EFFICACY AND SAFETY OF METHOTREXATE VERSUS ACITRETIN IN CHRONIC PLAQUE PSORIASIS

Sahibzada Mahmood Noor[1], Neelum Ayub[2], Mohammad Majid Paracha[3]

[1-3] Department of Dermatology, Lady Reading Hospital, Peshawar - Pakistan.
Address for correspondence:
Dr. Mohammad Majid Paracha
Associate Professor, Department of Dermatology, Lady Reading Hospital, Peshawar - Pakistan.
Email: drmajid_68@hotmail.com
Date Received:
August 31, 2016
Date Revised:
December 18, 2016
Date Accepted:
December 30, 2016

ABSTRACT

Objectives: To compare the treatment efficacy and safety of methotrexate with acitretin in chronic plaque psoriasis.

Methodology: A total of 142 patients were enrolled, 71 patients in each group. Patients were randomly divided into two groups, A and B by lottery method. They were given methotrexate (25 mg injection deep I/M once weekly) or acitretin (0.4mg/kg orally daily). At the end of 24 weeks, response to treatment was evaluated in terms of reduction in PASI score. Safety of treatment was accessed in terms of laboratory investigations i.e. transaminase, triglycerides, platelets and white blood cells during treatment.

Results: In methotrexate group, an excellent response (PASI-75%) was noted in 38 (53.5%), good response (PASI-50%) in 13 (18.3%), fair response (less than 50% reduction in PASI) in 4 (5.6%), and no response was observed in 1(1.4%) patients. In acitretin treated group excellent response was noted in 18 (25.3%), good response in 27 (38.0%), fair response in 8 (11.2%), and no response was observed in 5 (7.04%) of patients.

Conclusion: Methotrexate is better option for treatment of moderate to severe plaque psoriasis than acitretin.

Key Words: Methotrexate, Acitretin, Chronic Plaque psoriasis

This article may be cited as: **Noor SM, Ayub N, Paracha MM. Efficacy and safety of methotrexate versus acitretin in chronic plaque psoriasis. J Postgrad Med Inst 2017; 31(1): 4-7.**

INTRODUCTION

Psoriasis is a chronic relapsing, non-contagious skin disease . Chronic Plaque Psoriasis is the most prevalent form of the disease although several other distinctive clinical forms are recognized. Psoriasis is a common, T cell mediated disease in which genetic and environmental influences have a critical role[1,2]. The most characteristic lesion consists of chronic, sharply demarcated, dull red, scaly plaques, particularly on extensor aspects of the body and scalp[3]. It affects approximately1- 2 percent of the world's population[4,5].

Psoriasis Area and Severity Index (PASI) developed in 1978, by Fredricksson and Pettersson, is used to evaluate the severity of psoriasis. This index analyzes four regions of the body (head, trunk, upper and lower limbs) in relation to erythema, induration (thickness), desquamation (scaling) of the plaques, and body surface area (BSA) affected. Scores from 0 to 4 based on intensity of erythema, induration and scaling are used to rate severity of psoriasis[6].

Patients with mild disease usually require only topical treatment however those with moderate to severe disease generally require phototherapy, ciclosporin, methotrexate and acitretin. These drugs are used in combination or in rotation to minimize the side effects[7,8].

The choice of treatment is influenced by short-term as well as long-term considerations, including severity of the disease, effectiveness of a given medication and its side effects, the patient's quality of life, and the cost of treatment[9,10]. Methotrexate and acitretin are commonly employed in the treatment of chronic plaque psoriasis in our set up. There is no study comparing the efficacy and safety of these drugs in the treatment of psoriasis. This quasi experimental study was aimed to determine whether acitretin alone is more effective than methotrexate alone, in terms of reduction in the PASI and evaluation of safety profile and thus enabling the health professionals in developing appropriate treatment protocol with minimum side effects and high efficacy.

METHODOLOGY

The study was conducted in Department of Dermatology, Lady Reading Hospital, Peshawar from March 2010 to September 2011, after taking permission from the hospital ethical committee.

A total of 142 patients with chronic plaque psoriasis were included in this study i.e.71 patients in each group.

