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METHOTREXATE IN ALLERGIC CONTACT DERMATITIS: A RETROSPECTIVE CASE SERIES

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Abstract

Background: Methotrexate (MTX), a folate antimetabolite, is currently approved for and the majority of the currently available data delves into its application in psoriasis and atopic dermatitis, leaving its potential in allergic contact dermatitis (ACD) grossly understudied barring a few case series and studies showing promising results.

Objective: To evaluate the efficacy and tolerability of methotrexate in treating allergic contact dermatitis.

Methods: We performed a retrospective chart review of 14 patients who were diagnosed clinically and a positive patch test with allergic contact dermatitis and started on methotrexate therapy. Out of these, 4 patients were lost to follow up and a single patient had to discontinue methotrexate due to decrease in blood hemoglobin levels. Out of the 14 patients, 9 completed 3 months of methotrexate therapy and were evaluated. Demographic and treatment-associated data were collected from the medical records managed at the dermatology department of tertiary care centre.

Results: In the nine patients evaluated, the mean improvement of Eczema Area Severity Index (EASI) score was 72.23%. One patient achieved >90% improvement, while five others showed >70% reduction in EASI. The least response (45.63%) was noted in a patient with an 8-year disease history treated with 7.5 mg/week MTX. MTX was well tolerated in the majority; one patient discontinued therapy due to anaemia and was excluded from the evaluation.

Conclusion: Methotrexate is a relatively well-tolerated and effective treatment for allergic contact dermatitis with robust efficacy.

Keywords: allergic contact dermatitis, contact dermatitis, methotrexate

Introduction

Allergic Contact Dermatitis is a common, often chronic, contact dermatitis (CD) with many clinical presentations. It is a T-cell mediated type IV (delayed type) hypersensitivity response to the exposure to haptens in sensitized individuals. The reaction develops in two phases, sensitization and elicitation phases. Presenting as pruritic, erythematous papules, vesicles and/or plaques initially limited to the site of initial exposure. Later on, it can auto-eczematize to other distant cutaneous sites as well.

Identification of the involved allergens, although important, is often unidentifiable and in many cases unavoidable.[1] Due to the debilitating nature of the disease and its significant impact on the patient's quality of life, a combination of symptomatic and immunosuppressive therapy is often required for the pharmacological control of the disease. These include corticosteroids, immunomodulators, antihistamines and emollients. Although corticosteroids are most widely studied and the mainstay of the treatment, various immunomodulators such as azathioprine, mycophenolate mofetil, INF-γ antagonists such as cyclosporine and PUVA has been used. However, there are not enough reports on the use of methotrexate with no clinical trial reported as of yet.

Material and methods

This was a retrospective case series of fourteen proven cases of allergic contact dermatitis treated at a tertiary care hospital with regular follow-ups up to 3 months since initiation during a period of 10 months from May 2024 to February 2025. Patient details in history and investigations including complete blood counts, liver function tests, renal function tests, chest x-ray, Mantoux test, routine urine microscopy and serological investigations for hepatitis B, hepatitis C, HIV and VDRL were performed as a baseline. Complete blood counts, liver and renal function tests were repeated in every subsequent follow-up at one week followed by twice weekly and monthly follow-ups. The severity of the disease was evaluated using Eczema Area Severity Index (EASI) at each month and added to the records.[2] The patients in this study were patch tested with the Indian Standard Series (ISS) Battery with 20 allergens approved by the Contact & Occupational Dermatoses Forum of India (CODFI).[3] Along with MTX, short course oral steroid for initial flare-up, topical steroids of appropriate potency, oral Folic Acid supplementation, and oral antihistaminic for symptomatic management were provided to the patients. Treatment response was observed by clearance of lesions, reduction in EASI scores and along with any adverse effect that were recorded.

Results

This series includes 14 patients who were clinically diagnosed with allergic contact dermatitis. Out of these, 4 patients were lost to follow up and a single patient had to discontinue methotrexate due to decrease in blood hemoglobin levels. The remaining 9 patients who were completed 3 month of methotrexate, evaluated in this case series. The mean age of the cases was 56 and the mean duration of the disease was 4.58 years. MTX was given at a weekly dose of 5, 7.5 or 10mg depending upon clinical judgment.

Among the cases, the average initial EASI was 15.64 while the mean EASI at the end of 3 months of therapy was 3.91 with a mean percentage of improvement being 72.23%. A single patient observed an improvement of EASI more than 90% while 5 out of the remaining 8 patients observed over 70% improvement of the scores. Least response was observed in a case of a 61 year male with a disease course of 8 years treated by 7.5 mg/week MTX with 45.63% improvement of the EASI. (Table 1) (Figure 1-2)

Out of the 10 patients that continued to follow up, majority of the patients observed no significant side effects relevant to MTX therapy with a single patient having to discontinue the therapy due to reduction in hemoglobin (10.6 mg/dL to 6.8 mg/dL) and were shifted on alternate therapy and referred to a physician for management of the same.

