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Review Article

Effectiveness of Methotrexate Versus Cyclosporine in the Management of Moderate to Severe Atopic Dermatitis- Meta-Analysis of Randomised Controlled Trials

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ABSTRACT

Objective: To compare the effectiveness of Methotrexate (MTX) versus Cyclosporine (CyA) in the patients of moderate to severe atopic dermatitis (AD)

Study Design: Systematic review and meta-analysis.

***Methodology*:** After formulating our research team and PICO question rationally, a search strategy and literature search were carried out as per Cochrane guidelines. Full-text articles were retrieved after title and abstract screening per our inclusion criteria. The whole search process was documented in the form of a PRISMA flow chart. Team members made and filed data extraction sheets, and qualitative data synthesis was performed. Afterwards, a meta-analysis was carried out, involving a total of 03 randomized controlled trials. Revman was used to process the continuous and dichotomous data collected for our outcomes. RoB 2 was used to assess the risk of bias in the included studies. Grade pro-GDT was used to summarize the findings in the table.

Results: Pooled results from 3 RCTs showed that CyA in a 2.5mg/kg dose is better than MTX @0.4 mg/kg/week at 12 weeks in AD. At follow-up, MTX maintains better disease control, i.e., until 24 weeks post-treatment. MTX has a better safety profile than CyA.

***Conclusion*:** MTX and CyA are both effective drugs for moderate to severe AD, but they have their pros and cons.

Keywords: Atopic dermatitis, Ciclosporin, Cyclosporine, Meta-analysis, Methotrexate.

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INTRODUCTION

Atopic eczema or dermatitis is a chronic remitting and relapsing, intensely itchy cutaneous disease with a variety of symptoms manifesting in individuals with a history of atopy in themselves or family members. Atopic spectrum includes hay fever, bronchial asthma and atopic dermatitis (AD). Having an age of onset in childhood, it affects approximately 7 to 17% of children. It may persist into adulthood in up to 60% of patients.[1] AD is one of the most common chronic dermatitis in children and adults with a prevalence of 10-20%.[2] The pathogenesis consists of complex interactions among multiple factors, i.e., susceptibility genes, environmental factors, skin barrier defects, and immunologic factors. There is a clear correlation between filaggrin gene mutations and AD. Aberrant expression of epidermal proteins caused by type 2 T-helper cells increases the risk of sensitization to allergens.[3]

Almost ten different diagnostic criteria are being used to diagnose AD. The frequency of their usage worldwide in published literature is Hanifin and Rajka criteria (41.0%), UK refinement of the Hanifin and Rajka criteria (9.0%), Japanese Dermatological Association criteria (4.2%), and American Academy of Dermatology criteria (3.8%).[4] Major features of the Hanifin and Rajka criteria include pruritus, dermatology in classical morphology and distribution, chronic/relapsing dermatitis, and personal or family history of atopy. Minor items include dry skin, Ichthyosis or Hyper linearity of palms or Keratosis pilaris, Elevated total serum IgE levels, Positive skin prick test, Early age of onset, Susceptibility to skin infections, Hand and foot eczema, Nipple eczema, Cheilitis, Frequent conjunctivitis, Dennie- morgan and few other features. [5]

There are more than 60 measurement scales to assess the intensity and extent of disease, disease progress, and skin barrier function in AD. SCORAD (SCORing Atopic Dermatitis) score, created and validated by the "European Task Force on AD" in 1993, is the most frequently used. It includes clinician assessment of AD severity and extent, along with patients' symptoms of pruritus and disturbed sleep. Eczema Area and Severity Index (EASI) and Patient-oriented Eczema Measure (POEM) are other user-

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friendly scales for clinical practice. SCORAD scores of 10-28.9 indicates mild, 29-48.9 moderate,49-103 severe atopic eczema.[6]

