

## Folate with methotrexate: big benefit, questionable cost

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SIR, In their recent report<sup>1</sup> Salim et al. present a randomized, double-blind, placebo-controlled exploratory study investigating the impact of folic acid supplementation on the efficacy of methotrexate (MTX) in the treatment of psoriasis. There is abundant evidence that concomitant folate supplementation with either folic or folinic acid can reduce the incidence of MTX-related side-effects and allows for greater drug tolerability.<sup>2,3</sup> Importantly, multiple studies in patients with rheumatoid arthritis have failed to show a difference in MTX efficacy when folate is added. The present study is a well-designed, albeit small trial ( $n = 22$ ) comparing the addition of folic acid vs. placebo to the drug regimen of patients taking MTX for stable psoriasis. The mean Psoriasis Area and Severity Index (PASI) score rose from 6.4 at baseline to 10.8 after 12 weeks of therapy in the folic acid group, with the largest change occurring at week 3 when one subject presented with a 'marked flare' of psoriasis. The placebo arm mean PASI score was relatively stable, moving from 9.8 to 9.2 after 12 weeks. The observed difference in mean PASI change between the two groups was statistically significant ( $P < 0.05$ ). The authors conclude that daily supplementation of 5 mg folic acid reduces the efficacy of low-dose MTX in the treatment of psoriasis.

While the trends in PASI scores were different between the treatment groups in this trial, the clinical relevance of these small changes is unclear. Furthermore, the observed differences in disease severity could be due to multiple potential confounding factors. The demographics, MTX treatment history and baseline disease severity were notably different between the two study arms. Specifically, the placebo arm had a younger mean age (54 vs. 60 years), higher mean baseline PASI score (9.8 vs. 6.4), longer mean duration of prior MTX use (99 vs. 47 months) and higher mean cumulative MTX dose (4.2 vs. 2.1 g). Furthermore, all patients in the

study were using individual, concurrent, uncontrolled topical therapies. In addition, patient compliance as assessed by study medication counts was higher in the placebo arm (90% vs. 78%). Finally, and most importantly, the baseline PASI scores of both groups were low and therefore susceptible to proportionally large random fluctuations. It is our experience that PASI scores  $< 10$  are unreliable in terms of measuring and comparing disease severity. Furthermore, the dose of folic acid used in this study was higher than the 1 mg daily<sup>2</sup> or 5–10 mg weekly<sup>3</sup> often recommended for the reduction of MTX side-effects. For the above reasons, it is not clear that folic acid use has a clinically significant impact on MTX efficacy in psoriasis, and future large-scale studies are needed. We agree with the authors that even if folate does reduce the efficacy of MTX, the associated reduction in MTX toxicity could provide a net benefit to folic acid supplementation. In light of the well-established benefits of folate supplementation and debatable effects on efficacy, folate supplementation is still warranted when treating psoriasis patients with MTX.

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## References

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- 2 Strober BE, Menon K. Folate supplementation during methotrexate therapy for patients with psoriasis. *J Am Acad Dermatol* 2005; **53**:652–9.
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Conflicts of interest: none declared.

## News and Notices

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### International Short Course on Dermoscopy

Date: July 17–21, 2007

Venue: Department of Dermatology, Medical University of Graz, Auenbruggerplatz 8, A-8036 Graz

Organizer: Medical University of Graz, Department of Dermatology

Type of Event: Course

Language: English

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Description: This course is for residents in dermatology and for dermatologists from universities or private practice as well as for physicians or nurses interested in the diagnosis of pigmented skin lesions.