Pediatric Rheumatology

Poster presentation

Methotrexate does not primarily affect Foxp3+ regulatory T cells in poly-articular juvenile idiopathic arthritis

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Background

Methotrexate (MTX) is the most widely used disease modifying anti-rheumatic drug in juvenile idiopathic arthritis (JIA), inducing long-lasting remission in many patients. It usually takes 6–12 weeks before anti-inflammatory effects are clinically noticed, suggesting modulatory effects on T cells. We examined the effect of MTX on (induced) regulatory T cells (T_{reg}) in JIA.

Materials and methods

We sampled 11 patients with active poly-articular JIA (poly-JIA) prior to and 3–6 months after initiating MTX. Moreover, 11 poly-JIA patients in remission on MTX were sampled prior to and 3–6 months after withdrawal of MTX. Frequency and characteristics of Foxp3+CD4+T_{reg} and effector T cell subsets were analyzed by flowcytometry. Function of T_{reg} was evaluated in suppression assays. Responses to human heat shock protein 60 (HSP60) were studied in proliferation assays.

Results

MTX-treatment resulted in a decrease of Foxp3+CD4+ T_{reg} (3,7% to 2,8% of CD4+T cells). Suppressive function of T_{reg} was not altered by MTX. Interestingly, stimulation with anti-CD3 resulted in increased proliferation of CD4+CD25- effector T cells after 3 months MTX compared to pre-MTX. Moreover, proliferative responses to human HSP60 increased after MTX-treatment. The quality of the HSP60-response changed with a less pro-inflammatory cytokine profile in supernatants after MTX-treatment. When JIA-patients in remission on MTX-treatment withdrawed MTX, the frequency of T_{reg} increased (3,2 to 3,8% of CD4+ T cells) but their suppressive function remained unchanged.

Conclusion

MTX seems to exert its immune-modulating effects not by affecting Foxp3+ T_{reg}. Instead, we observed changes in effector T cells and HSP60 specific T cells.