Treatment of AD involves a stepwise approach tailored according to disease severity. Besides basic management and flare prevention, mild disease requires using low-potency topical corticosteroids (TCS) on a need basis; in moderate to severe AD, mid-potency TCS should be regularly used. Topical calcineurin inhibitors and crisaborole are steroid-sparing FDA-approved options. Patients with severe disease, not responding to other measures, may require systemic treatment options, i.e. Dupilumab or immunosuppressants. Systemic corticosteroids may bridge steroid-sparing treatment options like phototherapy, ciclosporin, Methotrexate, azathioprine, or mycophenolate mofetil.[7-9] Out of these options, Dupilumab is easily available and is not cost-effective in our resource-poor clinical settings. Phototherapy is available but is not feasible for most patients as they have to visit the hospital twice or thrice weekly. Ciclosporin (CyA) is the most used drug for patients with moderate to severe AD.[9] The occurrence of nephrotoxic side effects limits long-term management with ciclosporin. Methotrexate (MTX) has been used as an off-label drug treatment in our setting for atopic dermatitis. It was given only weekly, and folate supplementation was required during treatment. It is well tolerated in other inflammatory dermatological indications like psoriasis, etc. Data from the Health Improvement Network in the UK in 2019 showed that the most commonly prescribed immunosuppressant was Methotrexate (43.3%). Ciclosporin was prescribed for 16.9% of cases.[10] Therefore we wanted to analyze worldwide data comparing these two drugs in AD management as one of these, i.e., CyA is the gold standard in its management, and MTX is cost-effective and more feasible to use in the form of weekly dosage. No systematic review or meta-analysis comparing these two drugs is available (although network meta-analysis comparing multiple treatment modalities in atopic dermatitis are available).[8] Therefore, we did this systematic review to compare MTX with CyA, assessing the clinical effectiveness of both drugs and comparing adverse event profiles. A preliminary literature search on PubMed shows only 3 network meta-analyses comparing systemic immunomodulatory drugs in atopic dermatitis.[11,12] The last one was published in Dec 2023.[8] An RCT study comparing Methotrexate vs Cyclosporine in Atopic dermatitis was done in Egypt 2013.[13] PubMed shows two more RCTs done in the context, one in 2018 and another in 2023.[14,15] We have aimed to synthesize knowledge from the available RCTs on the subject.

METHODOLOGY

We followed the protocol for literature search as per the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement updated in 2020[6]

Population: Patients with moderate to severe atopic dermatitis (Adults and Children)

Intervention: Methotrexate (Oral or subcutaneous)

Comparison: Ciclosporin

Outcomes: Clinical improvement (as measured by improvement in SCORAD or O-SCORAD) and frequency of adverse and serious effects.

Search Strategy

03 free scientific databases, namely PubMed, Cochrane Library, and Google Scholar were sorted out for studies in the literature comparing Methotrexate with ciclosporin in the management of moderate to severe atopic dermatitis. Manual searching for additional relevant publications was also done, including searching clinical trials registries, i.e., clinical trials .gov.

The PubMed search yielded 128 results, but after the application of the filter of RCT, only three studies turned up. RCT about the required search gave 132 results in Google Scholar .3641 results came in the English language from Cochrane Library, including 1633 From Embase after the application of the filter of clinical trials was narrowed down to 23 clinical trials matching our search.

Study Selection

Three reviewers independently included published literature using the following criteria:

Inclusion Criteria: The studies included were: 1) clinical randomized controlled trials (RCTs); 2) the participants of the study had moderate to severe atopic dermatitis; 3) the studies compared Methotrexate for one group with ciclosporin for the other group; 4) the main outcome measures of the study included improvement of the SCORAD and side effects of both drugs; 5) Availability of full-text articles.

Exclusion Criteria: The following types of trials were excluded: 1) Studies lacking either Methotrexate or ciclosporin as intervention and control, 2) Quasi-experimental clinical trials; 3) Studies lacking the main outcomes we desired.

RESULTS

Three reviewers screened titles and abstracts to exclude other study designs, narrative reviews, and published protocols. When a study was available on more than one website, including Research Gate, only the most recent article was retrieved. Three studies were finally selected.

Table-I: Keywords and Medical Subject Headings Used for the PubMed Search

"Methotrexate"[All Fields] OR Methotrexate"[MeSH Terms]	AND	"ciclosporine" [All Fields] OR "Cyclosporine" [All Fields] OR "Cyclosporine"[MeSH Terms] OR ("cyclosporins" [MeSH Terms] OR "Cyclosporine" [MeSH Terms]	AND	"atopic dermatitis" [All Fields] OR "atopic eczema"[All Fields] OR "dermatitis, atopic" [MeSH Terms] OR "dermatitis, atopic" [MeSH Terms])

