver and its side effect are difficult to monitor.[16]

Azathioprine has a long history of being safely used by rheumatologist, gastroenterologist and dermatologist. Azathioprine not only have immunosuppressive effect but also possess anti inflammatory properties and in dermatology it is primarily used for immunobullous disorders like pemphigus.[14] Azathioprine is easy to monitor and carries less side effects in comparison to Methotrexate.[49,50] So, in view of availability of many modalities of treatment it is worthwhile to study and compare the effects of Methotrexate and Azathioprine in chronic plaque type Psoriasis, which would add to the future trends in the management of Psoriasis and would help the suffering patients.

Aims and Objectives: To evaluate the effect of Methotrexate and Azathioprine and to know the comparative effect of Methotrexate against Azathioprine in chronic plaque type Psoriasis

II. Materials And Methods

The study was a randomised double blind control hospital based study conducted in Department of Dermatology, Venereology & Leprosy**,** Rajendra Institute of Medical Sciences (RIMS), Ranchi. The subjects were recruited for the study by simple random sampling technique. The treatment trial was of 20 weeks which include 12 weeks of hospitalization and 8 weeks of follow up between December 2013 to December 2015. Patients with 18 to 60 years age of either sex and who were diagnosed as chronic plaque type Psoriasis were included and patients with History of any current or previous malignancy, pregnant or lactating women, history of diabetes mellitus, Epilepsy, HIV positive patients, known hypersensitivity to Methotrexate and Azathioprine, patients taking any systemic therapy with steroids, immunomodulators and cytotoxic drugs in previous 2 months, patients using topical treatment with formulations containing active agents as steroids, tar or dithranol in previous 2 weeks, TLC less than $3x10^9$/l, platelets count less than 50,000/mm3 and hemoglobin less than 9 gm/dl were excluded from the study.

A special designed semi structured Performa, included various socio-demographic variables (age, sex, education, religion, marital status, socioeconomic status) and clinical variables (clinical diagnosis, age of onset , duration of illness, treatment details) was applied. Psoriasis Area and Severity Index (PASI)[46] is used to assess the skin area involved and the severity of the dermatological illness. Severity assessment is done along a 0-4 scale (0-no lesion, 4-severest possible lesion) for the three target symptoms of erythema, infiltration and desquamation. The total PASI score, ranging from 0.0 to 72. PASI is considered an objective measure and it is widely used in research purpose. Though Psoriasis Area and Severity Index (PASI) has limitations, it remains the gold standard.[20,39] Limitations of the PASI system includes expression of very different aspects of Psoriasis in one single figure and inter-observer variability.

Complete blood count, liver functions tests, blood urea and creatinine levels, ECG and chest X-RAY were done before start of treatment. Screening for hepatitis B and C was also done. Patients were randomized using block randomization method into either: Group A which received Methotrexate in a dose of 15 mg weekly for 12 weeks. Group B received Azathioprine in a dose of 2 -3 mg/kg/day for 12 weeks. Severity of Psoriasis was assessed by measurement scores according to PASI scale. The PASI was scored on 0, 4, 8 and 12 weeks.Clearance of PASI from the base line levels were taken as percentage of clearance and interpretation of the results was done as follows: excellent response = ≥80% clearance; good response = 70 to 79 % clearance; fair response = 50 to 69 % clearance; and poor response = ≤49 % clearance. Group A patients receiving Methotrexate had their complete blood counts weekly for first two weeks and thereafter fortnightly. Liver and Renal function tests were done weekly for the first 2 weeks and then fortnightly thereafter until the completion of the study. Group B patients receiving Azathioprine had their complete blood counts were done weekly for the first 2 weeks then fortnightly for another 10 weeks Liver function test was done fortnightly till the completion of study**.**

Data was analyzed using Statistical Packages for Social Sciences (SPSS Version 22). Descriptive statistics was used to define the sample characteristics. For testing the variance among socio demographic and clinical variables, chi square test was applied for discrete variables and independent t-test was applied for continuous variables.

