- [2] Sanz I. *Nat Rev Rheumatol* 2016;12(12):700–2.
 [3] Omri HE, et al. *Clin Med Insights Blood Disord* 2015;8:1–7.
 [4] Fervenza FC, et al. *Clin J Am Soc Nephrol* 2010;5(12):2188–98.
 [5] Lahiri M, et al. *Best Pract Res Clin Rheumatol* 2015;29(2):290–305.
 [6] Thiel J, et al. *Arthritis Res Ther* 2017;19(1):101.
 [7] Einarsson JT, et al. *Clin Rheumatol* 2017; Dec;36(12):2743–2750.

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THU0555

GUIDELINES FOR JUVENILE IDIOPATHIC ARTHRITIS MANAGEMENT: IS THERE A ROOM FOR COMBINED METHOTREXATE AND LEFLUNOMIDE THERAPY IN THE TREATMENT RECOMMENDATIONS

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Objectives: To set recommendations for the management of children and adolescents living with JIA and assess whether there is a room for combined methotrexate and leflunomide therapy, adopting treat to target approach.

Methods: the treatment guidelines were developed based on systematic review, local studies, formal consensus and feedback. Initiation of methotrexate or leflunomide was recommended for polyarticular JIA children who, after 3 month of treatment, did not respond to methotrexate or leflunomide monotherapy, or those whose DMARD dose could not be optimised; a new management step was introduced where a combination of both medications was administered. This was a multicentre study including 76 JIA patients who had been treated with the combination of methotrexate plus leflunomide. All patients were classified according to the International League of Associations for Rheumatology (ILAR) criteria. Recorded data included: demographics, JIA subtype, reason for starting combined treatment, treatment duration, withdrawals, causes of discontinuation, efficacy and safety. Patients were classified as “responders” or “non-responders”. Responders were those patients with articular improvement $\geq$ ACR-Paediatric 30 and/or ocular improvement according to the Standardisation of Uveitis Nomenclature Working Group (SUN) definitions. Efficacy was assessed at 3, 6- and 12 month and outcomes were compared to methotrexate monotherapy.

Results: Out of the 76 children there were, oligoarthritis (34%), polyarthritis (31%), systemic JIA with synovitis (>4 joints) (20%), and psoriatic arthritis (15%). Mean age at initiation of combined therapy 10.2 ± 3.4 years, mean disease duration is 9.4 ± 4.8 months. The combined therapy was superior to methotrexate alone and did not significantly increase the rate of adverse events. ACR-Ped 30 was achieved in 64% at 3 months, 75% at 6 months. This was superior to methotrexate alone (37.3% and 53.8%; $p < 0.01$ at 3- and 6 months respectively). At 1 year, 81% reached Ped 30, 74.5% reached ACR-Ped 50, 64% achieved ACR-Ped 70 whereas 51% met ACR-Ped 90 criteria. There were no serious adverse events. One of the two DMARDs was stopped in 51% of the children; of them: 25% were due to adverse events, clinical remission in 25% whereas 21% were switched to anti-TNF therapy according to guidelines due to inefficacy or loss of efficacy. All patients who had had uveitis responded well and achieved clinical remission.

Conclusions: For the children with polyarticular JIA who did not respond to monotherapy with methotrexate, combination of methotrexate and leflunomide treatment appeared to be efficacious and maintain a durable response. The current recommendation would be to use combined methotrexate and leflunomide in children with polyarticular JIA who are either intolerant to higher methotrexate doses or who did not have a satisfactory response to methotrexate. The combination should be considered prior to the use of a biologic agent.

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THU0556

IMPACT OF METHOTREXATE ON GROWTH IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is a heterogeneous group of chronic inflammatory disease which could be responsible for functional impairment and severe growth disturbance. Conventional disease-modifying antirheumatic drugs, such as methotrexate (MTX), may improve growth velocity especially by regulating systemic inflammation.

Objectives: The objective of this study was to evaluate the effect of MTX on growth parameters in pre-pubertal children with JIA and to determine the factors affecting the growth velocity.

Methods: We assessed height and changes in the height standard deviation score (SDS) at disease onset, at the onset of MTX and at the last follow-up visit in a cross-sectional study of JIA children. All patients were pre-pubertal when MTX began and were followed for at least 6 months afterward. We compared growth parameters (height, growth rate, weight and body mass index (BMI)) in responders and non-responders to MTX. The growth rate was defined as the number of millimetres of height acquired during 1 year. Associations between changes in the height SDS and discrete variables were evaluated using chi-square or Fisher's exact tests. The significance level was set at 0.05.