Search string used was (("Cyclosporine"[MeSH Terms] OR "Cyclosporine"[All Fields] OR "ciclosporin"[All Fields] OR "ciclosporine"[All Fields] OR "cyclosporin"[All Fields] OR "Cyclosporine s"[All Fields] OR "cyclosporins"[MeSH Terms] OR "cyclosporins"[All Fields] OR "Cyclosporines"[All Fields] OR ("Cyclosporine"[MeSH Terms] OR "Cyclosporine"[All Fields] OR "ciclosporin"[All Fields] OR "ciclosporine"[All Fields] OR "cyclosporin"[All Fields] OR "Cyclosporine s"[All Fields] OR "cyclosporins"[MeSH Terms] OR "cyclosporins"[All Fields] OR "Cyclosporines"[All Fields])) AND ("methotrexate"[MeSH Terms] OR "methotrexate"[All Fields] OR "methotrexate s"[All Fields] OR "methotrexates"[All Fields]) AND ("dermatitis, atopic"[MeSH Terms] OR ("dermatitis"[All Fields] AND "atopic"[All Fields]) OR "atopic dermatitis"[All Fields] OR ("atopic"[All Fields] AND "dermatitis"[All Fields]) OR ("dermatitis, atopic"[MeSH Terms] OR ("dermatitis"[All Fields] AND "atopic"[All Fields]) OR "atopic dermatitis"[All Fields] OR ("atopic"[All Fields] AND "eczema"[All Fields]) OR "atopic eczema"[All Fields])))

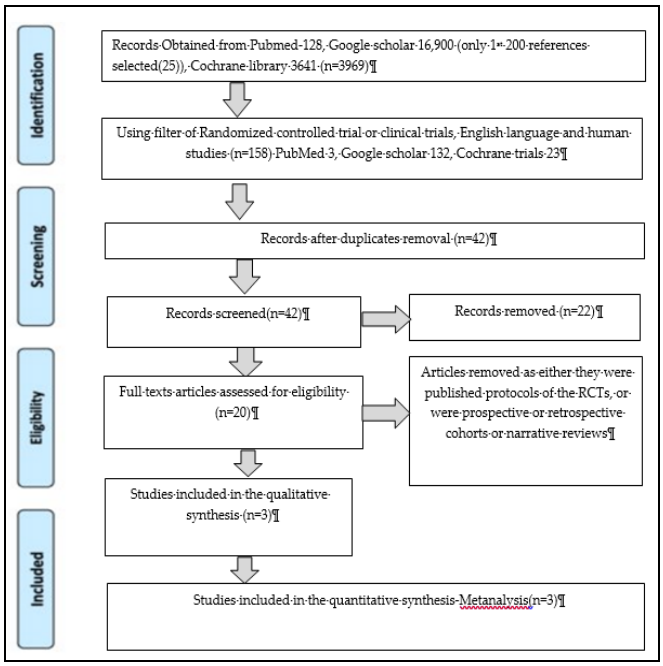


Figure-1: Flow chart for study Inclusion in meta-analysis based on PRIS

Data Extraction

Three reviewers independently extracted data from the studies using a pre-planned data extraction sheet, resolving disagreements by discussion and consensus amongst the team members. Variables extracted from the three studies included the country where the study was conducted and the year of publication, including the journal's name, sample size, and No. of dropouts; demographics of the population like age; inclusion and exclusion criteria; treatment protocol; length of treatment and follow-up; Study outcomes; Frequency of recorded side effects with the drugs; and conclusion.

Statistical Analysis

The outcomes mentioned before were pooled in this analysis using Review Manager software version 5.2. Meta-analysis was done using a random-effects model. There was no evidence of methodological heterogeneity as all studies were randomized controlled trials and could be easily pooled together. For dichotomous outcomes, risk ratios were assessed using the Mantel-Haenszel method. We used Standard Mean differences for continuous outcomes as the outcome measure was SCORAD in 2 studies and O-SCORAD in one. A 95% confidence interval was taken with the inverse variance method. Statistical heterogeneity was measured using I2, and if it showed values >50% and *p*-values of <0.10, it was taken as a large degree of heterogeneity among the included studies. We planned to explore it by checking data entry errors, conducting subgroup or regression analysis, conducting sensitivity analysis, and reconsidering the effect measure per guidelines in the Cochrane Handbook of Systematic Reviews. [17]

Assessment of the Risk of Bias

The risk of bias assessment of randomized controlled trials comprehensive tool, i.e. RoB2, was used to assess the risk of bias in all included studies. It