III. Observation And Results

The data gathered were consolidated, coded and subjected to appropriate statistical analysis. According to table 1 majority of patients belongs to 36 to 60 years of age i.e. 60 % and 64% in patients received Methotrexate and Azathioprine respectively. Majority of patients were male in both the groups i.e. 70% and 74% respectively. 58% and 46% patients were educated above 12^{th} standard in patients received Methotrexate and Azathioprine respectively. Majority of the patients were hindu, married and of lower socioeconomic status in both groups. The difference was not statistically significant between between both the groups in

sociodemographic profile. Mean duration of illness was 10.84±6.70 and 13.04±5.75 in Methotrexate and Azathioprine groups respectively. This difference was not statistically significant (P= 0.08). Mean PASI score was 17.47±8.84 and 15.90±8.97 in Methotrexate and Azathioprine groups respectively. It also showed no statistically significant difference (p=0.38). (Table 2).

After 4 weeks of Methotrexate treatment, 70% patients showed PASI clearance less than 49%, and 6% patient showed more than 70%. After 4 weeks of Azathioprine treatment, 88% patients showed PASI clearance less than 49%, and 2% patient showed more than 70% response. After 8 weeks of Methotrexate treatment, 26% patients showed PASI clearance less than 49%, and 32% patient showed more than 70% PASI clearance. After 8 weeks of Azathioprine treatment, 58% patients showed PASI clearance less than 49%, and 10% patient showed more than 70% PASI clearance. After 12 weeks of Methotrexate treatment, 14% patients showed PASI clearance less than 49%, and 54% patient showed more than 70% PASI clearance. After 12 weeks of Azathioprine treatment, 40% patients showed PASI clearance less than 49%, and 28% patient showed more than 70% PASI clearance.There was no statistically significant difference (p=0.09) found in PASI clearance after 4 weeks while this difference was significant after 8 weeks (p=0.01) and 12 weeks (p=0.02) of treatment. After 12 weeks of therapy with Methotrexate, 31 (62%) cases were relapsed within 8 weeks of stopping Methotrexate while 37 (74 %) cases were relapsed within 8 weeks of stopping Azathioprine but this difference was not statistically significant (p=0.20).(Table 4)

Side effects were present in 34% of the patient who had received Methotrexate and 30% of the patients who had received Azathioprine which include nausea, vomiting, diarrhea , abdominal pain, fatigue, headache, arthralgia, elevated liver enzymes, thrombocytopenia and leucopenia. Most common side effects were of gastrointestinal type in both the group and nausea –vomitting constitute the majority.(Table 5)

IV. Discussion

Azathioprine has been widely used for various autoimmune and inflammatory disorders. Azathioprine is very safe to use and with Thio Purine Methyl Transferase (TPMT) discovery and its available testing, we can avoid dreaded side effects like myelosuppression.[14] Routine examination like complete blood count and liver function test provide aids to monitor hepatotoxicity and myelosuppression during the course of study. Azathioprine acts by inhibiting purine metabolism and cell division through incorporation of its metabolite into the DNA and RNA.[15] But exactly it is not clear, how this mechanism leads to immunosuppression. Other reason for using Azathioprine is its easy availability and relatively cheap, considering the need of developing countries. There had been very few trial of Azathioprine use in Psoriasis.

The socio-demographic parameters were assessed in the two study groups. There was no significant difference between patients received Methotrexate and Azathioprine in terms of age, sex and education which was in accordance to our study plan. In our study majority of patients belongs to 36-60 years of age (Table 1), which was in concordance with study of *Haider et al*[21] which showed majority of patients belong to age group of 40±12 years. Another study of *Yui Yi* [22] , largest study in china which showed age of onset was 36 years. *Dhir et al* [23]also found the age range 35 to 67 years in their study. In *Karn et al* [24] study the mean age of Psoriasis patients was also 39.48 ± 11.74. In present study 72% of patients were male (Table 1), which is also similar to *Haider et al.*[21] findings where 61.6% were males. *Dhir et al*[23] also reported majority of patients were male (75%). *Karibasappa and George*[25] also found majority of patients were male in his study (60%). In *Dayal et al*[26] and *Icen m et al*[27] studies also showed overall incidence was higher in males than in females.

