

Letter to Editor

Methotrexate in refractory chronic urticaria

Vitorino Modesto dos Santos¹, Taciana Arruda Modesto Suga²

¹Department of Medicine, Armed Forces Hospital and Catholic University, ²American Society of Neurophysiology and Dermatology, Brazil.

Dear Editor,

Chronic spontaneous urticaria (CSU) may become refractory chronic refractory urticaria (CRU) to first-generation antihistamines even with up to 4-fold the usual dosage, increasing the disease burden; one option is to use methotrexate (MTX) plus the second-generation antihistamines.^[1-6] MTX may affect the bone marrow causing pancytopenia and the oral and gastrointestinal epithelial cells, with the development of mucositis and hemorrhagic ulcerations.^[7-10] MTX adverse effects are usually of low or moderate intensity, but the cumulative levels in cases of renal dysfunction favors the overdose toxicity and more severe outcome.^[7-10]

We would like to emphasize the very recent article of this Journal by Yadav AK, describing the outcomes of 46 patients with mean age of 32.6 (\pm 9.68) years and CSU, who underwent oral MTX (15 mg weekly) plus folic acid, and the oral desloratadine (5 mg twice daily); there was a reduced urticaria activity and enhanced life quality index.^[6] The aim of the study was to evaluate the effectiveness of MTX oral pulse to manage patients with CRU; although longer periods with placebo-controlled studies are needed, the results indicated that MTX can be a safe effective option to treat patients who have CSU without response to elevated doses of second-generation antihistamines. With no severe adverse effect, only slightly elevated transaminases occurred in 15% of cases.^[6] The author concluded that MTX is a safe, well-tolerated, and effective option to treat CSU cases that do not respond to elevated doses of second-generation antihistamines.^[6] The results of the study show a promising, economical, and simplified therapeutic advance; notwithstanding, it seems opportune to call special attention to the eventual occurrence of adverse effects that have been described even in patients utilizing low MTX dosage.^[7-10] Clinical manifestations of toxicity include oral and gastrointestinal ulcerations, rash, alopecia, anaphylaxis, pancytopenia, immunosuppression, and lung or liver fibrosis.^[7-10] Potentially, toxic MTX level varies according to the time of last drug ingestion, ranging

from over than 10.00 μ mol/L in 24 h, and 1.00 μ mol/L in 48 h, till 0.20 μ mol/L in 72 h. High doses can be by logistical mistake or accidental excessive MTX ingestion.^[9] An ingestion of MTX up to 25 mg per week is considered a low dose of the medicament. We would like to emphasize on the need to enhance the suspicion index among healthcare workers about a possible unsuspected or underdiagnosed low-dose toxicity evolving without early control.^[9] Special care must be taken in case of patients with some cognitive or visual deficits, who should not be in charge of controlling their weekly routine medication-taking schedules. They may also have difficulty interpreting and/or reporting symptoms to their caregivers. In conclusion, the option of utilizing MTX to better control the refractory cases of urticaria should be welcome, because this surely will benefit a large number of patients; however, an accurate follow-up must be employed to actively search for adverse effects.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Choi JH, Lee DH, Song WJ, Choi M, Kwon JW, Kim GW, *et al.* The KAAACI/KDA evidence-based practice guidelines for chronic spontaneous urticaria in Korean adults and children: Part 2. Management of H1-antihistamine-refractory chronic urticaria. *Allergy Asthma Immunol Res* 2020;12:750-70.
2. Garbayo-Salmons P, Expósito-Serrano V. Chronic spontaneous urticaria refractory to cyclosporine add-on omalizumab successfully treated with methotrexate add-on. *Dermatol Ther* 2020;33:e14469.
3. Sandhu J, Kumar A, Gupta SK. The therapeutic role of methotrexate in chronic urticaria: A systematic review. *Indian J Dermatol Venereol Leprol* 2022;88:313-21.
4. Unsel M. Efficacy of drug therapies in antihistamine refractory chronic spontaneous urticaria: Real life data. *Asian Pac J Allergy Immunol* 2021. doi: 10.12932/AP-270820-0948.
5. Unsel M. Safety of methotrexate in chronic urticaria unresponsive to omalizumab. *Iran J Allergy Asthma Immunol* 2021;20:500-4.

*Corresponding author: Vitorino Modesto dos Santos, Department of Medicine, Armed Forces Hospital and Catholic University, Brasilia-DF, Brazil. vitorinomodesto@gmail.com.

Received: 02 March 2024; Accepted: 07 March 2024; Epub Ahead of Print: 16 May 2024 Published: XXXXXX DOI: 10.25259/IJSA_15_2024

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms. ©2024 Published by Scientific Scholar on behalf of Indian Journal of Skin Allergy

6. Yadav AK. Study of effectiveness of methotrexate oral pulse in refractory chronic urticaria. *Indian J Skin Allergy* 2024. doi: 10.25259/IJSA_28_2023.
7. Arce IL, Vicari P, Figueiredo VL. Methotrexate intoxication: Diagnostic difficulty case report. 2021;43(Suppl 1):S47-8.
8. Chamorro-Petronacci C, García-García A, Lorenzo-Pouso AI, Gómez-García FJ, Padín-Iruegas ME, Gándara-Vila P, *et al.* Management options for low-dose methotrexate-induced oral ulcers: A systematic review. *Med Oral Patol Oral Cir Bucal* 2019;24:e181-9.
9. Schelzel G, Palicherla A, Tauseef A, Millner P. Low-dose methotrexate toxicity leading to pancytopenia: Leucovorin as a rescue treatment. *Proc (Bayl Univ Med Cent)* 2024;37:339-43.
10. Shrestha R, Ojha SK, Jha SK, Jasraj R, Fauzdar A. Methotrexate-induced mucositis: A consequence of medication error in a rheumatoid arthritis patient. *Cureus* 2023;15:e46290.

How to cite this article: Santos VM, Sugai TA. Methotrexate in refractory chronic urticarial. *Indian J Skin Allergy*. doi: 10.25259/IJSA_15_2024