Results: We enrolled 36 pre-pubertal children with JIA (24 boys and 12 girls) who had been treated with MTX orally. Median patient age was 6.2 years^{4–13} at the onset of MTX and 8.4 years [6.1–14.9] at the latest follow-up. The median disease duration was 2.7 years [2.5–5.3]. Twenty-one patients (58.3%) had oligoarticular JIA, 2 patients (5.5%) had systemic JIA, 10 (27.7%) had polyarticular JIA and 3 (8.3%) had enthesitis-related arthritis. Nineteen children (52.7%) had received corticosteroids during an average period of 1.7 years [0.6–3] with a mean of 10 mg/day of prednisone or equivalent. The median duration of MTX at the latest follow-up was 3.1 years [0.62–5.5] with a mean MTX dose of 10 mg/m²/week.^{10–15} Twenty-eight patients responded to MTX treatment and 8 did not. There were no significant differences between the responders and non-responders for age at treatment initiation, disease duration and mean MTX dose. At MTX onset, no significant differences between the two groups in terms of height ($p = 0.52$), growth rate ($p = 0.08$), weight ($p = 0.74$) and BMI ($p = 0.9$) were found. One year after MTX therapy, mean height (0.2 versus -1.1 ; $p = 0.03$), mean growth rate (0.5 versus -2.9 SDS; $p = 0.01$), mean weight (0.4 versus -2.3 SDS; $p = 0.01$) and mean BMI (0.6 versus -1.9 ; $p = 0.04$) were significantly higher in the responder group than in non responders, respectively. At the latest follow-up, this increase was significantly maintained for growth rate ($p = 0.001$) and height ($p = 0.002$) in the responder group. In the multivariate analysis, patients who required more than 10mg/m²/week of MTX, systemic JIA and patients with reliance on steroids had a significantly lower growth velocity after the onset of MTX ($p < 0.01$, $p = 0.02$, $p = 0.02$ respectively).

Conclusions: In our study, the increase in growth parameters in pre-pubertal children with JIA was associated with a better control of the disease activity under MTX therapy.

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THU0557

THERAPEUTIC DRUG MONITORING OF BIOLOGICALS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA): AN OVERVIEW OF CURRENT PRACTICE IN ANTI-TNF THERAPY

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Background: Juvenile idiopathic arthritis (JIA) is the most prevalent paediatric rheumatic disease.¹ Long term complications include physical disability and a decreased quality of life.^{2,3} Since the introduction of anti-TNF drugs for JIA, its prognosis has improved significantly.¹ Personalised medicine is the next step to improve treatment in JIA. Anti-TNF trough levels and demonstration of the presence of anti-drug antibodies (ADA) could help individualise treatment decisions in JIA patients, but evidence supporting this is missing.

Objectives: To describe cross-sectional data of anti-TNF trough levels and ADA, combined with decision effects, in children with JIA.

Methods: Patients' records in children with JIA using etanercept, adalimumab or infliximab were retrospectively checked for measurements of anti-TNF trough levels and ADA. Anti-TNF trough concentrations and ADA were measured using an enzyme-linked immunosorbent assay (ELISA) and antigen-binding test. Data on age, sex, JIA subtype, reason for testing and the decision effect of trough level or presence of ADA on the current therapy were collected.

Results: Eighty-one anti-TNF trough levels were measured in 45 children with JIA. A wide variety of anti-TNF trough levels was found. Therapeutic drug concentrations, according to adult ranges in RA and IBD,^{4,5,6} were found in 11 (58%) patients on etanercept (n=19), 2 (14%) on adalimumab (n=14) and 8 (17%) on infliximab (n=48). Four patients on adalimumab and one patient on infliximab showed ADA. All of these five patients had non-detectable drug trough levels. Reasons for testing trough level and/or presence of ADA were loss of response (20%), partial or no response (40%), measurement after dosage increase (2%), remission (17%), uveitis flare (9%) and allergic reaction (11%). Treatment decisions were influenced by trough levels in 70/81 (86.4%) of measurements and in 5/5 (100%) of patients with ADA.

Abstract THU0557 – Figure 1. Dose vs Concentration (etanercept, adalimumab, infliximab)

Conclusions: Measuring anti-TNF trough levels and ADA was a valuable tool in making personalised treatment decisions in JIA. Treatment changes included dose/frequency increase, or stopping and switching treatment in the presence of ADA combined with undetectable drug levels. More data are needed to access optimal therapeutic drug levels in anti-TNF treatment in JIA and to implement this strategy more widely.