Table-II: Study Characteristics and Patients

Study ID	Study 1	Study 2	Study 3
Title of the study	Methotrexate Versus Cyclosporine in Adults with Moderate-to-Severe Atopic Dermatitis: A Phase III Randomized Noninferiority Trial	Methotrexate versus Cyclosporine in the treatment of severe atopic dermatitis in children: a multicenter experience from Egypt	Efficacy and safety of ciclosporin versus methotrexate in the treatment of severe atopic dermatitis in children and young people (TREAT): a multicentre parallel group assessor-blinded clinical trial
Corresponding Authors	Catherine Goujon	Mohamed A. El-Khalawany	Carsten Flohr
Country where study was conducted and year of publication and Journal in which published	France 2017 J ALLERGY CLIN IMMUNOL PRACT	Egypt 2013 Eur J Pediatr	UK 2023 Br J Dermatol
Sample size	N=97 MTX=50 CyA=47	N=40 MTX=20 CyA=20	N=103 MTX=51 CyA=52
No.of Drop outs	27 in MTX group 10 in CyA group	Nil	13 MTX 07 CyA
Mean age of population in years	32±9 in MTX group 33±10 in CyA group	11.16±1.52 - MTX 10.30±2.82 - CyA	9.82 (4.01)-MTX 10.34 (4.21)-CyA
Inclusion criteria	Patients with chronic moderate-to severe AD as per the diagnostic criteria of the UK Working Party Having score of >15 on SCORAD index Inadequately responding to TCS or TCIs.	8–14 years old patients with severe AD who were either unfit or not responding to phototherapy	2 -16 years; severe recalcitrant AD; having inadequate response to potent TCS.
Exclusion criteria	The use of systemic CS or immunosuppressants within 4 weeks before the inclusion Contraindication to MTX or CyA	Chronic or recurrent infection or uncontrolled systemic diseases. History of organ transplantation or cancer Herpes zoster within 2 months before the study. Hypersensitivity for either drug	Previous exposure to biologics or systemic immunosuppressants Usage of systemic steroids in past 28 days Having phototherapy within past 6 weeks A serious co-morbid medical condition .
Treatment protocol	Patients were either given MTX 15 mg/wk in a single oral dose or CyA 2.5 mg/kg/d divided in 2 oral doses). For patients not achieving SCORAD 50, after 8 weeks, doses were, increased to 25 mg/wk and 5 mg/kg of body weight/d respectively for further 16 weeks. Patients in MTX group received 5 mg folate daily, except on the day of drug intake.	Group A was treated with MTX with initial dose of 5 mg (test dose); then a dose of 7.5 mg weekly dose was continued till the end of the treatment period, administrated orally in three divided doses with 12-h interval. Folic acid 400 µg was given once following the day of MTX dose. Group B was treated with CyA 2.5 mg/kg/day (oral in two divided doses)	Patients were randomly either given oral CyA (4 mg/ kg daily) or MTX (0.4 mg/ kg weekly) for 36 weeks and Follow up was done for 24 weeks
Length of treatment	24 weeks	12 weeks	36 weeks
Length of follow up	-	12 weeks after treatment period	24 weeks
Primary outcome measures	Primary: achieving SCORAD 50 at 8 weeks. Secondary: achieving EASI 50 and a DLQI value of ≤5 at 8 weeks & patients achieving all these 03 scores at 12, 16, 20, and 24 weeks.	Absolute reduction in SCORAD at the end of the treatment	Primary (i) o-SCORAD at 12 weeks; and (ii) time to first relapse after treatment completion.
Frequency of adverse effects	35 (30%)-MTX 68(55%)-CyA	43-MTX 52-CyA	407-MTX 369-CyA
Serious adverse events	1 in CyA group		7-MTX 5-CyA
Conclusion	MTX @15mg/week is less efficient than CyA in improving moderate-to-severe AD at 8 weeks. Increasing the dose of MTX to 25 mg/week resulted in significant improvement at week 20 comparable to that observed with Cyclosporine and with a better safety profile.	MTX or CyA in low doses are relatively safe and better-tolerated drugs for severe AD in children. CyA induces a rapid response while MTX has the benefit of inducing longer remission period.	CyA acts quicker, while MTX induces better disease control after treatment stoppage.

included assessment of selection bias, selection bias, performance bias, detection bias, attrition bias and selective reporting bias. Based on these items, each included study was rated as having low, unclear, or high bias.[18] No blinding was done in the three studies included besides blinded assessment of results. Therefore, this was recorded as a bias, making the evidence uncertain.

