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Original Article

Comparative efficacy of methotrexate and hydroxyurea in treatment of psoriasis

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Abstract

Background Psoriasis is a common, genetically determined, inflammatory and proliferative disease of the skin. In contrast to the general belief that psoriasis is incurable, most of the patients are treated with different modalities showing variable responses. Moreover, considerable percentage of patients can be benefited by proper selection of treatment modality.

Objective we compared the efficacy of two drugs, methotrexate and hydroxyurea, the use of which is supported by immunopathogenic basis of origin of psoriasis in the treatment of psoriasis.

Patients and methods A total of 40 patients of psoriasis having more than 20% body surface involvement during a one year period were alternatively allocated to group A and group B and treated with methotrexate 15mg per week and hydroxyurea 500mg twice a day respectively for three months. The patients were evaluated for response and side effects at 1, 2 and 3 months of treatment. The severity of disease was evaluated by PASI scoring using the method of Ramsay and Lawrence and the results of two groups were statistically compared.

Results In group A, on methotrexate, the percentage reduction at one month was 47.21±8.70, which increased to 66.20±10.77 and 81.90±12.08 on two and three months of treatment respectively while in patients on hydroxyurea, the percentage reductions in score were found to be 40.47±15.32, 55.74±15.27 and 73.68±18.59 at one, two and three months.

Conclusion Both methotrexate and hydroxyurea were equally effective in the treatment of psoriasis. Also methotrexate lead to a faster clearance of disease in early course of treatment though both drugs had similar efficacy at the end of three months.

Key words Psoriasis, methotrexate, hydroxyurea, PASI.

Introduction

Psoriasis is a common genetically determined, inflammatory and proliferative disease of the skin, characterized by chronic, sharply demarcated, dull red, scaly plaques, particularly on the extensor prominences and in the scalp.[1] It has a worldwide distribution with prevalence varying according to race and geographical location. In contrast to the general belief that psoriasis is an incurable disease, most of the patients treated with different modalities show variable responses. Although, a universal good response may or may not be achieved, it is important that a considerable percentage of patients are benefited by proper selection of treatment modality. The local treatments

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include use of tar preparations, dithranol,[2] vitamin-D analogues[3] and topical corticosteroids[4] while in the systemic treatment, the alternatives are antimetabolites like methotrexate, corticosteroids, retinoids, hydroxyurea and cyclosporine.[5] Out of these, the use of drugs like methotrexate[6] and hydroxyurea[7] is supported by the immunopathogenic basis of origin of psoriasis.[8] We compared the efficacy of these two dugs in the treatment of psoriasis.

Patients and methods

A total of 40 patients of psoriasis having at least 20% involvement of body surface area, during one-year period, constituted the study material. We had excluded pregnant females, lactating mothers, immunocompromised patients, patients with active form of infection anywhere in the body, patients of psoriasis suffering from any other disease, and the patients in pediatric age group. The patients were alternatively allocated into two groups, group A and group B. The group A patients were given tablet methotrexate 5mg 12 hrly for three doses a week i.e. a total dose of 15 mg/week. This was continued for three months. Group B patients were given capsule hydroxyurea 500mg orally twice a day for three months. In each group, during the first visit of patient, detailed history was taken and thorough clinical examination was done. During the first visit of patient investigations like complete blood counts, Liver Function Tests, Renal function Test, Random Blood Sugar, Electrocardiogram, and X-ray chest (PA view) were done. The patients were called on follow-up and evaluated for response and side effects every week for first month and then fortnightly for next two months. Severity of the disease was evaluated by PASI scoring using the method of Ramsay and Lawrence[9] and the grading was done as follows: remission >75% reduction in PASI score; marked improvement, 50-75% reduction in PASI; moderate improvement, 25-50% reduction in PASI score; and no improvement, <25% reduction in PASI.

At the end of the three months PASI score was compared with the pretreatment values in each group.

Results

Group A and group B were found to be similar in age distribution of patients. The mean age in group A was 44.80$\pm$13.36 years, while in group B, the mean age was 44.25$\pm$9.78 years with no statistically significant difference. In the sex distribution, both groups had a male preponderance. In the group A, out of the total of 20, there were 14 males and 6 females, and in group B there were 16 males and 4 females

The duration of illness varied widely in patients but the mean duration of illness in both groups was similar. In group A, it was 8.60$\pm$5.88 years and in group B, the same was 11.50$\pm$10.77 years.

