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Letter to Editor

Methotrexate in refractory chronic urticaria

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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 (± 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 µmoL/L in 24 h, and 1.00 µmoL/L in 48 h, till 0.20 µmoL/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.

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