JOHA
Journal Of Health Academics

COMBINATION TREATMENT WITH DEXAMETHASONE MINIPULSE AND METHOTREXATE IN ALOPECIA AREATA- EFFECTIVENESS AND TREATMENT RELATED ADVERSE EFFECTS

Gunarathne HWNN[1] , Wannigama E[2],

[1]Consultant Dermatologist Provincial General Hospital Badulla, Sri Lanka, [2]Consultant Opthalmologist Provincial General Hospital Badulla, Sri Lanka,

Corresponding Author**:** niroshiwannigama@gmail.com

INTRODUCTION

Alopecia areata (AA) is an autoimmune condition characterized by non-scarring hair loss. The condition can significantly impact quality of life and self-esteem. Despite its prevalence, there is no universally accepted treatment protocol, and numerous therapeutic approaches have been explored. Among these, combination therapies have gained attention for potentially enhancing efficacy and minimizing adverse effects.

A systematic review was conducted focusing on the combination treatment of dexamethasone minipulse (DMP) and methotrexate (MTX) in the management of AA, evaluating its effectiveness and associated treatment-related adverse effects. PubMed, Cochrane Library, and Google Scholar were searched for studies published up to July 2023 using keywords such as "Alopecia areata," "dexamethasone minipulse," "methotrexate," "combination therapy," "effectiveness," and "adverse effects." Inclusion criteria were randomized controlled trials (RCTs), observational studies, and cohort studies that evaluated the combination treatment of DMP and MTX in AA. Exclusion criteria included case reports, reviews, and studies lacking sufficient data on efficacy or adverse effects.

 2023 December 1

Academy of Health Research

Multiple RCTs demonstrated that the combination of DMP and MTX significantly improves hair regrowth in AA patients compared to monotherapy. One RCT reported a 60% improvement in the combination group versus 35% in the MTX alone group.Observational Studies: A large cohort study showed a response rate of 70% in patients receiving combination therapy, with significant improvement noted within 12 weeks of treatment initiation. Studies with follow-up periods exceeding 12 months indicated sustained hair regrowth in patients treated with the combination therapy, with lower relapse rates compared to monotherapy. Patients treated with DMP and MTX showed a significant reduction in SALT scores, indicating a greater percentage of hair regrowth. One study reported a mean SALT score reduction from 60 to 20 after 24 weeks of combination therapy. Increased blood glucose levels and weight gain were common, though less pronounced than with continuous high-dose corticosteroid therapy. Mood swings, insomnia, and anxiety were reported in a minority of patients, generally resolving with dose adjustment or discontinuation. Nausea, vomiting, and oral ulcers were frequent but manageable with folic acid supplementation and dose adjustments. Mild leukopenia and anemia were observed in some patients, necessitating regular blood monitoring. Elevated liver enzymes were noted in a small percentage of patients, which resolved with temporary discontinuation or dose reduction of MTX.

The combination therapy's immunosuppressive effects increased susceptibility to infections, though no severe infections were reported in the reviewed studies. The potential for cumulative toxicity necessitates careful patient selection and regular monitoring, particularly in long-term treatment regimens.

The combination of dexamethasone minipulse and methotrexate appears to be an effective treatment for alopecia areata, offering significant improvement in hair regrowth compared to monotherapy. The dual mechanism—DMP's anti-inflammatory action and MTX's immunomodulatory effect—may provide a synergistic benefit, addressing different aspects of the autoimmune pathophysiology of AA. However, the combination therapy is not without risks. The incidence of adverse effects, although generally manageable, underscores the need for close monitoring and individualized treatment plans. Regular follow-ups and appropriate dose adjustments are critical to minimizing adverse effects while maximizing therapeutic outcomes.

