

## Original Article

# The efficacy and safety of oral methotrexate in chronic eczema

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**Abstract** *Background* Eczema is an extremely common skin problem in our society. Sometimes, chronic eczema becomes resistant to the conventional therapies. Hence, there is a need for an efficacious and safe treatment of patients with recalcitrant, chronic eczema.

*Objectives* To assess the efficacy and safety of low dose methotrexate (MTX) in chronic eczema.

*Patients and methods* The study was carried out in the Dermatology Department, Unit-I, Mayo Hospital, Lahore, for one year duration with sixty patients of chronic eczema, using purposive non-probability sampling technique. Severity of eczema was assessed using Eczema Area and Severity Index (EASI). A reduction of 50% or more in EASI score, after three months of therapy, was considered as effective treatment. Patients in the study group were administered 0.1 mg/ kg body weight of MTX once weekly for three months. Patients of control group were given placebo in the form of folic acid 5 mg tablets once daily for three months. The safety of MTX was judged by clinical and laboratory evaluation of patients on weekly follow-up.

*Results* All the study group patients had a reduction of 50% or more in EASI score whereas none in the control group had similar reduction. The clinical & laboratory evaluation of the patients on MTX showed no abnormality, signifying methotrexate's safety in the dose used.

*Conclusions* Methotrexate proved to be an efficacious and safe modality of treatment in patients of chronic eczema.

### *Key Words*

Chronic eczema, methotrexate, eczema area and severity index.

## Introduction

Eczema, also called dermatitis, is defined as an inflammatory response of the skin to endogenous and/ or exogenous stimuli.<sup>1,2</sup> It is an acute, sub-acute or chronic inflammatory dermatosis characterized by papules, vesicles, erythema, scaling, pruritus, lichenification and dyschromia.<sup>1</sup> Histopathological appearance depends on the type of eczema; spongiosis and intraepidermal clefts predominating in acute eczema and hyperkeratosis with parakeratosis

and acanthosis being the features of chronic eczema whereas the microscopic features of both acute and chronic eczemas are seen in varying degrees in sub-acute and acute exacerbation of chronic eczema.<sup>1</sup>

MTX, an anti-metabolite, is a synthetic analogue of folic acid.<sup>3,4</sup> It was initially used for hematologic malignancies.<sup>3,4</sup> It has been used recently in different nonmalignant diseases including rheumatoid arthritis, graft-versus-host disease and many skin disorders like psoriasis, dermatomyositis, systemic sclerosis, morphea, cutaneous sarcoidosis and different types of eczema.<sup>3-5</sup> The mechanism of action of MTX activity in skin diseases is due to folate

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antagonism and decreased cell proliferation, suppression of inflammatory cell chemotaxis & inhibition of monocytic/ macrophage activation and lymphocytic function.<sup>3,6-8</sup>

Chronic eczema results in loss of working hours, morbidity and psychological complications leading to a severe impact on quality of life.<sup>9,10</sup> Treatment of chronic eczema often poses a considerable challenge to the dermatologist and the patients often fail to respond to conventional therapies, making their lives miserable. Hence, the present study was planned to find out the efficacy and safety of low dose MTX in recalcitrant eczema.

### Patients and methods

This was an open clinical trial (quasi-experimental study) carried out in the Department of Dermatology Unit-I, King Edward Medical University/ Mayo Hospital, Lahore, during the period from April, 2005 to April, 2006. Sixty patients of either sex, 18 to 65 years of age, with chronic eczema, were enrolled. Those patients were excluded from the study who had been on oral steroids or other eczema modifying drugs, mentally handicapped or patients who had co-morbidity. Those patients in whom the use of MTX was relatively or absolutely contraindicated, like pregnant & lactating females, were also excluded from the study.

After informed consent, a detailed history and complete clinical examination, with type & severity of eczema, was recorded in a proforma using EASI score. The four main anatomic sites were assessed: head (h), upper extremities (u), trunk (t) and lower extremities (l), roughly corresponding to 10%, 20%, 30% and 40% of body surface area, respectively. These percentages were converted into fractions of one

i.e. 10% corresponding to 0.1, 20% corresponding to 0.2, 30% corresponding to 0.3 and 40% corresponding to 0.4 and then these figures were applied in the following formula for the calculation of EASI score:

$$\text{EASI} = 0.1 \{ \text{erythema}(E)_h + \text{induration}(I)_h + \text{oedema}(O)_h + \text{papulation}(P)_h + \text{excoriation}(Ex)_h + \text{lichenification}(L)_h \} \text{area}(A)_h + 0.2 \{ E_u + I_u / O_u / P_u + Ex_u + L_u \} A_u + 0.3 \{ E_t + I_t / O_t / P_t + Ex_t + L_t \} A_t + 0.4 \{ E_l + I_l / O_l / P_l + Ex_l + L_l \} A_l$$

E, I, O, P, Ex, and L are assessed according to a 3-point scale where 0=no symptoms, 1=slight, 2=moderate, 3=marked. *A* is assigned a numerical value based on the extent of lesions in a given anatomic site: 1=<10%, 2=10-29%, 3=30-49%, 4=50-69%, 5=70-89% and 6=90-100%.