Current findings of Mean duration of illness of 10.84±6.70 and 13.04±5.75 years in Methotrexate and Azathioprine groups respectively are supported by *Dhir et al*[23] in which mean duration of illness was 11.6 years (1-25 years) and *Karisappa et al*[25] study in which duration of illness was 2-23 years. It is also supported by *Singh and Rai*[28] study. Current findings of Mean PASI score of 17.47±8.84 and 15.90±8.97 in Methotrexate and Azathioprine group respectively, supported by *Haider et al*[21] study, where mean PASI was 14.8±4.2, it is also supported by *Singh and rai*[28] study where mean PASI was 19.90 ± 10.64, 20.44 ± 12.28 and 19.95 ± 9.80 for three different groups. *Dayal et al*[26] also found mean PASI 16.82 ± 3.90 SD and 21.6 ± 4.42 SD in two different groups. Also *In Karn et al* [24] study mean PASI score at base line was 23.34 ± 1.12 and 21.25 ± 1.07 for 2 different groups.

After 4 weeks of Methotrexate treatment, 70% patients showed PASI clearance less than 49%, and 6% patient showed more than 70%. In ***Karn et al***[24] study, mean baseline PASI was 23.34 ±1.12 and after 4 weeks it was 15.60±0.72 which showed less than 40 percent clearance while in another study by ***Masuria et al***[29]complete clearance of Psoriasis was seen in 40% of patients in 4 weeks. In another study by ***Flystrom et al***[35] baseline PASI of 14.1±7 changed to 9.3±6.1. *Vijayshree and Kumar*[44] who also gave similar results in which 60.38 % patients showed PASI clearance less than 60.

After 4 weeks of Azathioprine treatment, 88% patients showed PASI clearance less than 49%, and 2% patient showed more than 70% response. Comparing with the study done by *Vijayshree and Kumar*[44] who also gave similar results in which more than 80% improvement was seen in only 2.4% patients and they also found

64.26% patients show reduction less than 60% of patients which was again consistent with our findings. *Greeves and Dawber*[30] showed improvement of only 25% in PASI clearance, in half of the patients after 6 weeks of Azathioprine treatment.

After 8 weeks of Methotrexate treatment, 26% patients showed PASI clearance less than 49%, and 32% patient showed more than 70% PASI clearance, which was comparable to *Haider et al*[21] study in which 60 percent of patient showed PASI-75 after 8 week of treatment and twenty nine (40%) patients had an almost complete remission during the 8 weeks of treatment i.e. showed >90% PASI clearance. In another study by *Opmeer BC et al*[31], mean baseline PASI score before treatment was 14.8±4.2 and at the end of 8 weeks of treatment was 4.9±4.3. In *Karn et al.,*[24] study, mean baseline PASI was 23.34 ±1.12. and after 8 weeks it was 9.45 ± 0.52. In 2015 study of *Singh and Rai*[28] PASI-75 achieved after 8 weeks. In *Malik & ejaz*[32] study, 73% patients had PASI clearance >80% and 45% had >60% clearance in 8 week. *Vijayshree and Kumar*[44] who also gave similar results in which 35.6% patients showed PASI clearance less than 60%.

After 8 weeks of Azathioprine treatment, 58% patients showed PASI clearance less than 49%, and 10% patient showed more than 70% PASI clearance. Comparing with the study done by *Vijayshree and Kumar*[44] who also gave similar results in which 42.8 % patients showed PASI clearance less than 60% and 9.5% patient showed PASI clearance more than 80% after 8 weeks of Azathioprine treatment.

After 12 weeks of Methotrexate treatment, 14% patients showed PASI clearance less than 49%, and 54% patient showed more than 70% PASI clearance. In *Karn et al*[24] study, the mean percent reduction of PASI score from base week to 12 weeks of treatment, was found to be 76.63± 1.79 for Methotrexate. In a similar study done by *Opmeer BC et al.*[31] base line PASI score was 13.4 ± 3.6 and at the end of 16 weeks it was 5.0± 4.5. *Akhyani et al*[34] also found that PASI -75 was achieved in 73.3% of patients on Methotrexate. *Flystrom I et al*[35] also found change from baseline at 12 weeks was 58% in the Methotrexate group. In the study by *Sandhu et al*[36], the mean PASI change at 12 weeks was 98% in the Methotrexate group.