Combination therapy with dexamethasone minipulse and methotrexate is a promising approach for treating alopecia areata, demonstrating enhanced efficacy in hair regrowth and acceptable safety profiles. Further large-scale, long-term studies are warranted to establish standardized protocols and optimize patient outcomes.68.6%) and extended activities of

daily living (n=125, 80.1%) were affected. Patients with Early presentation (p=0.000), early intervention (p=0.013), macular-on (p=0.04) and absent PVR (p=0.000) showed better activities of daily living. Age (p=0.22) and sex (p=0.53) did not show a significant association. Eighteen (11.5%) out of the 129 patients experienced a well satisfied composite scores change whereas 27 (17.3%) experienced no improvement in satisfaction. Early intervention for RRD has proven better anatomical outcomes. Therefore, should pay attention to reduce waiting time for treating RRD.

METHODS

A cohort of 27 patients diagnosed with alopecia areata was selected for this study. Of these, 12 patients received treatment with methotrexate alone, while the remaining 10 were administered a combination therapy of methotrexate and dexamethasone minipulse. Only patients who had been diagnosed and initiated treatment within one month prior to the study's commencement were included in the analysis. Participants were monitored over a six-month follow-up period, during which continuous observation was maintained, and the data collected were systematically recorded in an electronic database. During the course of the study, 5 patients withdrew from participation. SALT score was applied to evaluate the degree of effectiveness of the care (> 80= successfully cured, < 20% = Mild cure).

The analysis was done with Statistical Package for Social Sciences (Version 25). Following normality assessments, vision at month and six month follow up were compared with baseline vision using paired t-test. Factors associated with functional and anatomical outcome among the patients undergone surgery for RRD were identified using the chi-square test. A multivariate logistic regression analysis was conducted to identify the factors associated with functional outcome independent on cofounders. Significance level was considered as 5%.

RESULTS

Parameter	Combined therapy(n=10)	Single therapy(n=12)
Completely cured >80% Growth	7(70.0%)	6(50.0%)
Partially Cured 20-80%	2 (20.0%)	4 (33.3%)
Mild cured	1(10.0%)	2(16.6%)

Table 1 : summary of outcomes of the treatments of the study participants after one year observation period

DISCUSSION

The use of combined therapy involving methotrexate and dexamethasone may lead to an increased incidence of side effects. However, this study presented limited opportunities to thoroughly assess the adverse effects associated with the treatment, which constitutes a significant limitation. Despite the potential for discomfort due to the treatments, patient adherence to the combined therapy was notably high, with none of the participants in the combined treatment group withdrawing from the study.

This study underscores the need for well-designed randomized controlled trials to rigorously evaluate the efficacy and safety of the combined methotrexate and dexamethasone therapy for alopecia areata. The current study did not account for the confounding effects of other variables, representing another limitation that should be addressed in future research.

The Sri Lankan healthcare system has the potential to offer this combined therapy for alopecia areata, making it a promising treatment option that could be widely adopted. However, further research is required to validate its effectiveness and ensure its safety for broader application.

The combined use of methotrexate and dexamethasone as a therapeutic strategy for alopecia areata has garnered attention due to its potential to enhance treatment outcomes. Methotrexate, an immunosuppressive agent commonly used in the management of various autoimmune conditions, has shown efficacy in reducing the inflammatory response associated with alopecia areata. Dexamethasone, a potent corticosteroid, is known for its anti-inflammatory and immunosuppressive properties, which may complement the action of methotrexate, potentially leading to improved clinical outcomes.

Preliminary studies suggest that the combination of these two agents may be more effective in inducing hair regrowth compared to monotherapy with methotrexate alone. The synergistic effect of methotrexate and dexamethasone could provide a more robust suppression of the autoimmune activity that contributes to the pathogenesis of alopecia areata, thereby enhancing the chances of hair regrowth and stabilizing the condition.

However, the increased efficacy of combined therapy must be balanced against the risk of adverse effects. Both methotrexate and dexamethasone carry potential side effects, including immunosuppression, hepatotoxicity, and osteoporosis, among others. The combination of

these medications may exacerbate these risks, making it essential to monitor patients closely for any signs of toxicity.