DISCUSSION

Ciclosporin is recommended as a first-line option for short-term management of moderate-to-severe AD cases not responding to topical regimens and phototherapy. Unfortunately, the efficacy of CsA is not long-lasting, and the rapid relapse of AD symptoms is expected after drug withdrawal, with a

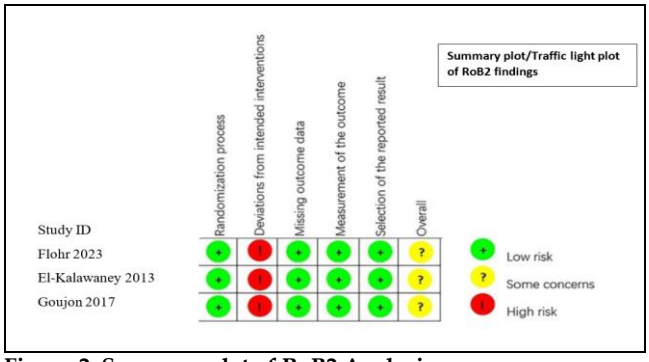


Figure-2: Summary plot of RoB2 Analysis

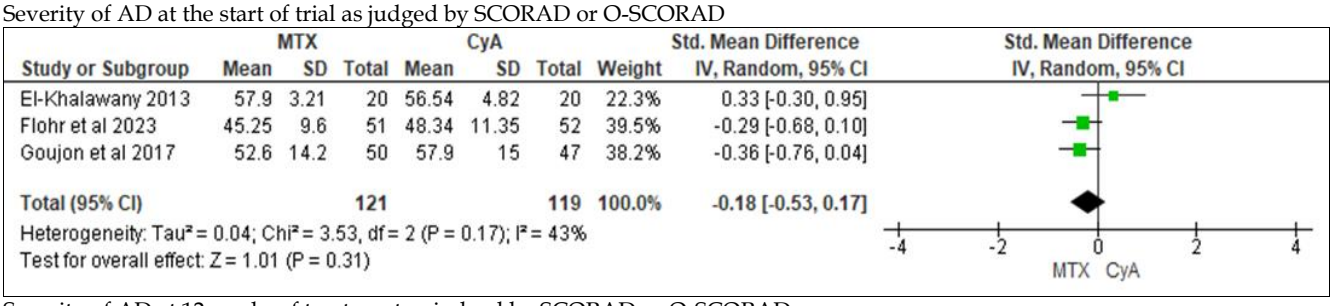
reported relapse rate of 23.5%-54.8%. Compounding the issue, long-term use of CsA is not recommended as it can cause renal toxicity. Methotrexate, on the other hand, is a chemotherapeutic drug. Low doses, i.e./ 100th of the chemotherapeutic dose, can manage various inflammatory diseases, especially psoriasis, in dermatological practice. It is an off-label drug to manage moderate-to-severe AD in adults and children. [19]

Results of our study showing pooled results from 3 RCTs indicate that, as far as effectiveness in ameliorating the symptoms of moderate to severe atopic dermatitis is concerned, ciclosporin, even in a low dose of 2.5mg/kg body weight, is better than methotrexate @0.4mg/kg/week at 12 weeks. In a retrospective study of patients receiving MTX, with a mean treatment duration of 20.4 months, 55.6% were considered responders, and 44.4% were non-responders. The mean treatment duration in CsA patients receiving AD was 13.2 months. 65.9% of patients were responders, and 34.1% were non-responders. These results match the results of our study. [20]

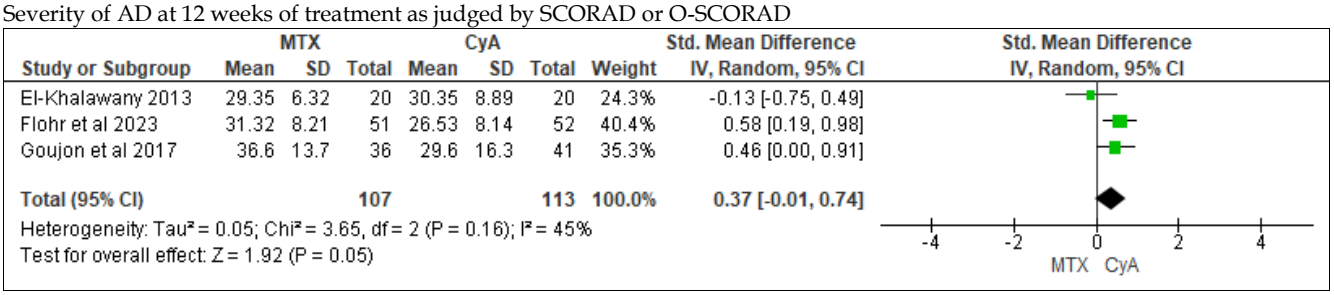
A network metanalysis published in 2023, including 149 RCTs, shows with high-certainty evidence that high-dose Upadacitinib is the most

