Pediatric Rheumatology

Poster presentation

Single-nucleotide polymorphisms in the folate pathway are associated with response to methotrexate treatment in juvenile idiopathic arthritis

MW Heijstek*[1], NM Wulffraat[1], Y Eken[1], SMF Pluijm[2], CMA Rademaker[1] and R de Jonge[2]

Address: [1]University Medical Center Utrecht, dept. of pediatric immunology, Utrecht, Netherlands and [2]Erasmus Medical Center, Rotterdam, USA
* Corresponding author

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Background

Insight into factors associated with outcomes of methotrexate (MTX) treatment may contribute to more individualized treatment of juvenile idiopathic arthritis (JIA). In this study, associations of SNPs in genes encoding folate pathway enzymes with MTX efficacy and adverse effects in JIA patients were evaluated.

Methods

Genotypes were determined in an observational cohort of 183 JIA patients that had been systematically followed at 3 months intervals. The following SNPs were determined: methylenetetrahydrofolate reductase (MTHFR) 677C>T and 1298A>C, methionine synthase reductase (MTRR) 66A>G, thymidylate synthase (TS) 2R/3R and Reduced Folate Carrier (RFC) 80G>A. MTX efficacy and adverse effects were compared among genotypes during the first year of treatment and at long-term follow up.

Results

The MTHFR 1298CC variant was associated with MTX efficacy (OR 3.3, 95%-CI 1.0–10.2) after 3 months, while MTHFR 677T-allele carriers had a lower chance of early good clinical response (OR 0.4, 95%-CI 0.2–0.9). The MTHFR 1298C-allele was also associated with MTX efficacy after long-term follow-up (OR 1.8, 95%-CI 1.0–3.4).

Regarding adverse effects, MTHFR 677TT was associated with liver toxicity in the first year of MTX use (OR 10.4, 95%-CI 2.2–48.6). MTRR 66G-allele carriers were more likely to have gastrointestinal intolerance during the first 3 months of treatment (OR 9.9, 95%-CI 1.3–76.9).

Conclusion

Polymorphisms in the MTHFR and MTRR genes are associated with methotrexate efficacy and adverse effects. Genotyping may add in predicting response to MTX treatment in JIA patients.