

Summary

Objective: To investigate whether methylenetetrahydrofolate reductase (MTHFR) C677T and A1298C polymorphisms and erythrocyte concentration of methotrexate (EMTX) could serve as predictors of methotrexate (MTX) efficacy and toxicity in patients with juvenile idiopathic arthritis (JIA).

Methods: Genetic analyses and EMTX and folate assessment were performed in 69 JIA patients treated with MTX and classified as full responders (n=51, disease inactivity) or nonresponders (n=18, less than 30 % improvement in paediatric ACR30 criteria while on 15 mg/m²/week parenteral MTX for at least 3 months).

Results: Nonresponders were treated with the higher median MTX dose (17.2 vs 12.6 mg/m²/week, P<0.0001), and accumulated more EMTX (217 nmol/L vs 106 nmol/L, P<0.02) and erythrocyte folates (763 nmol/L vs 592 nmol/L, P=0.052) than responders. Analysis of MTHFR allele and genotype frequencies in relation to response failed to detect association. The frequency of any adverse effect was 29.4 % in responders and 33.3 % in nonresponders (P=0.77). The frequency of 677T allele was elevated in patients with adverse effects (52.4 % vs 20.9%, OR=3.88; 95% CI: 1.8–8.6; p<0.002). The probability of any adverse effect was significantly higher in patients with 677TT when compared to 677CC genotype (OR=55.5; 95-% CI: 2.9–1080; p<0.001).

Conclusion: MTHFR genotyping may have a predictive value for the risk of MTX associated toxicity in JIA patients. Despite the lack of therapeutic effect, nonresponders accumulate adequate concentrations of EMTX.