Table-III: Forest plots of Treatment Outcomes

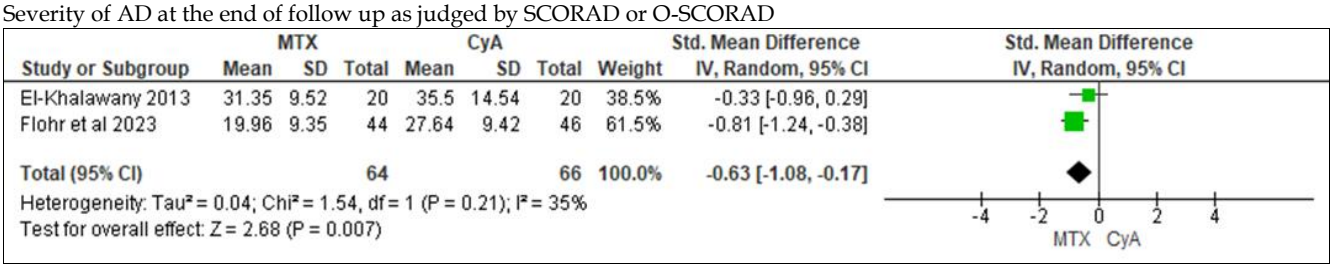
Severity of AD at the start of trial as judged by SCORAD or O-SCORAD



Severity of AD at 12 weeks of treatment as judged by SCORAD or O-SCORAD



Severity of AD at the end of follow up as judged by SCORAD or O-SCORAD



Total adverse events reported

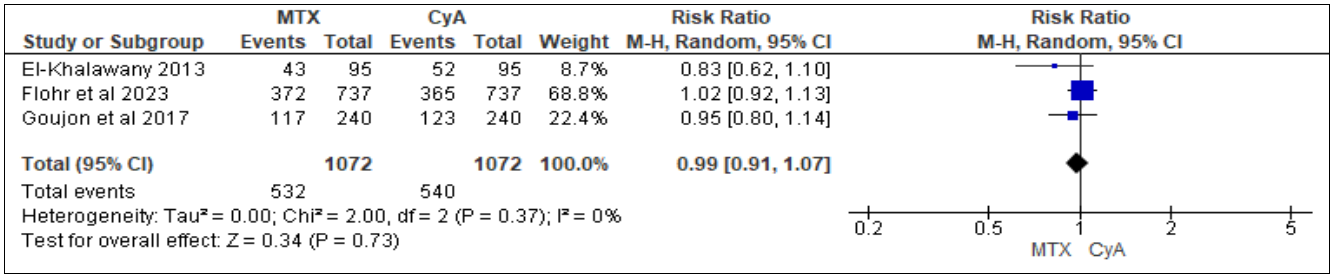
In the study by Flohr et al we have eliminated fatigue from the adverse effects as it was affecting the statistical heterogeneity and is a non-specific symptom, which can be caused by atopic dermatitis as well.

effective systemic treatment option for AD. High-dose Cyclosporine is among the most effective (low certainty) systemic treatment options, with a mean difference of -13.38 in EASI score showing improvement in disease severity with a 95% credible interval of -17.01 to -9.83. There was low-certainty evidence for low-dose cyclosporin and Methotrexate. Each produces a mean difference in EASI scores of -6.73 and -6.88, respectively. [8]

reaching the maximum dose of 25 mg; stopping after 03 months if there is no improvement and a maintenance dose of 5 - 7.5 mg. [21]

Our metanalysis results show that the safety profile of Methotrexate is better than that of ciclosporin. Side effects encountered with both drugs mentioned in RCT by Flohr et al. include eczemas, headache, GI symptoms, mouth ulcers, decreased GFR, infections like nasopharyngitis and decreased