After 12 weeks of Azathioprine treatment, 40% patients showed PASI clearance less than 49%, and 28% patient showed more than 70% PASI clearance. *Du Vivier et al*[37] gave the Azathioprine upto a dose of 300 mg per day and 66% of the patients were responded. In the study of *Hewitt et al*[38] complete remission was reported in 20% of the subjects, almost complete remission in 30%, good response but incomplete remission in 45% and no response in 5%. *Greaves and Dawber*[3] used reduction in area of involvement as outcome assessment. In 50% of the subjects there was 0-25% reduction, in 20% there was 25-50% reduction, in 10% there was 50-75% reduction and in 20% there was 75-100% reduction. Reduction of Psoriasis efflorescences was the outcome assessment by *Weitgasser et al*[40]. Forty subjects (60%) had complete remission, 20 (30%) had partial reduction and 6 (10%) had no significant reduction. In the series of *Le Quintrec et al.*[41] complete remission was found in 80% of the subjects, incomplete remission in 10% and in 10% of the subjects there was a relapse of the Psoriasis. Complete remission was attained in 91% of the subjects in the study of *Baum et al*[42] and 9% had marked improvement.

After 12 weeks of therapy with Methotrexate 31 (62%) cases were relapsed within 8 weeks of stopping Methotrexate while 19 (38%) were not relapsed. After 12 weeks of therapy with Azathioprine, 37 (74%) cases were relapsed within 8 weeks of stopping Azathioprine while 13 (26%) cases were not relapsed. There was no statistically significant difference (p=0.20) found in relapse within 8 weeks of stopping Methotrexate and Azathioprine.

Our findings are supported by *Singh and Rai* [28] who observed relapse in 36.5 % of cases after 12 weeks of stopping Methotrexate. In another study by *Karibasappa et al*[25] Methotrexate in the dose of 15mg/week was given to 20 patients with chronic plaque Psoriasis, till remission (4-12 weeks), followed by a maintenance dose (5mg/week) for 8 weeks. All patients were found to have relapsed within 6-12 weeks of stopping Methotrexate. *Kravetz and Balsam*[53] for first time used Azathioprine in Psoriasis; they used 2 mg/kg daily in 12 patients, 1-4 courses with improvement. In majority of the patients, it relapsed within 1.5-6 months after the last dose. *Greaves and Dawber*[30] used 2.5 mg/kg/day for 6 weeks in 10 patients with 25% clearance of the lesions in 5 patients within 2-6 weeks duration. Relapse was seen 1 month after stoppage of Azathioprine. *Feldges and Barnes*[54] used 2.5 mg/kg/day in 10 patients for 4 ½ months to 5 ½ years with almost complete clearance of skin lesions in 6 patients. Azathioprine was discontinued after remission lasting for 1 year. However, the lesions relapsed after stoppage of treatment. In 1974, *Du Vivier et al.*[37] used 100- 300 mg Azathioprine daily for 2-24 weeks with 75-100% clearance of Psoriasis lesions with maintenance dose of 75-200 mg daily in 13 out of 29 patients. One patient who was free of the lesions developed relapse 6 months after complete stoppage of Azathioprine.

Side effects were present in 34% of the patients who had received Methotrexate and 30% of the patients who had received Azathioprine, which include nausea, vomiting, diarrhea , abdominal pain, fatigue, headache, arthralgia, elevated liver enzymes, thrombocytopenia and leucopenia. Most common side effects were of gastrointestinal type in both the groups and nausea,vomiting constitute the majority. Fatigue and elevated liver enzymes were more common in Methotrexate group. Transient thorombocytopenia and leucopenia were seen in

2% of the patients receiving Methotrexate but revert back to normal after receiving folinic acid supplement which the patient missed during the therapy. Serious side effects like Pulmonary fibrosis and Secondary leukemia was not seen and is probably due to their low dose usage in dermatology in contrast with other branches where they are primarily given in higher doses for various transplantation and cancers.

Our findings has been supported by *Karn et al*[24] who also reported that gastrointestinal side effects were the most common to occur with Methotrexate. In his study he found about 30.43% of the patients of Methotrexate group were suffered from elevated liver enzymes, while in our study it is limited to only 10%. This difference can be attributed to patients selection criteria in our study. *Trivedi et al*[51] *and Sturdevant et al*[52] reported most common adverse effects of Azathioprine were gastrointestinal including nausea, vomiting, and diarrhea.

