PHARMACOTHERAPY

Is monitoring methotrexate polyglutamates useful?

Given the wide variation in individual responses to methotrexate therapy for rheumatoid arthritis (RA), factors that predict which patients will respond to this treatment and at what dose have obvious clinical potential. Concentrations of the products of intracellular glutamation of methotrexate, red blood cell (RBC) methotrexate polyglutamates, have previously been shown to negatively correlate with disease activity in patients with RA. In contrast to these results, however, new research by Stamp *et al.* found no relationship between these two parameters.

“The clinical significance of our results is uncertain, but they suggest there is a group of patients in whom disease remains active despite higher methotrexate doses and higher drug concentrations,” says lead investigator Lisa Stamp.

Consistent with previous studies, the results did show a positive correlation between increased RBC folate concentrations and increased disease activity. “It is possible,” says Stamp, “that folate concentrations are more important

than methotrexate polyglutamate concentrations in determining drug response.”

The study of 192 patients receiving long-term methotrexate therapy was designed to mimic real-life clinical practice, with participants being assessed at a single visit for disease activity, adverse effects related to therapy and relevant blood tests. However, this cross-sectional design precluded comparisons between different dosing strategies and responses; other limitations to the study include the relatively small sample size and heterogeneity within the patient population.

“A prospective, longitudinal, well-powered study carefully examining the effects of RBC folate and methotrexate polyglutamate levels on methotrexate efficacy and toxicity may help clarify some of these issues,” says Prabha Ranganathan of Washington University School of Medicine. “A test to predict methotrexate efficacy and toxicity will be a great advance in rheumatology and welcomed by rheumatologists as

methotrexate remains the gold standard of therapy in RA.”

Sarah Price

Original article Stamp, L. K. *et al.* Methotrexate polyglutamate concentrations are not associated with disease control in rheumatoid arthritis patients receiving long-term methotrexate therapy. *Arthritis Rheum.* 62, 359–368 (2010)