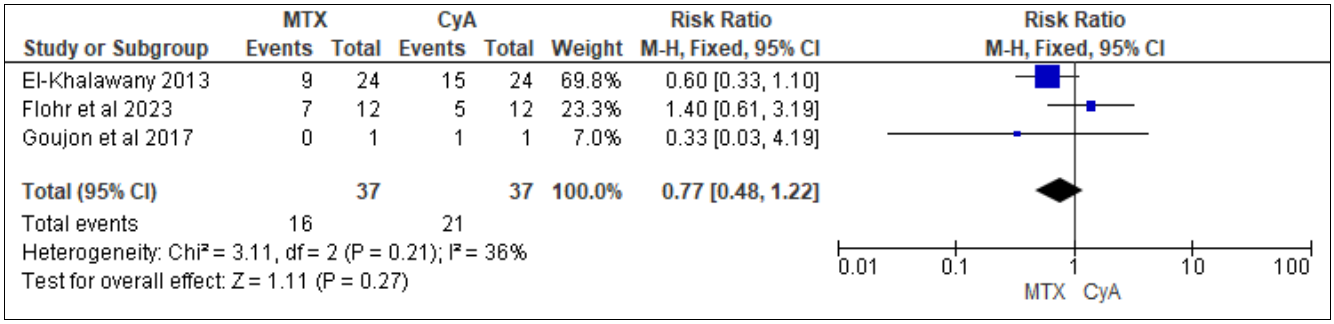
Table- IV: Forest Plot of Adverse Events Outcomes



Serious adverse events reported

Serious adverse effects were mentioned in the study by Flohr et al and Goujon et al, but in the study by El-Khalawany we calculated the frequency of adverse effects ourselves taking pancytopenia, leukopenia, deranged liver and renal profiles.

Table-V: Forest Plot of Serious Events Outcomes



Our meta-analysis shows that, at follow-up, Methotrexate maintains better remission rates or disease control and that it does so for a longer duration, i.e., 24 weeks post-treatment. This is in accordance with the results of a Korean retrospective study showing that 25.8% of patients on MTX remained stable for 03 months with an IGA score of 0-2 after stopping MTX. Their mean period of stability without MTX medication was 20.0±10.4 months. [19]

Goujon et al., in their open retrospective study on AD receiving low-dose MTX for 3 to 30 months, proposed MTX dosage schedules in moderate to severe AD in cases of no contra-indications for its prescription. It includes an initial weekly single dose of MTX, i.e. 15 mg, increasing to 5 mg weekly in case of inadequate response after 02months of treatment;

appetite. Nausea, decreased appetite, and oral ulcers were more common with MTX and decreased GFR with CyA. [21] A Few other side effects mentioned in another RCT by Goujon et al. include hypertrichosis, gingival hyperplasia, acne and hypertension with CyA.(14)Some serious side effects mentioned in this RCT included admission to the hospital indoor care for severe AD flare at 12 weeks in a patient on 2.5 mg/kg/d CyA. Another patient on MTX discontinued the study at week eight because of an increase in liver enzymes (4 x reference limit), and another patient on MTX discontinued at week 12 because of lymphopenia (900 cells/mL vs 1500 cells/mL as normal count). The last two were not considered serious side effects by the author. (14) In RCT done by El-Khalawany et al., a few other side effects mentioned were pancytopenia, thrombocytopenia, leukopenia and raised ESR, which

were more commonly seen with CyA. Anaemia was more prevalent in the MTX-treated group. Abnormalities in liver function tests were more common in the treated group. [13]

In a monocenter retrospective study comparing systemic treatment options for severe AD, the most frequent side effects were lymphopenia and infections. Mild lymphopenia was found in 1 patient receiving MTX (3.6%), one patient receiving CyA (2.3%) and one patient receiving combination therapy with MTX and AZA (14.3%). Common infections, such as folliculitis, conjunctivitis, and viral warts, occurred in 10.7% of patients in the MTX group and 7% in the CyA group. [20]