There was no significant difference in PASI clearance after 4 weeks of Methotrexate and Azathioprine treatment but statistically significantly difference found after 8 weeks (p=0.01) and 12 weeks (p=0.02) of treatment, i.e. patients received Methotrexate shown significantly higher PASI clearance (better response) in comparison to patients received azathioprone. There was no statistically significant difference (p=0.20) found in relapse within 8 weeks of stopping Methotrexate and Azathioprine.

Similar findings were also seen in studies by *Malik and ejaz*[32] who found at the end of week 8, the Methotrexate-treated group had a significantly greater percentage reduction in the PASI compared with that of the Azathioprine treated Group. In another study by *Mezzadara et al.*[43] who gave Azathioprine in very high doses to their patients i.e. 6 gram over a period of 18 days and then followed their patients for further ten weeks. They found Azathioprine to be comparable to Methotrexate in Psoriasis. *Du vivier et al*[37] concluded that patients showed poorer tolerance and clinical response to Azathioprine than to Methotrexate, and the drug will therefore represent an advance in therapy only if the long-term complications are significantly less. *Vijayshree and Kumar*[44] also observed that at the end of 8 week it was Methotrexate group that have shown better response in the form of reduction in PASI score in comparison to Azathioprine.

Strength of our study is that we have taken a drug naive population, it was a prospective study which included 3 months of hospitalization at a tertiary health care centre. Weakness of our study is that we could not remove the confounding facors like stress, effect of cold and infection. Sample size was also modest and futher clinical trial are needed over large sample size in order to find out the best drug which could maintain the long term remission and carries least side effect in management of this incurable disease.

References

[1]. Griffiths CEM, Camp RDR, Barker JNWN. Psoriasis. In: Burns D, Breathnach S, Cox N, Griffiths C, editors. Rook's textbook of dermatology. Oxford: Blackwell Science; 2010. pp. 20.1–20.60.

[2]. Christopher E.Psoriasis –Epidemiology and clinical spectrum. Clin Exp Dermatol 2001; 26:314-320.

[3]. Kavli G, Færde OH, Arnesen E et al. Psoriasis: familial predisposition and environmental factors. BMJ 1985; **291**: 999–1000.

[4]. Krueger G, Koo J, Lebwohl M, Menter A, Stern RS, Rolstad T. The impact of Psoriasis on quality of life: results of a 1998 National Psoriasis Foundation patient-membership survey. Arch Dermatol.2001;137:280–284.

[5]. Pearce DJ, Singh S, Balkrishnan R, Kulkarni A, Fleischer AB, Feldman SR. The negative impact of Psoriasis on the workplace. J Dermatolog Treat. 2006;17:24–28.
de Arruda LH, De Moraes AP. The impact of Psoriasis on quality of life. Br J Dermatol. 2001;144:33–36.

[6]. Feldman SR, Fleischer AB, Jr, Reboussin DM, Rapp SR, Bradham DD, Exum ML, Clark AR. The economic impact of Psoriasis increases with Psoriasis severity. J Am Acad Dermatol. 1997;37:564–569. doi: 10.1016/S0190-9622(97)70172-5.

[7]. Finlay AY, Coles EC. The effect of severe Psoriasis on the quality of life of 369 patients. Br J Dermatol. 1995;132:236–244.

[8]. Paul CF, Ho VC, McGeown C et al. Risk of malignancies in Psoriasis patients treated with cysclosporine: a 5 year cohort study. J Invest Dermatol 2003; 120:211–6.

[9]. Hunter GA, Simmons IJ, Thomas BM. A clinical trial of hydroxyurea for Psoriasis. Australas J Dermatol 1972; 13: 93–9.

[10]. Bos JD, Meinardi MMHM, van Joost T et al. Use of cyclosporin in Psoriasis. Lancet 1989; ii: 1500–2.

[11]. Spuls PI, Witkamp L, Bossuyt PM, Bos JD.A systematic review of five systemic treatments for severe Psoriasis. Br J Dermatol 1997; 137: 943-9.

[12]. Boztepe G, Karaduman A, Sahin S et al. The effect of maintenance narrow-band ultraviolet B therapy on the duration of remission for Psoriasis: a prospectiverandomized clinical trial. Int J Dermatol 2006; 45: 245-50.

