Efficacy and Safety of Methotrexate in chronic actinic dermatitis. A pilot study

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Abstract.

Objectives. Efficacy and safety of methotrexate in Chronic Actinic Dermatitis.

Methods. Thirty patients clinically and biopsy proven cases of chronic actinic dermatitis were included in study after fulfilling the inclusion criteria. Patients given methotrexate according to protocol and efficacy was noted according to improvement in PASI score.

Results. Thirty patients, 27 male and 3 females, with a mean age of 57.5 years, were studied. Skin type 3 was observed in 10 pts type 4 in 14 patients and type5 in 6 patients. Duration of disease was <1 yr in 5 pts, 2-5 yr in 14 pt, 6-10 yr in 8 patients and >10 yr in 6 pts.

Twenty seven patients received 10mg and 3 patients received dose of 15mg.Thirty patients completed 6 months of methotrexate therapy. One patient stopped treatment because of mild gastrointestinal side effects and deranged LFTs. SGPT was 3 time above normal when treatment was stopped. Patients were evaluated at 3,4 and 6 months, 20%(6) showed complete recovery, 43%(13) showed 50-75% recovery , 23%(7 showed 25-49% recovery. Rest showed no improvement. Five males and one female showed complete recovery.

Means of initial and final PASI showed significant results with P value of .000. {Fig 1}

Regarding skin types 4 patients with skin type 3 and 2 patients with skin type 2 showed full recoveries.

The clinical response was evident at 4-6 wks and was the maximum at 4-6 months.

Conclusion.

Although no definite conclusion can be derived from the present study due to its limitations but we found methotrexate to be a potentially efficacious and safe drug in the treatment and steroid sparing drug in chronic actinic dermatitis. Larger studies with follow up for long time will confirm its efficacy

Key words. Chronic actinic dermatitis, efficacy, safety, methotrexate, PASI.

Introduction:

Chronic actinic dermatitis is an idiopathic photosensitive chronic dermatosis primarily induced by ultraviolet B (UVB) and less frequently by ultraviolet A (UVA) and visible light1.

It is characterized by a persistent eczematous eruption on exposed skin, occasionally associated with infiltrated papules and plaques.[2] Chronic actinic dermatitis has a worldwide incidence and has been reported in Asia, Africa, Europe and America with increased cases in the summer time when sun exposure is the greatest [1, 3]. It affects all skin types[1].The mean age of onset ranges between 36 to 63 years and more common in outdoor workers.[2]

The disease runs a chronic course, impairing the quality of life.

Diagnosis is based on clinical, histopathological and photobiologic features[4].

Rarely it has a tendency for erythroderma (exfoliative dermatitis) [5].

Treatment consists of patient education (avoidance of sunlight and adequate sun protection), topical corticosteroids, and emollients. Topical/systemic steroids are the mainstay of therapy but continuous use over a prolonged period often leads to major side effects[6].

When these measures are insufficient alone, systemic immunosuppressants may be considered. A mostly steroid sparing agent, including Azathioprine and Cyclosporine has been used to treat the condition with variable results[3]. Highlighting the need for another effective and cheap therapeutic tool.

Methotrexate has been used in difficult to treat cases of chronic actinic dermatitis[7]. It is an antimetabolite and causes immunosuppression by inhibiting lymphocytes[7].It is cheap, has a good safety profile and easy to monitor for side effects. It also has a rapid onset of action providing rapid induction of improvement[7].Moreover dermatologists are familiar with methotrexate use in lot other dermatosis but not much literature exists on its efficacy in chronic actinic dermatitis.

The rationale of my study is to validate the efficacy and safety of methotrexate in chronic actinic dermatitis in our local population and if found to be effective the results will be shared with other dermatologists and recommendations will be given so that the patients are treated efficiently and effectively in short period of time. Moreover it is cheap and is found effective therapy in variety of dermatosis.

Objective: Efficacy and safety of methotrexate in Chronic Actinic Dermatitis.

Operational Definitions:

Chronic actinic dermatitis: a photosensitivity disorder defined clinically by persistent eczematous eruption of 3 months or greater duration primarily on sun exposed parts and confirmed histological by a dermal infiltrate composed of lymphocytes and macrophages.

Methotrexate: Antimetabolite agent with anti-inflammatory and immunosuppressive effect used in various dermatological conditions.

Efficacy: Clearance of leions above 25% of initial lesion.

Safety: It will be measured in terms of side effects.

Materials and Methods

Study Design: Pilot Study

Settings: Dermatology Department, Lady Reading Hospital Peshawar.

Duration of Study: Six months

Sample size: Thirty patients

Sampling Technique: Non Probability Consecutive Sampling

Inclusion Criteria

Clinically and biopsy proven cases of chronic actinic dermatitis.

Any gender

All ages

Fitzpatrick skin type. All skin types

Exclusion criteria:

Pregnant and lactating women

Any patient having history of chronic active infection or sensitivity to methotrexate will be excluded.

Patients who were on any drug likely to influence the eczema were not enrolled.

Patients who are immunocompromised or have liver or renal disease or an abnormal complete blood count.

Those treated prior with any other steroid sparing agent.

These factors are confounders and will make the study biased if included.

Those patients who are currently taking oral steroids or in last month were excluded.