Legends for table

Table 1: Demographic and clinical characteristics of the study patient

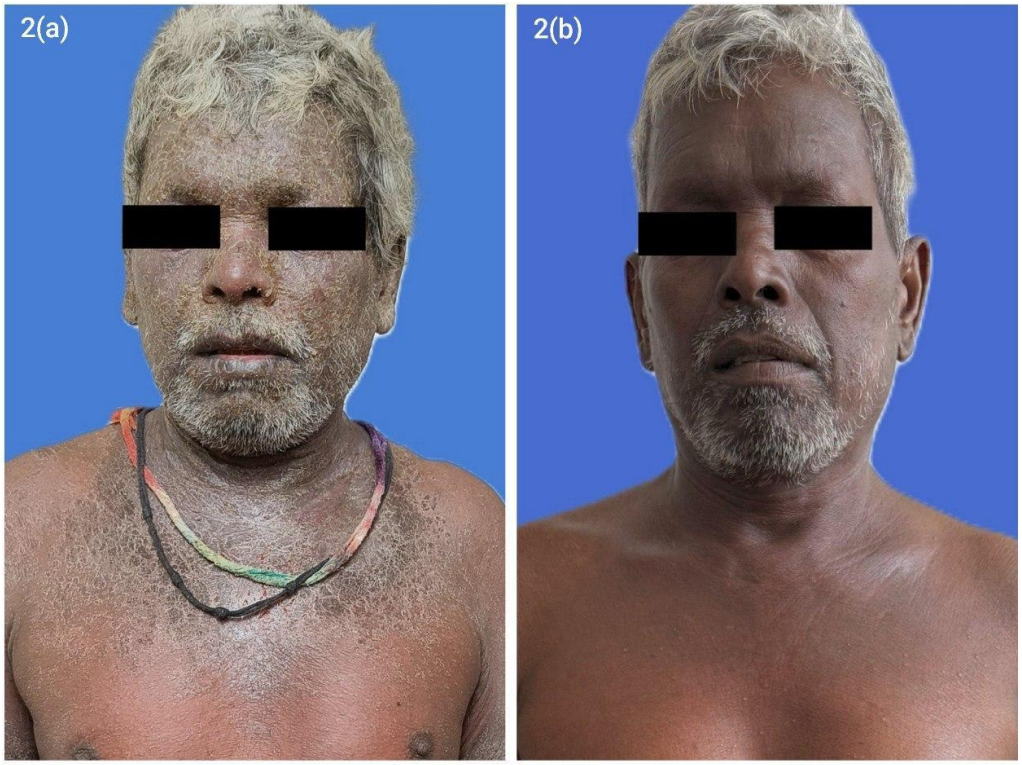
Serial No.	Age in years/Sex	Disease duration	Dose given	EASI		Improvement	Adverse Effects
				Before Treatment	Month 3		
1	42/M	3 months	5 mg/week	9.6	2.5	73.95%	No singnificant s/e
2	58/M	6 years	7.5 mg/week	16.3	4.5	72.39%	No singnificant s/e
3	81/M	2 years	5 mg/week	13.8	5.4	60.86%	No singnificant s/e
4	58/M	6 years	7.5 mg/week	30.9	2.3	92.56%	No singnificant s/e
5	70/M	20 years	10 mg/week	25.1	3.9	84.46%	No singnificant s/e
6	56/M	2 years	7.5 mg/week	17.8	8	55.10%	No singnificant s/e

7	35/F	6 months	5 mg/week	9.4	1.8	80.85%	No singnificant s/e
8	61/M	8 years	7.5 mg/week	10.3	5.6	45.63%	No singnificant s/e
9	43/F	2 years	5 mg/week	7.6	1.2	84.21%	No singnificant s/e

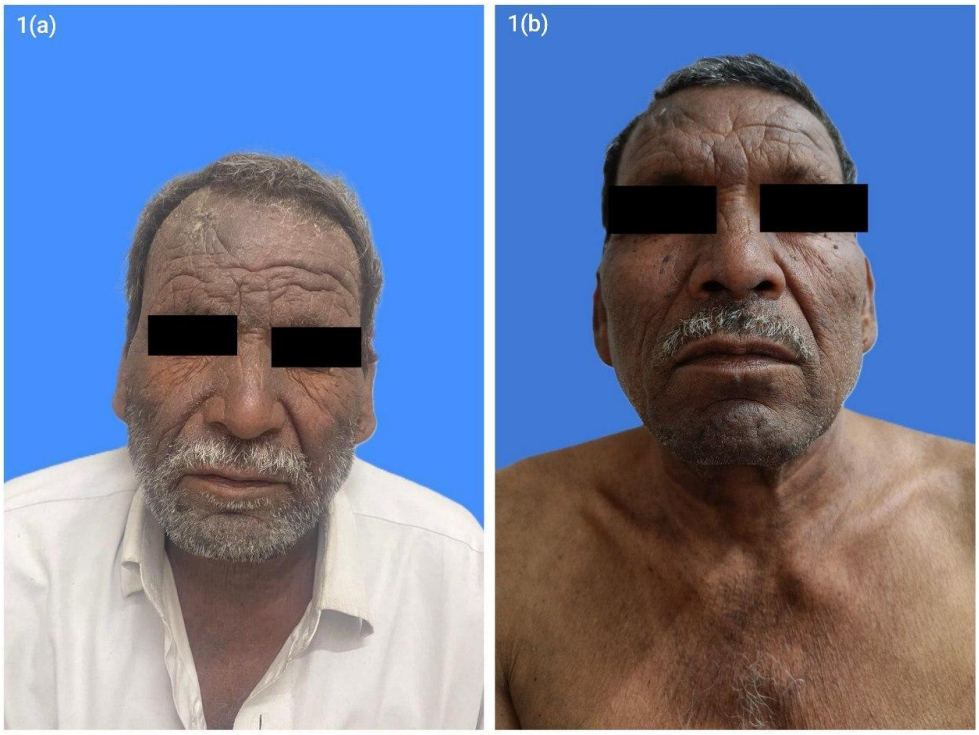
EASI = Eczema Area & Severity Index; s/e = side effects