[13]. Badalamenti,S.S.,Kerdel,F.A. Azathioprine. in: S.E.Wolverton(Ed.) ComprehensiveDermatologicTherapy. Saunders, Edinburgh, Scotland; 2013:182–189.

[14]. Loo TL, Luce JK, Sullivan MP, et al. Clinical pharmacologic observations of 6-mercaptopurine and 6-methythipurine ribonucleoside. Clin Pharmacol Ther 1968;14:180–94.

[15]. O'Quinn RP, Miller JL. The effectiveness of tumor necrosis factor alpha antibody (infliximab) in treating recalcitrant Psoriasis: A report of 2 cases. Arch Dermatol 2002;138(5):644–8.

[16]. Oh CJ, Das KM, Gottlieb AB. Treatment with anti-tumor necrosis factor alpha (TNF-alpha) monoclonal antibody dramatically decreases the clinical activity of Psoriasis lesions. J Am Acad Dermatol 2000;42(5):829–30.

[17]. Gordon KB, Langley RG, Leonardi C, et al. Clinical response to adalimumab treatment in patients with moderate to severe Psoriasis: Double-blind, randomized controlled trial and open-label extension study. J Am Acad Dermatol 2006;55(4):598–606.

[18]. Mehlis S, Gordon KB. Tumor necrosis factor (TNF) inhibitors . in: S.E. Wolverton (Ed.) Comprehensive Dermatologic Therapy. Saunders, Edinburgh, Scotland; 2013:307-318.

[19]. Puzenat E, Bronsard V, Prey S, Gourraud PA, Aractingi S, Bagot M, Cribier B,