It was observed that both the groups showed positive correlation between duration of illness and PASI score at beginning of the treatment. A coefficient of correlation of +0.15 in group A and +0.13 in group B was found between these two variables.

The effect of drugs was compared by assessing the change in PASI score at one, two and three months of treatment. In both the groups there was constant decrease in PASI score with treatment, but there was no statistically significant difference in the decrease in PASI score at the end of month 1, 2and 3. In group A the score decreased to 10.43±3.89 at one month of treatment. It further decreased to 6.63±2.73 and 3.33±2.09 at 2 and 3 months of treatment, respectively. Also the PASI score in group B had a decline coming down from the initial value of 22.01±11.97 to 13.14±8.73, 9.59±6.74 and 6.23±6.71 at 1 month 2 month and 3 month of treatment, respectively. So, although the values had a constant decline on treatment, the comparison of mean scores between two groups at start as well as on the follow-up showed no significant difference (**Table 1**).

Table 1 Mean PASI score in two groups at baseline and during therapy

	Comparison of Me 248 *Scores of Group A and Group B*			
	Start	*1 month*	*2 month*	*3 month*
Group A	19.97±7.50	10.43±3.89	6.63±2.73	3.33±2.09
Group B	22.01±11.97	13.14±8.73	9.59±6.74	6.23±6.71
t-value	0.64	1.27	1.81	1.84
p value	Non-significant	Non-significant	Non-significant	Non-significant

Table 2 Mean percentage reduction in PASI score in two groups.

	Mean Percentage Reduction in PASI Score		
	1 month	*2 month*	*3 month*
Group A	47.21 ± 8.70	66.20 ± 10.77	81.91 ± 12.08
Group B	40.47 ± 15.32	55.74 ± 15.27	73.68 ± 18.59
t-value	t= 1.71	t= 2.50	t= 1.66
p value	Non-significant	Significant	Non-significant

Table 3 Comparison of efficacy in two groups.

Grades of Improvement at 3 months		
	Group A	*Group B*
Remission (> 75% Reduction in PASI)	15 (75%)	9 (45 %)
Marked improvement. (50-75% reduction in PASI)	4 (20%)	8 (40 %)
Moderate improvement. (25-50% reduction in PASI)	1 (5%)	3 (15 %)
No improvement (<25% reduction in PASI)	0 (0%)	0 (0%)

We further compared the mean percentage reductions in the two groups. The percentage reduction in PASI score was calculated in each group at one month, two months and three months intervals. In group A the percentage reduction at one month was 47.21±8.70, which increased to 66.20±10.77 and 81.90±12.08 on two and three months of treatment respectively. In the other group the percentage reductions in score were found to be 40.47±15.32, 55.74±15.27 and 73.68±18.59 at one, two and three months. The percentage reductions of two groups at the three timings were

compared. It was seen that although the percentage reduction in PASI score was always more in case of group A patients, but the differences in the percentage reduction in PASI score was statistically significant at the end of second month only (**Table 2**).

It was seen that in both groups the maximum number of patients were in remission but it was more in group A with 75% patients in this grade while in group B 45% showed remission. Marked improvement was seen in 20% and 40% of patients in group A and B respectively (**Table 3**).

Also it was observed that a positive correlation existed between the duration of illness and the treatment outcome in form of % reduction is PASI score. The coefficient of correlation was seen to be +0.17 and +0.27 in group A and group B, respectively. So it was concluded that the longer duration of illness had a positive impact on the treatment outcome.

The side effects were recorded at one, two and three months of treatment. In group A, the hematological side effects were seen in one patient at one month and increased to 9 patients i.e. 45% of patients at 3 months of treatment. The gastrointestinal side effects appeared much earlier and persisted throughout the study with 50% of patients having gastrointestinal side effects at one and two months and 55% at three months. Hepatotoxic side effects in form of change in LFTs were seen only at 3 months of treatment in 25% of patients. No other side effect was seen in any patient.