The patients in the study group were administered 0.1 mg/kg body weight of methotrexate once weekly for three months. Patients of control group were given placebo in the form of folic acid, 5 mg tablets once daily for three months. Patients in both, study and control groups, were thoroughly counselled regarding their disease and management. On each follow up, clinical and laboratory evaluation of the patients was undertaken in order to assess the safety of methotrexate.

Efficacy was measured by comparing EASI score before treatment with EASI score after treatment in the study and control groups. A reduction of 50% or more in the EASI score at the end of three month period was considered as significant improvement and an effective treatment. SPSS windows software version 13 was used for statistical analysis. Since some of the outcome measures were of qualitative nature, chi square test was applied and student t test was used for quantitative values.

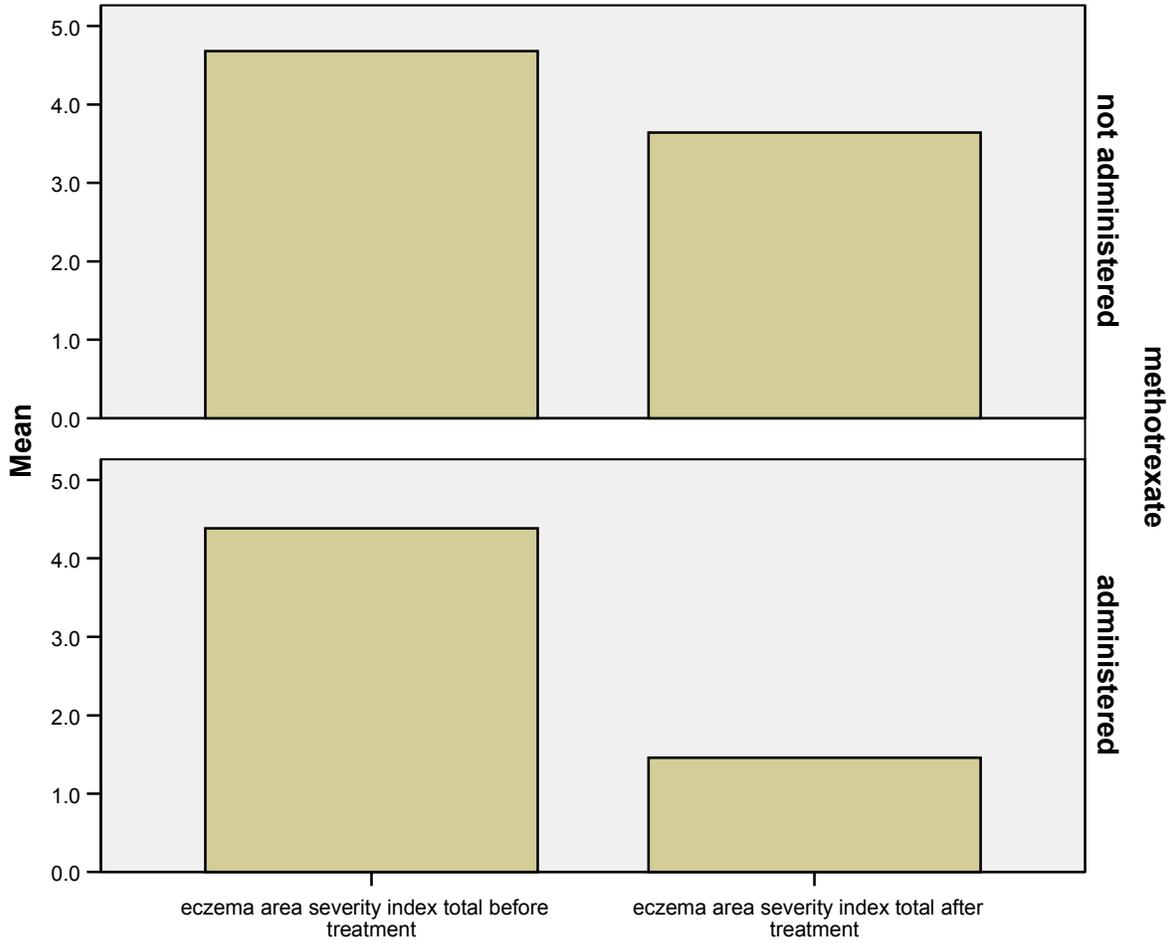


Figure 1 Eczema Area & Severity Index before and after treatment.