[20]. Joly P, Jullien D, Le Maitre M, Paul C, Richard-Lallemand MA, Ortonne JP, Aubin F. What are the best outcome measures for assessing plaque Psoriasis severity? A systematic review of the literature. J Eur Acad Dermatol Venereol. 2010 Apr;24 Suppl 2:10-6.
[21]. Haider S, Wahid Z, Najam-us-Saher, Riaz F. Efficacy of Methotrexate in patients with plaque type Psoriasis. Pak J Med Sci 2014;30(5):1050-1053.
[22]. Yui Yip S. The prevalence of Psoriasis in the mongoloid race. J Am Acad Dermatol 1984; 10: 965–8.
[23]. Dhir R, Tutakne MA, Chari KVR. Relapse in Psoriasis after Methotrexate Indian J Dermatol Venereol Leprol 1992;58:77-9.
24.Karn D, Amatya A, Khatri R. Comparative study of Methotrexate and Cyclosporine in the treatment of Psoriasis. Nepal journal of dermatology venereology and leprosy 2010; vol 9,1:15-21.
[24]. Karibasappa NA, George A. Relapse in Psoriasis after Methotrexate. Indian J Dermatol Venereol Leprol 1997;63:307-9.
[25]. Dayal S, Mayanka, Jain V K. Comparative evaluation of NBUVB phototherapy and PUVA photochemotherapy in chronic plaque Psoriasis. Indian J Dermatol Venereol Leprol 2010;76:533-7.
[26]. Icen M, Crowson CS, McEvoy MT, Dann FJ, Gabriel SE, Maradit Kremers H. Trends in incidence of adult-onset Psoriasis over three decades: a population- based study. J Am Acad Dermatol. 2009 Mar;60(3):394-401.
[27]. Singh SK, Rai T. Relapse in Psoriasis with two different tapering regimens of Methotrexate: A randomized open-label controlled study. Indian J Dermatol Venereol Leprol 2015;81:144-7.
[28]. Masuria B L, Bansal N K, Sharma M, Singhi M K, Mittal. A clinico histopathological outcome of 4 weeks Methotrexate pluse therapy in Psoriasis. Indian J Dermatol Venereol Leprol 1999;65:172-3.
[29]. Greaves MW, Dawber W. Azathioprine in Psoriasis. Br Med J 1970; 2 (5703): 237-8.
[30]. Opmeer BC, Heydendael VM, De Borgie CA, Spuls PI, Bossuyt PM, Bos JD, et al. Costs of treatment in patients with moderate to severe plaque Psoriasis: economic analysis in a randomized controlled comparison of Methotrexate and cyclosporine. Arch Dermatol. 2004;140(6):685-690.
[31]. Malik T, Ejaz A. Comparison of Methotrexate and Azathioprine in the treatment of Psoriasis: A randomized controlled trial. J Pakistan Association of Dermatologists 2010; 20: 152–157.
[32]. Heydendael VM, Spuls PI, Opmeer BC, de Borgie CA, Reitsma JB, Goldschmidt WF, Bossuyt PM, Bos JD, de Rie MA. Methotrexate versus cyclosporine in moderate-to-severe chronic plaque Psoriasis. N Engl J Med. 2003 Aug 14;349(7):658-65.
[33]. Akhyani M, Chams-Davatchi C, Hemami MR, Fateh S. Efficacy and safety of mycophenolate mofetil vs. Methotrexate for the treatment of chronic plaque Psoriasis. J Eur Acad Dermatol Venereol. 2010 Dec;24(12):1447-51.
[34]. Flyström I, Stenberg B, Svensson A, Bergbrant IM. Methotrexate vs.ciclosporin in Psoriasis: effectiveness, quality of life and safety. A randomized controlled trial. Br J Dermatol. 2008; 158(1):116-121.
[35]. Sandhu K, Kaur I, Kumar B, et al. Efficacy and safety of cyclosporine versus Methotrexate in severe Psoriasis: a study form north India. J Dermatol. 2003;30:458–463.
[36]. Du Vivier A, Munro DD, Verbov J. Treatment of Psoriasis with Azathioprine. Br Med J 1974; 1(5897): 49-51.
[37]. Hewitt J, Escande JP, Leibowitch M et al. [Trial therapy of Psoriasis with Azathioprine]. [French]. Bull Soc Fr Dermatol Syphiligr 1970; 77: 392-6.
[38]. Feldman SR, Fleischer AB Jr, Reboussin DM, Rapp SR, Exum ML, Clark AR, NurreL. The self-administered Psoriasis area and severity index is valid and reliable. J Invest Dermatol. 1996 Jan;106(1):183-6.
[39]. Weitgasser H, Weitgasser H. [Experiences with an ambulatory immunosuppressive therapy of generalized Psoriasis]. [German]. Hautarzt 1972; 23: 316-8.
[40]. Le Quintrec JL, Menkes CJ, Amor B. Severe psoriatic rheumatism. Treatment with Azathioprine. report of 11 cases. Rev Rhum Mal Osteoartic 1990; 57: 8159.
[41]. Baum J, Hurd E, Lewis D et al. Treatment of psoriatic artthritis with 6-mercaptopurine. Arthritis Rheum 1973; 16: 139-47.
[42]. Mezzadra G. Therapeutic experience with Azathioprine in Psoriasis. G Ital Dermatol Minerva Dermatol 1972; 47: 72-6.
[43]. Vijayashree J, Kumar JS. Study of Effect of Methotrexate on Psoriasis in Comparison with Azathioprine. Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 41, October 12, 2015: 6916-9.
[44]. Fredriksson T, Pettersson U. Severe Psoriasis—oral therapy with a new retinoid. Dermatologica 1978; 157: 238–44.
[45]. Mattoo SK, Handa S, Kaur I, Gupta N, Malhotra R. Psychiatric morbidity in Psoriasis: Prevalence and correlates in India. Ger J Psychiatry. 2005;8:17–22.
[46]. Kumar V, Mattoo SK, Handa S. Psychiatric morbidity in pemphigus and Psoriasis: A comparative study from India. Asian J Psychiatr. 2013;6:151–6.
[47]. Patel AA, Swerlick RA, McCall CO. Azathioprine in dermatology: The past, the present, and the future. J Am Acad Dermatol 2006; 55: 390-1.
[48]. Wolverton SE. Optimizing clinical use of Azathioprine with newer pharmacogenetic data. Arch Dermatol 2009; 145: 707-10.
[49]. Trivedi CD, Pitchumoni CS. Drug-induced pancreatitis: an update. J Clin Gastroenterol 2005;39:709–16.
[50]. Sturdevant RAL, Singleton JW, Deren JJ, et al. Azathioprine-related pancreatitis in patients with Crohn's disease. Gastroenterology 1979;77:883–6.
[51]. Kravetz RE, Balsam T. Treatment of Psoriasis with mercaptopurine. Arch Dermatol. 1961;84:597–600.
[52]. Feldges DH, Barnes CG. Treatment of psoriatic arthropathy with either Azathioprine or Methotrexate.Rheumatol Rehabil. 1974;13:120–4.