REFERENCES:

- [1] Blazina S, et al. *Paediatr Drugs* 2016;18(6):397–412.
- [2] Tambralli A, et al. *J Rheumatol* 2013;40(10):1749–55.
- [3] Haverman L, et al. *Rheumatology (Oxford)* 2012;51(2):368–74.
- [4] Kneepkens EL, et al. *Ann Rheum Dis* 2015;74(10):1825–9.
- [5] Pouw MF, et al. *Ann Rheum Dis* 2015;74(3):513–8.
- [6] Singh N, Dubinsky DC. *Gastroenterol Hepatol (NY)* 2015;11(1): 48–55.

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THU0558

INCREASED FREQUENCY OF FEBRILE SEIZURES IN TWO PERIODIC FEVER SYNDROMES: FAMILIAL MEDITERRANEAN FEVER AND PFAPA SYNDROME

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Background: Fever and the fear of febrile seizure risk in parents are a common reason that lead parents to seek care in childhood emergency departments. The most frequently seen periodic fever syndromes in Turkey are periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis (PFAPA) syndrome and familial Mediterranean fever (FMF). There is lack of data regarding the frequency of febrile seizures in periodic fever syndromes.

Objectives: To document the frequency of febrile seizure in patients with Familial Mediterranean Fever and PFAPA syndrome.

Methods: Patients with FMF and PFAPA, who were diagnosed according to Turkish paediatric FMF diagnostic criteria and Marshall criteria, were enrolled to the study. Past medical history of all subjects from postnatal six months to 6 years of age were assessed in terms of febrile seizure. Clinical, demographic and laboratory data of both patient groups were obtained from patient files. The frequency of febrile seizure in both disease groups was compared with the prevalence in healthy children of a previous Turkish study.

Results: A total of 417 FMF and 157 PFAPA subjects were recruited to the study with a female frequency of 49.9% and 42.8%, respectively. The mean age of the FMF and PFAPA patients at study time was 12.4±4.5 years and 5.3±2.1 years, respectively. The mean age at disease onset was 5.1±3.8 (IQR: 2–7) years in FMF group, whereas it was 21±16.5 months (IQR: 10–30) in PFAPA group. The frequency of febrile seizure in FMF and PFAPA syndrome was similar (8.4% versus 8.6%, p>0.05). Among the subjects with febrile seizure, 42.9% (n=15) in FMF group and 30.8% (n=4) in PFAPA group underwent electroencephalography. The EEG result of all subjects were reported to be normal. While 8 subjects with febrile seizure (22.9%) in FMF group required anticonvulsant therapy, 2 patients (15.4%) in PFAPA group used anticonvulsant treatment. Among the PFAPA subjects with febrile seizure (n=13), 53.9% (n=7) underwent tonsillectomy. Thereafter, 85.7% (n=6) of the patients with tonsillectomy never experienced a febrile seizure.

Both the FMF and PFAPA syndrome group were found to have a higher frequency of febrile seizure compared with the healthy subjects of the previous Turkish study (FMF versus healthy children: 8.4% versus 3.2%) (PFAPA syndrome versus healthy children: 8.6% versus 3.2%); and this was statistically significant (p<0.001). However, the frequency of febrile seizure in FMF did not differ from the patients with PFAPA syndrome (8.4% versus 8.6%, p>0.05).

Conclusions: Compared to the healthy children, the frequency of febrile seizure in FMF and PFAPA syndrome was significantly increased. The recurrent fever, which is the main shared manifestation of these two diseases, is possibly a trigger for febrile seizure. This increased frequency of febrile seizure in both periodic syndrome seems to be a result of recurrent fever, other than a neurologic involvement of the FMF itself.

REFERENCES:

- [1] Barut K, Sahin S, Adrovic A, Sinoplu AB, Yucel G, Pamuk G, et al. *Familial Mediterranean fever in childhood: a single-center experience. Rheumatology international* 2018;38(1):67–74.
- [2] Yakinci C, Kutlu NO, Durmaz Y, Karabiber H, Egri M. Prevalence of febrile seizure in 3637 children of primary school age in the province of Malatya. *Turk J Trop Pediatr* 2000;46:249–50.

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THU0559

THE PERFORMANCE OF THE NEWLY PROPOSED EULAR/ACR CLASSIFICATION CRITERIA IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS-A PRELIMINARY STUDY

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Background: The sensitivity and specificity of the ACR-1997 and SLICC-2012 classification criteria in juvenile-onset systemic lupus erythematosus (SLE) are already studied. In previous reports, the main limitations of the ACR-1997 and