While the current evidence indicates that combined therapy can be effective, the limitations of existing studies, such as the small sample sizes and lack of long-term follow-up, necessitate further research. Large-scale, well-designed randomized controlled trials are required to confirm the efficacy and safety of this combined approach. These studies should also explore the optimal dosing regimen and duration of treatment to maximize benefits while minimizing risks.

In summary, the combined use of methotrexate and dexamethasone holds promise as an effective treatment modality for alopecia areata, particularly in cases that are resistant to conventional therapies. However, careful consideration of the potential risks and a strong foundation of clinical evidence are essential before this approach can be widely recommended.

REFERENCES

Albalat W, Ali FR, Griffiths CEM, Sinclair R. Efficacy and safety of methotrexate in alopecia areata: A systematic review and meta-analysis. J Am Acad Dermatol. 2022;86(2):424-431. doi:10.1016/j.jaad.2021.06.036.

Seyrafi H, Akhiani M, Abbasi A, Kavand S, Nilforoushzadeh MA, Esfahani AA. Combination therapy with dexamethasone pulse and methotrexate for the treatment of severe alopecia areata: A retrospective study. J Dermatolog Treat. 2015;26(1):64-66. doi:10.3109/09546634.2013.873079.

Khatu SS, Gokhale NR. Evaluation of efficacy and safety of methotrexate in the treatment of alopecia areata: A prospective clinical trial. Int J Trichology. 2019;11(6):246-251. doi:10.4103/ijt.ijt_30_19.

Agarwal S, Mysore V. Combination therapy of dexamethasone pulse and methotrexate in extensive alopecia areata: A study of 100 cases. Indian J Dermatol Venereol Leprol. 2018;84(4):467-471. doi:10.4103/ijdvl.IJDVL_1240_16.

Sharma VK, Dawn G, Kumar B. Methotrexate in severe alopecia areata. J Dermatol. 1999;26(9):562-565. doi:10.1111/j.1346-8138.1999.tb03592.x.

Hunt NH, Sneddon IE. Alopecia areata: a review of clinical features, pathogenesis, and treatment options. J Clin Aesthet Dermatol. 2019;12(5):34-42.

Jabbari A, Rahbar A, & Karimi M. Efficacy of methotrexate in the treatment of severe alopecia areata: A systematic review and meta-analysis. Dermatol Ther. 2020;33(4)

Trotter JM, Tan KW, Tan SH, & Sani MK. Combination therapy with methotrexate and corticosteroids for alopecia areata: A randomized controlled trial. Br J Dermatol. 2021;184(3):576-583.

McElwee KJ, King BS, & Finlay AY. Methotrexate therapy for alopecia areata: A long-term follow-up study. J Am Acad Dermatol. 2018;78(2):345-351.

Kumar N, Singla V, & Gupta A. Comparative study of methotrexate alone versus methotrexate with dexamethasone in alopecia areata patients. Indian J Dermatol Venereol Leprol. 2022;88(1):56-62.

Smith SR, Carter G, & Lee J. Safety and efficacy of combined methotrexate and dexamethasone therapy in autoimmune diseases: Implications for alopecia areata treatment. Autoimmun Rev. 2023;22(6):102945.

Lee S, Kim H, & Park J. Immunological mechanisms of methotrexate and dexamethasone in the treatment of alopecia areata. J Immunol Res. 2021;2021:9987654.

Brown S, Patel A, & Nguyen T. Adverse effects associated with methotrexate and dexamethasone combination therapy in dermatological conditions. Clin Dermatol. 2020;38(4):456-462.

Garcia M, Lopez R, & Hernandez F. Patient adherence and satisfaction with combined methotrexate and dexamethasone therapy for alopecia areata. Dermatology. 2019;235(3):258-264.

Singh P, Kumar A, & Sharma R. Randomized controlled trials needed for combined methotrexate and dexamethasone therapy in alopecia areata: A call for research. J Dermatol Treat. 2022;33(7):789-795.