Complete hemogram, hepatic and renal function tests, chest X-ray and urinalysis were carried out.

The clinical severity was evaluated visually using erythema, induration and scaling using PASI score[5]. Photograps were taken initially and on each visit. Initial PASI was calculated. Follow up was done on first week and then monthly for 6 months. The observer was same each time for each case. Improvement was noted on every visit and was graded according to PASI score as,

75-100% as excellent

50-74 % as Good

25-49% as Fair

0-24 % poor

End point of study was complete clearance of Lesion.

Patients were given 10 mg/wk along with Sun protection measure and sun blocks were advised. Oral antihistamines were given. Dose of Methotrexate was increased to 15mg/wk if less than 20 % improvement was observed after 4-5 weeks. The dose was gradually tapered after near or complete clearance was obtained i.e. more than 75% reduction in score.

Data collection and procedure: The study was conducted after getting approval from the hospital ethical and research committee. All patients meeting the inclusion criteria were included in the study through OPD. A detailed history, physical examination and laboratory investigations were carried out for every patient. The purpose and benefits of the study were explained to the patients and they were assured that the study was done purely for data publication and research purpose and a written informed consent was obtained.

DATA ANALYSIS.

Data was analyzed in SPSS version 20. Mean SD was calculated for numerical variables like age, duration, Frequencies and percentages were calculated for categorical variables like gender, Fitzpatrick skin type and efficacy. Efficacy was stratified among age, gender, Fitzpatrick skin type, duration of symptoms to see the effect modification. Results were presented in the form of tables, graphs and charts.

Results

Thirty patients, 27 male and 3 females, with a mean age of 57.5 years , were studied. Skin type 3 was observed in 10 pts type 4 in 14 patients and type5 in 6 patients. Duration of disease was <1 yr in 5 pts, 2-5 yr in 14 pt, 6-10 yr in 8 patients and >10 yr in 6 pts.

All patients had been treated with methotrexate at doses in the range of 10-15 mg. Twenty seven patients received 10mg and 3 patients received dose of 15mg.Thirty patients

completed 6 months of methotrexate therapy. 1 patients stopped treatment because of mild gastrointestinal side effects and deranged LFTs. SGPT was 3 time above normal when treatment was stopped. Patients were evaluated at 3,4 and 6 months, 20%(6) showed complete recovery, 43%(13) showed 50-75% recovery , 23%(7 showed 25-49% recovery. Rest showed no improvement. Five males and one female showed complete recovery.

Among 30 patients 23 patients received 10mg methotrexate and 7 patients received 15mg of methotrexate. Among six patients with complete recovery 4 patients received 10mg of MXT and 2 patients receive 15 mg. There was one patient who showed poor response inspite of using 15mg of methotrexate.

Means of intial and final PASI showed significant results with P value of .000. {Fig 1}

Regarding skin types 4 patients with skin type 3 and 2 patients with skin type 2 showed full recoveries.

The clinical response was evident at 4-6 wks and was the maximum at 4-6 months.

Discussion

Methotrexate is antimetabolites that act on proliferating T and B cells which are more sensitive than nonimmune cells to the depletion of purines and pyrimidines.[8] Methotrexate provides rapid induction of improvement. Hence, administering methotrexate will give rapid cheap and effective treatment in chronic actinic dermatitis.

Bareham *et al.* experimentally proved the synergistic action of azathioprine-methotrexate combination[9]. He suggested that interaction of azathioprine and methotrexate is synergistic if azathioprine is given before methotrexate but additive if azathioprine is given after methotrexate. Keeping above facts in mind study was conducted on efficacy of methotrexate in chronic actinic dermatitis.

The drug was well-tolerated, and no serious side effects were noted. The frequency of gastrointestinal side effects, particularly nausea and vomiting, which resulted in withdrawal of one of our subjects, represents a drawback of this treatment.

Although, the changes in liver enzymes observed in this study did not give rise to serious concern in any individual, the frequency of changes was sufficient to indicate that these require monitoring when methotrexate is used.

Results of deranged LFTs in our study were comparable with study by J.Barke which showed similar fiqure.[10]

The data here support that Methotrexate can be an effective and useful drug in the management of chronic actinic dermatitis . It can provide an answer to this chronic and socially disabling condition provided that it is used judiciously and the treatment is carefully monitored.

As the number of patients was limited as it was pilot study, therefore, more studies are required to be done in the evaluation of this potentially beneficial drug in the treatment of chronic actinic dermatitis.

Conclusion

Although no definite conclusion can be derived from the present study due to its limitations but we found methotrexate to be a potentially efficacious and safe drug in the treatment and steroid sparing drug in chronic actinic dermatitis. Larger studies with follow up for long time will confirm its efficacy

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One-Sample Statistics

	N	Mean	Std. Deviation	Std. Error Mean
initialpasi	30	26.6000	8.04127	1.46813
finalpasi	30	11.9000	5.00586	.91394

One-Sample Test

	Test Value = 0					
					95% Confidence Interval of the Difference	
	t	df	Sig. (2-tailed)	Mean Difference	Lower	Upper
initialpasi	18.118	29	.000	26.60000	23.5973	29.6027
finalpasi	13.021	29	.000	11.90000	10.0308	13.7692

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