In group B, the hematological side effects were seen more often with 30% and 55% of patients having these at the end of second and third months of treatment respectively. The GI side effects were not seen in the patients of this group. Hepatotoxic side effects in form of change in LFTs were also not seen here. While the other side effects in form of pigmentation of lesional skin, nail changes, erythema of hands and face were found positive in 25% of patients at the end of two months and further increased to 40% at three months of therapy.

Discussion

The use of methotrexate for psoriasis dates back to 1958.[6] It interferes with the function of enzyme dihydrofolate reductase thereby blocking the DNA synthesis particularly in the S-phase of the cycle therefore inhibits the replication of rapidly proliferating cells in psoriatic plaques.

In our present study methotrexate showed remission in 75% patients, marked improvement in 20%, and moderate improvement in 5% of patients. Till now numerous studies have proven that more than 75% improvement in PASI score is achieved by different authors at the end of 12 weeks.

It has been observed that with hydroxyurea at the end of three months, 45% patients were in remission and marked improvement was seen in 40% of patients. Samuel *et al.*[10] had also observed similar results.

In our study, it was found that the duration of illness had a positive correlation with the PASI score at the start of treatment i.e. patients with longer duration of illness had greater severity of disease in the form of higher PASI score.

There is paucity of published studies on the comparative efficacy of methotrexate and hydroxyurea in treatment of psoriasis. We compared both drugs and found that differences in mean reduction in PASI in both groups was not statistically signifi- 250 at the end of first and third months but more percentage reduction in PASI score with methotrexate at 2 months indicated a better efficacy of methotrexate in early course of treatment. So it can be said that methotrexate led to faster clearance of disease in early course of treatment but both drugs had similar efficacy at the end of three months.

The side effects in both groups were observed. It was seen that methotrexate was associated with hematological side effects like leucopenia and thrombocytopenia; gastrointestinal side effects; and hepatotoxicity where as hydroxyurea was associated with hematological side effects and other changes like pigmentation of lesional skin, nail changes, erythema of face and hands etc. So hydroxyurea can be a viable alternative to methotrexate in patients with psoriasis who are either intolerant to methotrexate because of gastrointestinal side effects or in whom methotrexate is contraindicated because of hepatotoxicity.

References

1. Griffiths CEM, Camp RDR, Barker JNWN. Psoriasis. In: Burns T, Breathnach S, Cox N, Griffiths C, eds. *Rook's Textbook of Dermatology, 7th edn.* Oxford: Blackwell Science; 2004. p. 35.1-35.69.
2. Shroot B. Anthralin. In: Roenigk HH, Maibach HI, eds. *Psoriasis, 2nd edn*. New York: Marcel Dekker; 1991. p. 481-499
3. Greaves MW, Weinstein G D. Treatment of psoriasis. *N Engl J Med* 1995; **332**: 581-3.
4. Lebwohl M, Ali S. Treatment of psoriasis. Part 1. Topical therapy and phototherapy. *J Am Acad Dermatol* 2001; **45**: 487-98.
5. Lebwohl M, Ali S. Treatment of Psoriasis. Part 2. Systemic therapies. *J Am Acad Dermatol* 2001; **45**: 649-61
6. Mc Henry PM, Bingham EA, Callendw ME *et al*. Dynamic hepatic scintigraphy in screening of patients for methotrexate induced hepatotoxicity. *Br J Dermatol* 1992; **31**: 404-9.
7. Layton AM, Sheehan-Dare RA, Goodfield MJD, Cotterill JA. Hydroxyurea in the management of therapy resistant psoriasis. *Br J Dermatol* 1989; **121**: 647-53.
8. Parent D, Bernard BA, Desbas C *et al.* Spreading of psoriatic plaques: alteration of epidermal differentiation precedes capillary leakiness and anomalies in vascular morphology. *J Invest Dermatol* 1990; **95**: 333-40.
9. Ramsay B, Lawrence CM. Measurement of involved surface area in patients with psoriasis. *Br J Dermatol* 1991; **124**: 565-70.
10. Samuel L, Moschella, Michael A, Greenwald. Psoriasis with hydroxyurea. *Arch Dermatol* 1973; **107**: 363-68

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