Group A (those treated with methotrexate) & group B (those treated with acitretin). Patients were allocated to groups by lottery. Sampling was Purposive, non probability sampling. Inclusion criteria was both male and female patients of a stable chronic plaque psoriasis, age of 18 years and above and more than 20% body surface area involvement. Patients with predominantly guttate, erythrodermic or pustular psoriasis (as efficacy of acitretin has been proven in these forms of psoriasis) were enrolled. From group A we had loss of one patient while from group B, 7 patients did not complete the study.

Patients suffering from other skin diseases e.g. eczema, lichen plannus which could cause bias were excluded from the study. Pregnant or lactating females (both methotrexate and acitretin are teratogenic) therefore ethically these patients could not be enrolled in this study.

Abnormal liver function tests (1.5 times the upper normal limit of AST/ALT were not enrolled as methotrexate and acitretin would have further deteriorated liver function tests and the results of study could be biased). Abnormal lipid profile (cholesterol more than 230mg/dl and triglyceride more than 200mg/dl) and patients suffering from infectious hepatitis (hepatitis B, hepatitis C & HIV infected individuals) were also excluded.

Patients who fulfilled the inclusion criteria were enrolled for treatment with either methotrexate (25mg deep I/M once weekly) or acitretin (0.4mg orally daily) after informed consent. Efficacy was measured by reduction in PASI score every six weeks for 24 weeks till the completion of treatment. Efficacy was graded poor if there was reduction of 0 to 24 percent , fair for reduction of 25 to 50 percent , good for reduction in PASI score of 51 to 75, Excellent for a reduction of 76 to 100 percent . Safety was evaluated in terms of serial follow up of laboratory investigations. Transaminases, triglycerides, WBC and platelet count were estimated at 6, 12, 18 and 24 weeks for both the drugs.

Statistical analysis was performed using statistical package for social sciences (SPSS10.0 for windows). Frequencies and percentages were presented for gender. Means ± standard deviation were computed for age of patients, PASI score, Transaminases, Triglycerides, WBC and platelet count. Data was compared using chi-square test for PASI score for both drugs after 6, 12, 18 and 24 weeks to see the effectiveness of both drugs. P-value of less than or equal to 0.05 was considered as significant. Results were expressed in the form of tables.

RESULTS

A total of 142 patients were enrolled in the study. Number of male patients in the study were 85 while there were 57 female patients. In group A male and female patients were 40 and 31 respectively while in group B male and female were 45 and 26 respectively. The age of the patients ranged from 18-70 years. Mean age of enrolled patients was 40.99 years ±14.99. Response rate of both groups was same in both female and male patients. Outcome of the study groups is shown in table 1.

In methotrexate group, an excellent response (PASI-75%) was noted in 38 (53.5%), good response (PASI-50%) in 13 (18.3%), fair response (less than 50% reduction in PASI) in 4 (5.6%), and no response was observed in 1(1.4%) patients. Nine (12.6%) patients showed a rise in ALT reaching a maximum of 300mg/dl that required discontinuation of treatment and with subsequent follow up. Serial values of ALT done showed a downward trend reaching normal values. Five (7.0%) patients showed myelo-suppression and loss of follow up in this group was in 1 (1.4%) patient as shown in table 2.

In acitretin treated group excellent response was noted in 18 (25.3%), good response in 27 (38.0%), fair response in 8 (11.2%) and no response was observed in 5 (7.04%) patients as shown in table 1. In acitretin group 5 (7.0%) patient had their TG increased to more than 200mg/dl reaching a maximum of 380mg/dl thus requiring discontinuation of treatment and 1(1.4%) showed a rise in ALT as shown in table 3. These patients showed a downward trend of these abnormal values on serial follow up. This difference was not statistically significant between the two groups.

Patients in MTX group showed complaints of nausea, headache, body aches, vertigo but none required discontinuation of therapy. While in acitretin group patients presented with complaints of pruritis, mucocutaneous dryness, cheilitis, but none required treatment discontinuation.