Legends for Figures

Figure 1-2: Allergic contact dermatitis- before and after treatment



1(a) before treatment 1(b) after treatment (at 3month)



2(a) before treatment 2(b) after treatment (at 3month)

Discussion

Methotrexate (MTX) is one of the most commonly used oral immunosuppressive agents used in dermatology with a long history of safety and efficacy. Methotrexate is a folic acid analogue currently approved by the Food and Drug Administration (FDA) for the treatment of neoplastic diseases (cutaneous T-cell lymphoma and leukaemia), psoriasis, and rheumatoid arthritis.[4] It acts via various mechanisms of action including inhibition of DNA synthesis, inhibition of proliferation of lymphoid cells and migration of T-cells and adenosine mediated anti-inflammatory effects.[4] It functions by inhibiting purine and pyrimidine synthesis of DNA in rapidly dividing cells.[5,6] There is also evidence that it inhibits the migration of T cells to certain tissue locations and induces an anti-inflammatory effect by increasing adenosine production.[5,7]

There are very few reports on the use of methotrexate in allergic contact dermatitis, and there have been no controlled clinical trials on its use in this setting. Ashaki Patel et al. (2017) noted that MTX is a well-tolerated and effective treatment for ACD showing excellent efficacy despite persistent allergen exposure.[8] Handa et al. showed that methotrexate is as efficacious as azathioprine in the treatment of Parthenium hysterophorus allergic contact dermatitis, but with a shorter treatment time.[9] Additionally, methotrexate maybe useful in treating severe P. hysterophorus dermatitis that is unresponsive to conventional treatment.[10,11] Sharma published the results of 16 patients treated with methotrexate who were diagnosed with Parthenium dermatitis, confirmed by patch or photopatch testing and refractory to treatment with potent topical corticosteroids. Patients received methotrexate 15 mg/week with folic acid 5 mg/daily. Only seven patients followed up for 6 months out of which six noted an early improvement with a decrease in disease severity after 1 month.[11]

Atopic dermatitis patients treated with methotrexate showed a significant improvement of 42 % in SCORAD at 12 weeks, whereas patients treated with azathioprine showed a 39 % improvement.[12] However, patients on azathioprine experienced more adverse events, including gastrointestinal events, abnormalities in blood counts, and increased liver enzymes.[13] Garritsen et al. also showed that azathioprine was more likely than methotrexate to cause influenza-like symptoms, pancytopenia, and liver dysfunction.[14]

Our study demonstrated that MTX (5–10 mg/week) can significantly reduce disease severity in patients with chronic allergic contact dermatitis, with a mean EASI improvement of 72.23% over three months. MTX was generally well tolerated. Only one patient discontinued therapy due to a significant drop in haemoglobin. No hepatotoxicity or gastrointestinal disturbances were reported, suggesting good tolerability in this small sample size.

The limitation of this case series is the retrospective nature and the limited number of patients involved in this study. The number of cases reviewed is small, and specific to a demographic area. Therefore, these data cannot be easily generalized. The retrospective nature of this study means that it cannot fully evaluate the full potential of methotrexate as a treatment method in various subsets of allergic contact dermatitis. Moreover, owing to the retrospective nature of this study, there was no standardized dosage of methotrexate or definition of partial or complete response.

There are only few studies are present as of now that describe the use of methotrexate in patients of allergic contact dermatitis with no clinical trials done as of yet. With promise showed in the use of the drug in patients with persistent allergen exposure and the challenges that are involved in the avoidance of occupational exposure to these allergens. MTX appears to be a cost effective and viable potential alternative to the conventional treatments hence, the need for further research on its application in the disease is required.

Conclusion

Methotrexate is beneficial for the treatment of allergic contact dermatitis. Although research on its use in this case scenario is severely limited, it is an extensively studied drug with regards to its efficacy and safety. Its familiarity and promising results in this case series hint towards the feasibility of employing it as a mainstay treatment for moderate-severe cases of ACD which further demands more future studies, especially comparing it with other conventional treatment practices.

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