

## Psoriasis severity and inflammatory responses under concomitant treatment with methotrexate plus micronutrients for psoriasis vulgaris

Psoriasis vulgaris is a chronic immune-mediated skin disorder with a global prevalence of 2% (1). The pathogenesis of psoriasis is unknown (2). In psoriasis vulgaris, the affected epidermis is significantly infiltrated with immune cells and produces abnormal cytokines (3). Methotrexate (MTX) as the gold standard therapy for moderate to severe psoriasis exerts its effects as both an immune-modulatory and antimetabolite agent (4). Methotrexate applies its immunomodulatory effects by decreasing T cell-mediated inflammation at multiple steps, which causes inhibition of keratinocyte growth and down-regulates the endothelial expression of ICAM-1 and E-selectin (5, 6). Despite milder flares-ups and reduction of scales and erythema under micronutrient (MM) consumption (7, 8), the clinical efficacy of MM in psoriasis treatment has been neglected for decades. However, today the increasing numbers of treatment modalities with respect to diet regimen, complementary medicines, and combined therapies for psoriasis patients are controversial among dermatologists.

A double-blind, randomized trial, which performed in Mashhad University of Medical Sciences, Iran, and published in 2017, aimed to evaluate the efficacy of concomitant treatment with (MTX) plus MM in comparison with monotherapy with MTX only in psoriatic patients. 30 psoriatic patients (20 to 50) years old with a Psoriasis area and severity index (PASI score) > 10 that had not received MTX, phototherapy for at least 2 months, were divided randomly into two groups (A and B). Both groups were given oral MTX (0.2–0.3 mg/kg/week) for 12 weeks. In addition, Group B received one tablet of MM supplement daily. (PASI) was considered for efficacy of treatment with a defined reduction in PASI score by 75% from baseline and after 12 weeks of therapy, also the plasma concentrations of IL-1 $\beta$  and TNF- $\alpha$  level were measured using the enzyme linked immunosorbent assay (ELISA) technique. (9)

As a result, the PASI score decreased significantly in both treatment groups from the baseline to the end of 12 weeks of treatment ( $p = 0.001$ ). Although both groups had a similar PASI score ( $p = 0.69$ ) before the study, the PASI score decreased significantly differently between the groups after 12 weeks ( $p = 0.04$ ). The analysis showed that this significant reduction was to the benefit of Group B compared to Group A ( $p = 0.045$ ), also 13 (86.6%) patients in Group B and 8 (53.3%) patients in Group A attained a mild PASI score ( $\leq 10\%$  body involvement). IL-1 $\beta$  and TNF- $\alpha$  levels were significantly decreased in favor of Group B ( $p < 0.05$ ). There was a significant correlation between changes in both IL-1 $\beta$  and TNF- $\alpha$  levels and PASI score after the study ( $p < 0.05$ ). (9)

In conclusion, a significant decrease in IL-1 $\beta$  and TNF- $\alpha$  through better clinical response in patients that were treated with MTX plus MM compared to those treated with MTX only. Furthermore, double-blind randomized trials with a larger sample size are highly suggested to confirm or reject these results.

## References:

1. Nestle FO, Kaplan DH, Barker J. Psoriasis. *N Engl J Med*. 2009;361:496–509.
2. Sabat R, Philipp S, Höflich C, Kreutzer S, Wallace E, Asadullah K, et al. Immunopathogenesis of psoriasis. *Exp Dermatol*. 2007;16:779–98.
3. Nickoloff BJ, Qin J-Z, Nestle FO. Immunopathogenesis of psoriasis. *Clin Rev Allergy Immunol*. 2007;33:45–56.
4. Herman S, Zurgil N, Deutsch M. Low dose methotrexate induces apoptosis with reactive oxygen species involvement in T lymphocytic cell lines to a greater extent than in monocytic lines. *Inflam Res*. 2005;54:273–80.
5. Saleh A, Abuhilal M, Cheung B. Methotrexate in psoriasis: from A to Z. *J Turk Acad Dermatol*. 2010;4:04101r.
6. Dahlman-Ghozlan K, Ortonne JP, Heilborn J, Stephansson E. Altered tissue expression pattern of cell adhesion molecules, ICAM-1, E-selectin and VCAM-1, in bullous pemphigoid during methotrexate therapy. *Exp Dermatol*. 2004;13:65–9.
7. Duarte G, Barbosa L, Rosa M. The management of psoriasis through diet. *Psoriasis: Targets and therapy*. 2012;2:45–53.
8. Millsop JW, Bhatia BK, Debbaneh M, Koo J, Liao W. Diet and psoriasis, part III: role of nutritional supplements. *J Am Acad Dermatol*. 2014;71:561–9.
9. Yousefzadeh H, Jabbari Azad F, Banihashemi M, Rastin M, Mahmoudi M. Evaluation of psoriasis severity and inflammatory responses under concomitant treatment with methotrexate plus micronutrients for psoriasis vulgaris: a randomized double blind trial. *Acta Dermatovenerol Alp Pannonica Adriat*. 2017 Mar;26(1):3-9.

DONE BY PHARM.D STUDENT: HANEEN AL-BREZAT  
SUPERVISED BY PHARM.D: ESHRAQ AL-ABWEENY