DISCUSSION

Most of the patients in our study were having maximum PASI score at admission as shown in table 1. The reason for this observation was probably the low literacy rate and lack of health facilities being provided by the health authorities in our set up. Most of the patients who present to our hospital are usually from remote areas so in initial stages of the disease they go to quacks where they are mismanaged and when they come to us they are usually with full blown disease.

Treatment outcome of our study groups was measured by reduction in PASI score. There was no significant difference in percentage reduction in the PASI score on follow up at week 6 in both groups. However there was marked reduction in PASI score in both methotrexate group and acitretin group after 24 weeks of treatment. It was found that in methotrexate group excellent response, (PASI-75%) was seen in 38 patients

(53.5%). In acitretin group excellent response was noted in 18 patients (25.3%). This difference in responses was statistically significant and was much higher for the methotrexate group as compared to acitretin group. The p value was found to be 0.027 which was statistically significant.

The response rate of methotrexate group in our study was compared with the study conducted by Heydendael et al[11]. It was found that PASI-75 response was achieved by 40% patients at 16 weeks of treatment which is relatively less than the response achieved in our study group. The reason for this disparity with the referred study is probably due to the difference in the sample size which was 88 in the referred study and is less than our study sample size. Another reason could be the difference in dose of methotrexate given. They gave a maximum of MTX 22.5mg/week dose in their study population whereas we used 25mg/week in our patients. The third reason for the low response rate of the referred study could be early assessment of reduction in PASI score i.e. at 16weeks while we did our final assessment of PASI score reduction at 24 weeks.

When we compared our study with another study conducted by Naldi et al[4] there was disparity in the results from our study. PASI-50 response was taken as end point and achieved by 67% of study population after 24 weeks of treatment[3]. In our study the primary end point was a PASI-75 response that was achieved by 53.4% patients.

When we compared the response rate of the patients in acitretin group with other studies it was observed that our results were comparable with a study conducted by Gisondi et al[12]. PASI-75 response was achieved by 30% patients in the referred study while in our study PASI-75 was achieved by 25.35% patients. The reason for this similarity was probably due to the same dose of acitretin, same duration of treatment and same primary end point of study i.e. PASI-75 response at 24 weeks.

Table 1: Comparison of reduction in PASI score in both the treatment groups

No. of Visits	Drugs chosen for the Patients	n	Mean	Std. Deviation	P-value
PASI_6wk	Methotrexate	71	42.11	10.809	0.550
	Acitretin	71	43.35	13.699	
PASI_12wk	Methotrexate	71	27.86	16.023	0.010
	Acitretin	71	34.51	14.275	
PASI_18wk	Methotrexate	71	17.56	12.353	0.014
	Acitretin	71	22.93	13.382	
PASI_24wk	Methotrexate	71	8.85	9.672	0.027
	Acitretin	71	12.76	11.055	

Table 2: Safety profile of acitretin

No. of Visits	SGPT		TG		TLC		PLT	
	<40	>40	<200	>200	<4000	4000-11000	<150,000	150,000--- 350,000
6Wks	70	1	68	3	0	71	0	71
12Wks	70	1	67	4	0	71	0	71
18Wks	70	1	66	5	0	71	0	71
24Wks	71	0	67	4	0	71	0	71

Table 3: Safety profile of methotrexate

No. of Visits	ALT		TG		TLC		PLT	
	<40	>40	<200	>200	<4000	4000-11000	<150,000	150,000--- 350,000
6Wks	66	5	71	0	68	3	4	67
12Wks	62	9	71	0	69	2	5	66
18Wks	64	7	71	0	71	0	3	68
24Wks	68	3	71	0	71	0	1	70

However when we compared our study with a study conducted by Murray et al[13] they observed a PASI-75 response in 60% patients. This disparity between the two studies is due to the dose of acitretin as they used a higher dose i.e. 50mg as compared to 25mg in our study.

