Background: exercise is one of the main factors for the successful treatment of obesity. It is known that with increasing age, muscle strength (sarcopenic obesity) decreases in an obese patient, which can lead to early disability and an increased risk of falls. Regular exercise therapy increases the functional capacity of the cardiovascular system, prevention of obesity among the population, as well as treatment for persons with sarcopenia and obesity. Therefore, it is relevant to study muscle function in obese patients while using kinesiotherapy.

Objectives: was to estimate the affect of complex 3-week treatment with 4 kinesiotherapy methods on body weight loss and muscle function in patients with obesity.

Methods: 80 men and women aged 21-69 years old with alimentary obesity were enrolled in the study (mean age 52.4±11 years, weight 111.3±24.5 kg, BMI 40.3±8.1 kg/m², waist circumference WC 113.4±16 cm, hip circumference HC 124.2±16 cm). The complex kinesiotherapy administered daily for 3 week and included interactive sensorimotor trainings on double unstable platform, kine-siohydrotherapy in a pool, special complex of physical exercises in a gym and ergocycle trainings. Weight, WC, HC, fall number for last 3 weeks were measured at baseline and after the treatment was completed. Muscle strength and walking speed functional tests results assessment (10-meters-walk test, Up-and-go test, 4 special tests for back and abdomen muscle endurance to static and dynamic loading) were performed at baseline and in 3 weeks.

Results: there was a significant reduction in body weight (111.3±24.4 kg at baseline vs 107.9±23.1 kg in 3 weeks; p=0.000), in BMI (40.3±8.1 vs 39.1±7.7 kg/m²; p=0.000), in WC (113.4±15.9 vs 109.2±15.1 cm; p=0.000) and in HC (124.1±15.5 vs 119.7±14.1 cm; p=0.000) in treated obese patients. 10-meters-walk speed increased from 0.84±0.15 m/sec at baseline to 0.88±0.17 m/sec in 3 weeks (p=0.000). Up-and-go test results improved from 8.4±2.1 to 7.9±2.09 sec (p=0.000). We registered statistically significant elevation of the endurance to static loading in abdomen muscles from 13.1±9.7 to 16.49±12.8 sec (p=0.000) and in back muscles from 14.8±11.9 sec to 18.6±14.9 sec (p=0.000). The endurance to dynamic loading increased in abdomen muscles from 29.9±11.2 to 34.84±11.93 times (p=0.000) and also in back muscles from 9.1±7.4 to 12.2±9.2 times (p=0.000). Fall number markedly decreased from 0.14 ±0.34 at baseline to 0.0 (95%CI: 0.02; 0.25) after completion of treatment.

Conclusion: investigated complex treatment with 4 kinesiotherapy methods promotes body weight loss, WC and HC reduction in obesity. 3-week special training of obese patients is associated with increasing in gate speed and lower extremities muscle strength, and it also causes improvement in static and dynamic loading endurance of back and abdomen muscles. Those changes may probably improve balance function and decrease risk of falling in obese patients.

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Pediatric Rheumatology – Basic and translational science

POS0067

HIGH DEGREE OF INTER-PATIENT HETEROGENEITY IN SYNOVIOCYTE HYPERPLASIA AND IMMUNE CELLS INFILTRATION IN THE SYNOVIUM OF JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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Background: Increasing evidence indicates that synovial tissue analysis can deliver pathophysiological insights but also individual clinically-relevant information in adult-onset inflammatory arthritides. Little is known about synovial pathology in juvenile idiopathic arthritis, especially regarding inter-patient variability of histopathological features.

Objectives: To assess the heterogeneity of main synovial features (synovio-cyte hyperplasia and immune cells infiltration) in juvenile idiopathic arthritis (JIA) patients and a cohort of young adults (<30 years old) with early rheumatoid arthritis (RA).

