

Abstract

J Rheumatol. 2009 Mar;36(3):539-45.

Metaanalysis of methylenetetrahydrofolate reductase (MTHFR) polymorphisms affecting methotrexate toxicity.

Fisher MC, Cronstein BN.

New York University, Hospital for Joint Diseases, New York, NY 10003, USA.

OBJECTIVE: Methotrexate (MTX) is an effective therapy for rheumatoid arthritis (RA) but it is also associated with toxicity. Pharmacogenetics is the systematic evaluation of the role of genetic differences in the efficacy and toxicity of therapeutic interventions. Because the results of small pharmacogenetic studies are often misleading, we undertook a metaanalysis of published studies to determine the role of polymorphisms in the therapeutic efficacy and toxicity of MTX.

METHODS: A search of PubMed produced 55 publications, which were then reviewed for relevance to MTX toxicity and efficacy in patients with RA. To ensure that no study was missed, each polymorphism found was then entered as an independent search string and all results were reviewed again.

RESULTS: Only 2 polymorphisms [C677T and A1298C in methylenetetrahydrofolate reductase (MTHFR); total 8 studies] relevant to MTX metabolism and efficacy had sufficient data to allow a metaanalysis of their association with toxicity; there was no polymorphism with sufficient data to perform a metaanalysis of efficacy. In a fixed-effects model, the C677T polymorphism was associated with increased toxicity (OR 1.71, 95% CI 1.32-2.21, $p < 0.001$). The A1298C polymorphism was not associated with increased toxicity (OR 1.12, 95% CI 0.79-1.6, $p = 0.626$).

CONCLUSION: As pharmacogenetics evolves, more data are needed to assess the role of various polymorphisms for drug efficacy and toxicity. These results illustrate the paucity of reliable pharmacogenetic data on a commonly used antirheumatic drug and the potential role of pharmacogenetics in tailoring drug therapy for an individual patient.

PMID: 19208607

FREE FULL TEXT

