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Original research article

METHOTREXATE IN THE MANAGEMENT OF MODERATE TO SEVERE ATOPIC DERMATITIS

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Abstract: *The retrospective study was conducted in the Department of Dermatology from June 2021 to June 2022 to analyze the complication profile, adverse effects, and efficacy of methotrexate in patients with moderate to severe AD. The patients with moderate to severe AD were included in the study. The demographic data, clinical records, and response to MTX were analyzed. The clinical response was assessed as a decrease in itching, improvement in skin lesions, lesser use of topical CS, and assessment by the dermatologist. During the treatment, the patient's renal function, liver function, and complete blood count were assessed every month for three months. The study was conducted on 40 patients (17 female, 23 male). The mean starting dose was 13.8mg. The mean maintenance dose was 17.8 mg. The dose was gradually tapered after control of symptoms. 28 (70%) patients had clear responses, 7 (17.5%) had excellent, 3 (7.5%) had good, and 2(5%) patients had partial response. The mean duration of MTX therapy was 36.9 months. Due to disease control, MTX was discontinued in 8 (17.5%) patients. 4 (10%) patients remained clear, and treatment was restarted in 3 (7.5%) patients due to flare. Thirty-two patients were still on treatment at the time of the study. Nausea occurred in 4(10%) patients, fatigue in 3 (7.5%) and a transient increase in transaminases in 7 (17.5%) patients. 1 (2.5%)patient had a transient decrease in hemoglobin and platelet level; Hb was maintained at 106-120 g/L, and platelet level became normal. Methotrexate is safe and effective for the treatment of moderate to severe AD. Lower doses can control disease in the long term without posing any significant risks.*

Keywords: Atopic Dermatitis, Methotrexate, Skin inflammation

Introduction

Atopic dermatitis (AD) is an inflammatory skin disorder associated with physical, social, and psychological morbidity. Moderate to severe AD may not respond to treatment with calcineurin inhibitors or topical corticosteroids and may need second-line treatments like systemic immunosuppressants or phototherapy. As AD is a chronic disease and has varying individual prognoses, long-term therapy with systemic immunomodulatory drugs is challenging. The goal of treatment in moderate to severe AD involves stabilization of disease flares, therapeutic efficacy, and no significant adverse effect(Hernández-Martín et al., 2017).

Systemic immunomodulatory drugs like corticosteroids (CS), azathioprine, mycophenolate mofetil (MMF), methotrexate (MTX), and cyclosporine A (CsA) have been used for the treatment of moderate to severe AD. CS are effective, fast-acting drugs, but long-term use is associated with severe complications, including rebound phenomenon. Thus, CS should be used as a short-term therapy along with other non-steroid drugs for severe exacerbations. CsA is a first-line drug for short-term treatment of moderate to severe AD, which can not be treated by phototherapy and topical regimens (Patro et al., 2020; Seger et al., 2019). However, CsA does not have long-lasting efficacy and results in rapid relapse after drug withdrawal(Giavina-Bianchi and Giavina-Bianchi, 2019). A study reported a relapse rate of 22.4% to 55.8% after CsA withdrawal(Navarro-Triviño et al., 2023).

MTX was initially used for the treatment of myeloproliferative neoplasms, including lymphoma and acute leukemia. Low-dose MTX has also been used to treat various immune-related and inflammatory diseases. Studies show that MTX has effective results in patients with moderate to severe AD(Flohr et al., 2023; Singh et al., 2021). In this study, we will analyze the complication profile, adverse effects, and efficacy of methotrexate in patients with moderate to severe AD.

Methodology

The retrospective study was conducted in the Department of Dermatology from June 2021 to June 2022. The patients with moderate to severe AD were included in the study. The ethical review board of the hospital approved the study. The demographic data, clinical records, and response to MTX were analyzed. The clinical response was assessed as a decrease in itching, improvement in skin lesions, lesser use of topical CS, and assessment by the dermatologist. Clinical response was categorized as worsening of the condition, no response (<25%), partial (25%-50%), good (50%-75%), excellent (>75%), and clear.

These patients were clinically diagnosed with AD, which was not responsive to topical treatment or prednisone. Many patients also received systemic therapy or phototherapy.

MTX weekly doses (10 to 25 mg) were given orally or subcutaneously. Patients underwent chest x-ray, tuberculosis skin tests, and other laboratory tests before the beginning of treatment. During the treatment, the patient's renal function, liver function, and complete blood count were assessed every month for three months.

SPSS version 23.0 was used for data analysis. Data was expressed as mean (SD) or frequency and percentages.

Results

The study was conducted on 40 patients (17 female, 23 male). The mean age of the participants was 45 years. Details of previous treatments are shown in Table I. 2 (5%) patients were previously treated with MTX. The drug was stopped due to improvement in symptoms or adverse effects.

The mean starting dose was 13.8mg. The mean maintenance dose was 17.8 mg. The amount was gradually tapered after control of symptoms. 28 (70%) patients had clear responses, 7 (17.5%) had excellent, 3 (7.5%) had good, and 2(5%) patients had partial response (Table II). The mean duration of MTX therapy was 36.9 months. Patients were advised to increase the dose by 2.5-5 mg in case of flare. If disease control was achieved, the tapered maintenance dose was continued. 13 (32.5%) who had flare were prescribed antibiotics to treat secondary Staphylococcus Aureus infection. 16 (40%) patients were administered IM triamcinolone acetonide injection at least once during treatment.

At the start of MTX therapy, one patient was on a tapering dose of prednisone, one on cyclosporine, and one on valacyclovir. Due to disease control, MTX was discontinued in 8 (17.5%) patients. 4 (10%) patients remained clear, and treatment was restarted in 3 (7.5%) patients due to flare. Thirty-two patients were still on treatment at the time of the study.