Table-VI: Summary of Findings Table Made on Grade Pro GDT

Methotrexate compared to Ciclosporin in AD for Moderate to severe AD

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Certainty	What happens
		Without MTX	With MTX	Difference		
Disease severity at start of treatment (SCORAD/O-SCORAD) № of participants: 240 (3 RCTs)[1,2,3]	-	-	-	SMD **0.18 lower** (0.53 lower to 0.17 higher)	⊕⊕⊕⊕ High	
Disease severity at 12 weeks of treatment(SCORAD/O-SCORAD) № of participants: 220 (3 RCTs)[1,2,3]	-	-	-	SMD **0.37 higher** (0.01 lower to 0.74 higher)	⊕⊕⊕⊕ High	Methotrexate is not better than ciclosporin at 12 weeks as measured by SCORAD/O-SCORAD
Disease severity at the end of follow up(SCORAD/O-SCORAD) № of participants: 130 (2 RCTs)[1,3]	-	-	-	SMD **0.63 lower** (1.08 lower to 0.17 lower)	⊕⊕⊕⊕ High	Methotrexate is better than ciclosporin in maintain remission after stopping treatment.
Adverse events reported № of participants: 240 (3 RCTs)[1,2,3]	**RR 0.99** (0.91 to 1.07)	50.4%	**49.9%** (45.8 to 53.9)	**0.5% fewer** (4.5 fewer to 3.5 more)	⊕⊕⊕⊕ High	Side effect profile of MTX is better than CyA
Serious Adverse Events reported № of participants: 240 (3 RCTs)[1,2,3]	**RR 0.77** (0.48 to 1.22)	56.8%	**43.7%** (27.2 to 69.2)	**13.1% fewer** (29.5 fewer to 12.5 more)	⊕⊕⊕⊕ High	Serious side effect profile of MTX is also better than CyA.

**The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).*
CI: confidence interval; OR: odds ratio; RR: risk ratio; SMD: standardized mean difference

GRADE Working Group grades of evidence
High certainty: *we are very confident that the true effect lies close to that of the estimate of the effect.*
Moderate certainty: *we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.*
Low certainty: *our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.*
Very low certainty: *we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.*

The RCT by Goujon et al. and the fall, owing monitoring protocol, were included in our meta-analysis. Patients on MTX had weekly CBC during the first 12 weeks, then every four weeks until week 24. LFTs and serum creatinine were checked every four weeks. Patients on CyA had blood analyses every four weeks (including a CBC, serum creatinine, and LFTs). In addition, electrolytes, bilirubin, uric acid, blood sugar tests, and urine analyses were carried out every three months. [14]

In the Egyptian RCT included in our meta-analysis, laboratory tests done for all patients before starting treatment included CBC, ESR, BSR, RFTs, LFTs, hepatitis B and C serology, serum total Ig E, and urine analysis in addition to chest x-ray and Mantoux skin test. However, they have not mentioned any further monitoring. [13]

The 3rd RCT included in our meta-analysis, baseline tests for all, including Chest X-ray and Mantoux test, and weekly tests for myelosuppression in the MTX group, are vaguely mentioned with no details. [(21)]

We should follow the guidelines for monitoring when administering MTX or CsA to avoid these adverse effects and to take prompt action if monitoring shows some deranged findings. British Association of Dermatologists guidelines for safe and effective prescription of MTX (2016) mention it as an effective drug for eczemas, including AD, in both children and adults. According to these guidelines, monitoring during MTX therapy includes full blood count, liver function tests, and urea and electrolytes every 1–2 weeks for the first month and until a steady dosing regimen is achieved. If AST and ALT are greater than 2–3 times the normal, it requires withholding or decreasing the MTX dose and discussing it with a gastroenterologist. If Total WBC count < 3 × 10 9 cells /L, Neutrophils < 1 0 × 10 9 cells or Platelets < 100 × cells/ L, withhold MTX and discussion with a hematologist is required.[(22)(23)]

Guidelines on the use of CyA in dermatosis mention its effective usage in AD affected patients, either adults or children, whose disease is severe and refractory to other treatment options. Monitoring guidelines during drug usage state that serum creatinine should be measured fortnightly for the first 03 months, then monthly till treatment continues. For patients on > 12 months of continuous long-term treatment, yearly renal function should be done, including creatinine clearance, to estimate the glomerular filtration rate. Measure blood pressure every two weeks for 1st 02 months and then every month. They recommend that in AD, the starting dose should be 5 mg/kg /day tapered to 1.5–3 mg /kg/ day, and the duration of treatment should be 6–12 months. [24,25]

ACKNOWLEDGEMENT

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CONCLUSION

Both CyA and MTX are effective, well-tolerated treatment options for moderate to severe AD in both children and adults, not responding to topicals and phototherapy. CyA has a quicker onset of action, while MTX is better at maintaining remission after treatment discontinuation. As first-line novel systemic biologics and small-molecule prescribing are restricted by availability and cost issues in our part of the world having limited financial resources, these two drugs can provide a feasible and cost-effective alternative. Good quality RCTs are required to improve the quality of evidence regarding the efficacy of both drugs.

Conflict of Interest: None.

Authors Contribution

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

1,2: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

3,4: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

5,6: Conception, data acquisition, drafting the manuscript, approval of the final 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.

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