When the side effect profile of the methotrexate group of our study was assessed it was observed that 12% patients showed transient elevation in liver function tests & it reached a normal value after stopping treatment in a time period of about 4 to 8 weeks. When we compared this observation of ours with the study conducted by Gisondi et al[12] the results were almost similar. They reported that 13% of their patients showed a transient elevation in liver function tests. This similarity was probably due to the similar study designs of the two studies. However 7% of our study population showed myelo-suppression while in the referred study no myelo-suppression was observed. This disparity was probably due to the difference in dose as we used higher dose as compared to the dose used by Gisondi and his collegues[12].

On comparing acitretin safety profile, it was found that TG were elevated in 7% patients in the present study while it was in contrast to the study conducted by Ezquera et al[14]. They reported that acitretin resulted in elevation of triglycerides in 15% of their patients. This contrast between the two studies was probably due to the difference in age range of the two study populations. Mean age of the referred study population was 61 years which is more than our study population.

Lost to follow up in acitretin group was 9.8% patients. Our study was not sponsored as patient were unable to buy acitretin due to socioeconomic constraints. Contrary to the international studies which are usually sponsored, thus there is no loss of follow up in these studies[12]. In our set up the non-compliance in acitretin group was not because of side effects but due to non-affordability as this is an expensive drug for common man as compared to methorexate which does not put a lot of burden on patient's pocket.

CONCLUSION

A faster reduction in the PASI can be achieved by using methotrexate alone than by using acitretin alone in the treatment of moderate to severe chronic plaque psoriasis. Methotrexate has more side effects as compared to acitretin, which is a relatively safer drug.

REFERENCES

1. Mashhood AA, Imran A. Pathogenesis of psoriasis. J Pak Assoc Derma 2005; 15:42-54.
2. Berard f, Nicolas Jf. Physiopathologie du psoriasis. Ann Dermatol Venereol 2003; 130:837-42.
3. Fairhurst DA, Achcroft DM, Griffiths CE. Optimal management of severe plaque psoriasis. Am J Clin Dermatol 2005; 6:283-94.
4. Naldi L, Grifiths CE. Traditional therapies in management of chronic plaque psoriasis. Br J Dermatol 2005; 152; 597-615.
5. Cather J, Menter A. Novel Therapies for psoriasis. Am J Clin Dermatol 2002; 3:159-73.
6. Jacobson CC, Kimball AB. Rethinking the psoriasis area and severity index: The impact of area should be increased. Br J Dermatol 2004; 151:381-7.
7. Weinstein GD, White GM. An approach to the treatment of moderate to severe psoriasiswith rotational therapy. J Am Acad Dermatol 1993; 28:454-9.
8. Lebwohl M, Ali S. Treatment of psoriasis topical therapy and phototherapy. J Am Acad dermatol 2001; 45:487-98.
9. Lebwohl M Ali S. Treatment of psoriasis systemic therapies. J Am Acad dermatol 2001; 45: 649-64.
10. Griffith CE, Clark CM, Chalmers RJ, Li Wan Po A, Williams HC. Systemic review of treatment for severe psoriasis. Health Technol Assess 2000; 4:1-125.
11. Heydendael VM, Spuls PI, Opmeer BC, de Borgie CA, Reitsma JB, Goldschmidt WF et al. Methotrexate versus cyclosporine in treatment of chronic plaque psoriasis. N Engl J Med 2003; 349:658-65.
12. Gisondi P, Del Giglio M, Cotena C, Girolomani G. Combining Etanercept and Acitretin in therapy of chronic plaque psoriasis: a 24-week, randomized controlled, investigator-blinded pilot trial. Br J dermatol 2008; 158:1345-9.
13. Murray HE, Anhalt AW, Lessard R, Schacter RK, Ross JB, Stewart WD, Geiger JM. A 12 month treatment of severe psoriasis with acitretin: results of a Canadian open multicenter study. J Am Acad Dermatol 1991; 24:598-602.
14. Ezquerea GM, Regana MS, Millet PU. Combination of acitretin and oral calcitriol for treatment of plaque type psoriasis. Acta Derm Venereol 2007; 5:449-50.

CONTRIBUTORS

SMN conceived the idea, planned the study, and drafted the manuscript. NA and MMP helped acquisition of data and did statistical analysis. All authors contributed significantly to the submitted manuscript.