Nausea occurred in 4(10%) patients, fatigue in 3 (7.5%) and transient increase in transaminases in 7 (17.5%)patients. 1 (2.5%)patient had a transient decrease in hemoglobin and platelet level; hb was maintained at 106-120 g/L, and platelet level became normal.

Table I History of treatments

Treatment	Number (%)
Phototherapy	10 (25%)
Oral corticosteroids	16 (40%)
IM triamcinolone acetonide	11 (27.5%)
Azathioprine	6 (40%)
Cyclosporine	4 (10%)
Methotrexate	2 (5%)
Antibiotics	2 (5%)
Mycophenolate mofetil	2 (5%)

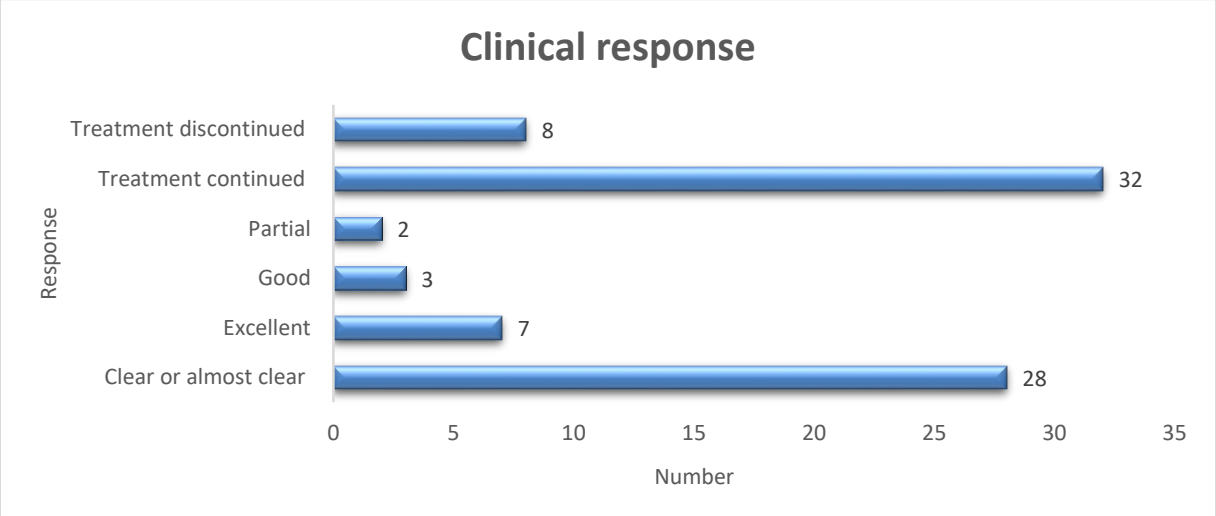

Figure 1: Clinical response of the patients

Table II Clinical response

Response	Number (%)
Clear or almost clear	28 (70%)
Excellent	7 (17.5%)
Good	3 (7.5%)
Partial	2 (5%)
Treatment continued	32 (80%)
Treatment discontinued	8 (17.5%)

Discussion

The findings of our study show that methotrexate therapy significantly improves AD and quality of life and is relatively safe. The majority of the patients had noticeable improvement. Due to disease control, MTX was discontinued in 8 (17.5%) patients. The findings show that low doses (10-25 mg) can be effective. These doses can be tapered after achieving disease control and maintained to prevent relapse. Patients showed initial signs of improvement after one month. There were minimal adverse effects. Liver fibrosis or any other serious complication was not reported in any patient. Previous studies have reported the use of methotrexate as a second-line treatment for AD. A study showed that the majority of patients with moderate to severe AD showed > 50% improvement in symptoms after MTX therapy. They gave a maximum dose of 22.5 mg until disease control(Shamim et al., 2023). Another study reported that methotrexate resulted in improved AD symptoms after two weeks with a dose of 10- 15 mg/ wk. They stated that it can be prescribed during flares and tapered after disease control(Purvis et al., 2019). A study reported that all AD patients treated with 10-20 mg MTX doses responded to the treatment after three weeks(Wollenberg et al., 2019). A previous study compared the efficacy of cyclosporine A and methotrexate. They reported that at 12 weeks, MTX resulted in a higher reduction in severity scoring for atopic dermatitis (SCORAD) score compared to cyclosporine A, though this difference was not significant(Barak Levitt et al., 2023). Another study compared the efficacy of azathioprine and MTX and reported that at 12 weeks, MTX resulted in 42% and azathioprine in a 39% reduction in symptoms(Drucker et al., 2022).

The adverse effects of MTX are mild and do not result in treatment discontinuation. Our results showed that nausea occurred in 4(10%) patients, fatigue in 3 (7.5%), and transient increase in transaminases in 7 (17.5%)patients. 1 (2.5%)patient had a temporary decrease in hemoglobin and platelet level; hb was maintained at 106-120 g/L, and platelet level became normal. A previous study also reported that MTX is safe for treating AD and did not return any significant complications (Davari et al., 2021). A study said that it could be an effective lower dose of 10-15 mg/wk(Voorberg et al., 2022), similar to the findings of our study. During early treatment, bridge therapy with triamcinolone acetonide or CS may be required along with MTX. However, these drugs are used intermittently, and short-term treatment with low doses of MTX reduces the risk of adverse effects noted with other aggressive therapies(Kimler et al., 2019).

Further studies on dose regimens, duration of remission and tapering of MTX are needed. The limitation of this study is its retrospective nature and small sample size. More extensive studies are recommended for further analysis.

Conclusion

Methotrexate is safe and effective for the treatment of moderate to severe AD. Lower doses can control disease in the long term without posing any significant risks.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.

Approved by the department Concerned.

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

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