Efficacy and Safety of Methotrexate in Chronic Actinic Dermatitis: A Pilot Study

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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 light. It is characterized by a persistent eczematous eruption on exposed skin, occasionally associated with infiltrated papules and plaques. 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. It affects all skin types. The mean age of onset ranges between 36 to 63 years and is more common in outdoor workers.

The disease runs a chronic course, impairing the quality of life. Diagnosis is based on clinical, histopathological and photobiologic features. Rarely it has a tendency for erythroderma (exfoliative dermatitis). Treatment consists of patient education (avoidance of sunlight and adequate sun protection), topical corticosteroids and emollients. Topical/systemic steroids are the mainstay of therapy however their prolong use results in side effects.

When these measures are insufficient alone, systemic immunosuppressants may be considered. Mostly steroid sparing agents, including Azathioprine and Cyclosporine has been used to treat the condition with variable results. Hence there is a need for another effective and cheap therapeutic tool.

Methotrexate has been used in difficult to treat cases of chronic actinic dermatitis. It is an antimetabolite and causes immunosuppression by inhibiting lymphocytes. 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. Moreover dermatologists are familiar with methotrexate use in lot other dermatosis. However literature on its efficacy in chronic actinic dermatitis is lacking.

The rationale of this pilot study is to validate the efficacy and safety of methotrexate in chronic actinic dermatitis in our local population and if found effective, the results will be shared with other dermatologists and recommendations will be given so that the patients are treated effectively.

METHODS

This pilot study was conducted at Department of Dermatology, Medical Teaching Institute Lady Reading Hospital, Peshawar, Pakistan for six months from 1st March 2017 to 31st August 2017. Thirty patients were included in the study and the sampling technique was non-probability consecutive sampling.

The study was carried out after approval from the hospital ethical and research committee. All patients meeting the inclusion criteria were included in the study through OPD. Written informed consent was taken from all patients participating in the study. A detailed history, physical examination and laboratory investigations were carried out for every patient.

Inclusion criteria for the study was: clinically and biopsy proven cases of chronic actinic dermatitis of any gender and age. All skin types (Fitzpatrick) were included in the study.
Pregnant and lactating women were excluded to prevent teratogenic effects of methotrexate and side effects in neonate as it is secreted in milk. Any patient having history of chronic active infection or sensitivity to methotrexate was excluded to prevent immune-suppression. Patients who were on any drug likely to influence the eczema, immune-compromised or have liver or renal disease or an abnormal complete blood count were also excluded to prevent further immune-suppression and alteration in liver and renal functions. Those patients treated prior with any other steroid sparing agent, patients who are currently taking oral steroids or in last month were also excluded from the study.

Complete blood examination, hemoglobin, total leukocyte count, liver and renal function tests, chest X-ray and urinalysis were performed.

The clinical severity was evaluated visually using erythema, induration and scaling using Psoriasis Area and Severity Index (PASI) score. Photographs 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 observed on every visit and was graded according to PASI score.

A response to 75-100% was considered excellent, 50-74% as good, 25-49% as fair and 0-24% as poor.

End point of study was complete clearance of lesion. Patients were continued on maintenance therapy after clearance of lesion. Patients were given 10mg/week 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 keeping eye on side effects.

Analysis of data was done using SPSS version 20 and 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

Thirty patients, 27 males and 3 females, with a mean age of 57.5±9.91 years were included in the study. Skin type 3 was observed in 10 patients, type 4 in 14 patients and type 5 in 6 patients. Duration of disease was <1 year in 5 patients, 2-5 years in 14 patients, 6-10 years in 8 patients and >10 years in 6 patients.

All patients in study were treated with methotrexate at a dose ranging from 10-15 mg. Twenty seven patients received 10mg and 3 patients received dose of 15mg. Twenty nine patients completed 6 months of methotrexate therapy. One patient stopped treatment because of mild gastrointestinal side effects and deranged liver function tests (LFTs). Serum glutamic pyruvic transaminase (SGPT) was 3 times above normal when treatment was stopped. Patients were evaluated at 1st week, then at 4th week and then monthly for 6 months. Six (20%) showed complete recovery, 13 (43%) showed 50-75% recovery, 7 (23%) showed 25-49% recovery while rest showed no improvement. Five males and a female showed complete recovery.

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

Means of initial and final PASI score showed significant results with P value of 0.000 (Table I).

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 weeks and was the maximum at 4-6 months.

DISCUSSION

Methotrexate is an antimitabolite that acts on proliferating T and B cells that are more sensitive than non-immune cells to the depletion of purines and pyrimidines. Methotrexate provides rapid induction of improvement. Hence, administering methotrexate will give rapid cheap and effective treatment in chronic actinic dermatitis. Bareham CR, et al. experimentally proved the synergistic action of azathioprine-methotrexate combination. 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.

Results of deranged LFTs in our study i.e. 10% were comparable with study by Salliot C and van der Heidje D, which showed 13% of raised LFTs. Two patients at a dose of 10mg while three patient at a dose of 15 mg showed side effects.

Methotrexate can induce variety of gastrointestinal side effects, vomiting, diarrohea and abdominal pain. These can occur with low or high doses of methotrexate. Hepatotoxicity is a sequel of long term use of methotrexate. An elevation in aminotransferases was observed in 7.5 to 26 percent of patients on long term treatment of rheumatoid arthritis and psoriatic arthritis patients with methotrexate. These observations are in accordance with side effects profile of methotrexate observed in our study. Hematological toxicity is rare with low dose of methotrexate. Prevalence of hematological toxicity is 3% among patients of rheumatoid
arthritis treated with methotrexate and incidence of pancytopenia is 1.4%. Hematological abnormalities were not observed in our patients. This may be due to the fact that small number of patients in our study.

CONCLUSION

The data here support that methotrexate can be an effective and useful drug in the management of chronic actinic dermatitis. It can provide a cure to this chronic disabling condition.

LIMITATIONS

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

REFERENCES


AUTHORS’ CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

MMP: Concept, acquisition of data, drafting the manuscript, critical review, final approval of the version to be published.

SMN: Study design, acquisition of data, final approval of the version to be published.

IU: Acquisition of data, final approval of the version to be published.

GU: Acquisition, analysis & interpretation of data, final approval of the version to be published.

AQK: Drafting the manuscript, final approval of the version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE

NIL

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