## Results

A total of 60 patients were enrolled in the study, out of which 30 patients were in the study group and 30 in the control group. All the patients were evaluable as no one dropped out from the study. There were 41 males and 19 females, suffering from chronic eczema of more than 3 months duration. The male to female ratio was 2.2:1. The age range noted was 18-65 years with a mean of 42.2 years. The age was less than 30 years in 12 patients, 30-50 years in 34 patients and more than 50 years in 14 cases. The difference between the mean ages in both groups (study and control) was statistically insignificant ( $p>0.05$ ). It was seen in our study that gender &

age group had no role to play in the improvement or otherwise of eczema i.e. they were not the confounding variables.

Forty percent of the patients were suffering from atopic dermatitis. Allergic contact dermatitis of hands due to cement exposure was seen in 15%, air-borne contact dermatitis in 13.3%, pompholyx in 11.7%, seborrhoeic dermatitis in 8.3%, lichen simplex chronicus in 5%, contact dermatitis to paraphenylenediamine and discoid eczema in 3.3% each. Methotrexate was given in a dose of 7.5 mg to 53.4 % of patients while 6.25 mg in 33.4% and 5 mg in 13.2% of cases once weekly.

The mean EASI score before treatment in both study and control groups was nearly the same. The decrease in EASI score after treatment in the study group was noted and compared with that of control group (a mean decrease of 68.16 in the study group while 21.4 in the control group) [Figure 1]. The difference was 46.7%, which was quite significant ( $p < 0.0001$ ). So, all the study group patients had a reduction of 50% or more in EASI score which was considered as effective treatment whereas none in the control group had 50% or more reduction in EASI score. Our results also showed that type of eczema had no influence on the efficacy status of methotrexate.

None of the patients in the study group reported any side effects and the clinical & laboratory evaluation of these patients showed no abnormality; thus signifying safety of methotrexate in the dose used.

## **Discussion**

The role of MTX in treating various types of eczema has already been established by many studies.<sup>3-5,11-13</sup> The present study was the first one which included sixty patients and had a control group receiving placebo to evaluate the efficacy and safety of low dose methotrexate for recalcitrant eczema. This study included patients with atopic eczema, allergic contact dermatitis, idiopathic pompholyx, seborrhoeic eczema and lichen simplex chronicus. Each of the above mentioned eczemas differ in the etio-pathogenesis, triggering & aggravating factors but have a similar final step in the outcome i.e. there is an inflammatory response of the skin to various endogenous and/ or exogenous factors & that is where methotrexate has its major action i.e. blocking the inflammatory cascade, which was clearly shown in our study. The present study also revealed that the type of eczema had

no influence on the efficacy status of the drug used for treatment, similar to other studies.<sup>1,2</sup>

Most of our patients were in the 30-50 years age group, similar to the trend seen worldwide.<sup>2,14</sup> A greater preponderance of males was observed as compared to females. This is again similar to an international studies.<sup>2,14</sup> and can be attributed to the fact that males are more prone to get this disease due to irritants, chemical and other allergens in their various occupational environments. All the study group patients had more than 50 % reduction in EASI score which was considered as effective treatment and the maximum reduction in EASI score was 81.8%. However, complete remission was not seen in any case. This shows that although MTX was able to reduce the severity of disease but it failed to completely resolve the eczema in the 3 months of treatment which also correlates with other international studies.<sup>6,11-13</sup> On the other hand, simple measures like avoidance of triggering and aggravating factors, led to a mean reduction of EASI score of 21.4% in the control group patients, which clearly shows the significance of such factors in the final outcome of management of eczema, similar to other studies.<sup>1,2,14,15</sup> Regarding the safety profile, no side-effects were reported and the results of relevant investigations remained in the normal range, showing the safety of drug in the dose used which is in accordance with the results of other studies.<sup>12,13</sup>

The results of our study confirm the efficacy of low dose methotrexate in mild to moderate chronic eczema. However, more randomized controlled trials are needed in order to assess the efficacy and safety of MTX in various types of chronic eczema with a longer follow-up period.

## Conclusion

Methotrexate in a low dose is an effective and safe therapy in patients of chronic, recalcitrant eczema.

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