Subclinical markers predict relapse in juvenile idiopathic arthritis post methotrexate withdrawal

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Elevated levels of the inflammatory biomarkers Myeloid Related Protein (MRP*) 8/14 predict an increased risk of relapse following withdrawal of methotrexate (MTX) therapy in children with juvenile idiopathic arthritis (JIA) who have achieved inactive disease status, according to a new study.

Effective treatment options are available to treat rhematic diseases, many of which have the potential to induce remission, defined as absence of signs or symptoms of disease. While there is evidence-based advice regarding when to initiate therapy in rheumatic diseases, there is no specific guidance on the timing of treatment withdrawal once a state of remission on medication is achieved. While this holds true for many autoimmune disease (such as Rheumatoid Arthritis, Crohn's disease, Ulcerative Colitis, or Autoimmune Hepatitis), in the case of MTX therapy for JIA, a continuation of MTX for 12 to 24 months after induction of remission has been proposed by researchers.1

The risk of relapse in JIA patients, once MTX is discontinued, is approximately 50%.2 However, the results of this study have shown that continuing MTX therapy past the point of remission does not affect the risk of relapses after withdrawal of therapy. Clinical (disease subtype, duration or dosage of therapy, duration of MTX therapy) or standard laboratory tests (c-reactive protein and erythrocyte sedimentation rate as measurements of inflammation) could not differentiate between patients

at-risk for relapse and those without this risk. However, MRP8/14 levels were significantly higher at MTX withdrawal in remission in those patients who subsequently developed relapses (715±140 ng/ml) compared to patients with stable remission (400±105 ng/ml; p=0.003).

Levels of MRP8/14 were especially high in patients with relapses occurring within 6 months, compared to 12 months. (955±270 ng/ml; p

Professor Dirk Foell of the University of Muenster, Germany, who conducted the study, said: "Methotrexate is effective in children with JIA and can induce a status of inactive disease. This is the first controlled trial analyzing the necessary time of treatment continuation once remission is achieved in a rheumatic disease. Our study shows that patients with elevated levels of MRP 8/14 may specifically benefit from prolonged treatment and also that a longer duration of MTX therapy after achieving remission does not influence the risk of relapse on patients with JIA. The results of our research help to make the case for the tracking of levels of biomarkers as predictors of treatment responses in this unique patient population."

In the PRINTO** study, 364 JIA patients with inactive disease for at least 3 months were randomised to receive additional MTX for either 6 or 12 months. Serum sample analysis using ELISA (Enzyme-Linked Immunosorbent Assay) was conducted in 188 patients to track MRP8/14 levels at 3 month baseline, and again at either 6 or 12 months according to study protocol. Patients were followed-up for at least 12 months after MTX discontinuation.

A log-rank analysis confirmed the differences in relapse rates between patients with MRP8/14 levels of 900ng/ml or above, compared to those with lower levels (p

At baseline, demographic and clinical characteristics were well balanced

and all patients had inactive disease status. 59 (31%) had the JIA subtype of persistent oligoarthritis, 27 (14%) extended oligoarthritis, 64 (34%) polyarthritis RF-negative, 10 (5%) polyarthritis RF-positive, 12 (6%) systemic and 16 (9%) other JIA subtypes. Patients had previously been treated with MTX at a dose of 11.6±2.8 mg/m2/week for 2.3±2.1 years. The overall rate of flares was 92/188 (49%) patients.

JIA is the most common inflammatory autoimmune childhood disease, affecting approximately 1 in 1,000 children. Despite advances in diagnosis and treatment options, it remains a chronic condition for most affected children with a significant disease burden.

Source: European League Against Rheumatism