Table 1: Comparing sociodemographic profile among patients received Methotrexate and Azathioprine.

Fischer's exact test was applied, where cell count was less than 5.

Variables		Patients received Methotrexate N=50 n (%)/ Mean(±SD)	Patients Received Azathioprine N=50 n (%)/ Mean(±SD)	t/χ2 /fisher's exact test	df	P
Age	18-35yrs	20(40%)	18(36%)	.17	1	.68
	36-60yrs	30(60%)	32(64%)			
Sex	Male	35(70%)	37 (74%)	.20	1	.66
	Female	15 (30%)	13 (26%)			
Education	<12th	21(42%)	27(54%)	1.44	1	.23
	≥12th	29 (58%)	23 (46%)			
Religion	Hindu	31 (62%)	34 (68%)	.40	1	.53
	Others	19 (38%)	16 (32%)			
Marital status	Married	37 (74%)	38 (76%)	.05	1	.82
	Single	13 (26%)	12 (24%)			
Socioeconomic status	Upper	4 (8%)	4 (8%)	.28	2	.87
	Middle	10 (20%)	8 (16%)			
	Lower	36(72%)	38 (76%)			

Table 2: Comparing duration of illness and baseline PASI among patients received Methotrexate and Azathioprine.

Variables	Duration of illness Mean(±SD)	Baseline PASI
Patients received Methotrexate N=50	10.84±6.70	17.47±8.84
Patients received Azathioprine N=50	13.04±5.75	15.90±8.97
P Value	.08	0.38
df	98	98

***indicates p <.05 **indicates p<.01**

Table 3: Comparing PASI clearance at week 4, 8 and 12 among patients received Methotrexate and Azathioprine.

PASI clearance	After 4 weeks		After 8 weeks		After 12 weeks	
	Patients received Methotrexate N=50 n (%)	Patients received Azathioprine N=50 n (%)	Patients received Methotrexate N=50 n (%)	Patients received Azathioprine N=50 n (%)	Patients received Methotrexate N=50 n (%)	Patients received Azathioprine N=50 n (%)
≥80%	0	0	6 (12%)	1(2%)	13(26%)	6(12%)
70-79%	3(6%)	1(2%)	10(20%)	4(8%)	14(28%)	8(16%)
50-69%	12(24%)	5(10%)	21(42%)	16(32%)	16(32%)	16(32%)
≤49%	35(70%)	44(88%)	13(26%)	29(58%)	7(14%)	20(40%)
χ2	4.9		12.91		10.48	
Df	2		3		3	
P	.09		**.01***		**.02***	

***indicates p <.05 **indicates p<.01 Fischer's exact test was applied, where cell count was less than 5.**

Table 4: Comparing relapse 8 weeks after stopping drugs.

	Patients received Methotrexate N=50 n (%)	Patients received Azathioprine N=50 n (%)	□2	df	P value
Relapsed	31 (62%)	37 (74%)	1.65	1	.20
Not relapsed	19 (38%)	13 (26%)			

***indicates p <.05 **indicates p<.01**

Table 5: Showing side effects of Methotrexate and Azathioprine.

Side effects	**Patients received Methotrexate N=50 n (%)**	**A Patients received Methotrexate N=50 n (%)**
present	17 (34%)	15 (30%)
Absent	33 (66%)	35 (70%)
Nausea and Vomitting	14 (28%)	10 (20%)
Diarrhea	3 (6%)	-
Abdominal pain	1 (2%)	2 (4%)
Fatique	12 (24%)	4 (8%)
Headache	5 (10%)	1 (2%)
Arthralgia	3 (6%)	2 (4%)
Elevated liver enzymes	5 (10%)	1 (2%)
Thrombocytopenia	1 (2%)	-
Leucopenia	1 (2%)	3 (6%)