Methods: Synovial biopsies were sampled using needle arthroscopy or ultrasound (US) guided biopsy during intra-articular joint injection. Tissue was embedded in paraffin then sections were stained with hematoxylin and eosin. Synovio-cyte hyperplasia (SH) and immune cells infiltration (ICI) was assessed by an experienced pathologist on a 0 – 3 scale where 0 represents the absence of the feature and 3 the highest level.

Results: 34 JIA patients (age (median ±SD): 15.5±6.47 years, oligo-articular JIA n=28/34, polyarticular JIA n=6/34, ANA-RF-ACPA positivity=56%-10%-3%) and 22 RA (age (median ±SD): 24.3±2.6 years, ANA-RF-ACPA positivity=10%-36%-32%) patients were included. Synovial tissue was obtained from knee (n=49/56), wrist (n=4/56) or metacarpophalangeal/intercarpalphalangeal joints (n=3/56), using US guided biopsy in 27% of patients and needle arthroscopy in 73%.

Individual scores of SH and ICI were correlated in both JIA (Spearman's r=0.503, p value=0.0024) and RA (Spearman's r=0.636, p value=0.0015). There was no significant difference in SH and ICI scores between the 2 groups (SH score (Q25-Q50-Q75) in JIA= 0.5-1.125-2 and in RA = 0.75-2-2; ICI score (Q25-Q50-Q75) in JIA= 1-2-2 and in RA = 0.75-2-2.25). Intra-group variability of the two assessed features was comparable between the 2 groups (SH coefficient of variation: 72.2% for JIA and 68.2% for RA; ICI coefficient of variation: 52.2% for JIA and 71.2% for RA). Within JIA patients, there was no significant difference in SH/ICI scores between groups based on ANA positivity, oligo or polyarticular involvement nor ongoing treatment.

Conclusion: Studying main histological features of synovitis, we found no difference between JIA and young RA patients. Furthermore, we report a similar degree of inter-patient heterogeneity in synovial pathological features of JIA and RA patients. These variations were not explained by common clinical characteristics. Whether they relate to different molecular signatures as suggested in adult RA will be further investigated using bulk tissue RNA sequencing.

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POS0068

HIGH LEVELS OF PORPHYROMONAS GINGIVALIS AND PREVOTELLA INTERMEDIA ANTIBODIES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Idiopathic juvenile arthritis (JIA) is a heterogeneous group of pathologies whose origin remains unknown at present (1). They are characterized by a systemic inflammatory and joint disease affecting children under 16 years of age. The current classification groups the different forms of JIA into 7 distinct entities (systemic forms, polyarticular forms with or without rheumatoid factors, oligoarticular forms, inflammatory arthritis associated with enthesopathies (ERA), arthritis associated with psoriasis and unclassifiable arthritis). Exact etiology of JIA is still unknown. To date, the various hypotheses put forward on the occurrence of JIAs integrate the genetic and environmental framework.

The link between periodontal disease and rheumatoid arthritis (RA) is largely reported. Recently, *Porphyromonas gingivalis* (*P. gingivalis*) infection explained the occurrence of arthritis in rodent and in RA (2). Several studies mention the beneficial effect of *P. gingivalis* treatment on disease activity.

Currently, there are very few studies on the prevalence of *P. gingivalis* in patients with JIA and the possible involvement of the germ in the development of inflammatory joint diseases in the pediatric population(3)(4).

Objectives: The objective of our study is to determine presence of high IgG antibodies against *P. gingivalis* and *Prevotella Intermedia* in a cohort of patients with JIA compared to a control population and to determine variation of level according to sub-classes of JIA.

Methods: Sera were obtained from 101 patients satisfying the ILAR classification criteria for JIA and in 25 patients with two other dysimmune disorders (type 1 diabetes and juvenile inflammatory bowel disease). Level of IgG antibodies against *P. gingivalis* and *Prevotella Intermedia* were obtained by homemade ELISA already used previously (5).

Results: In the JIA group, major children were oligoarthritis (47.5%), polyarthritis represents 31.7% of JIAs, ERA and systemic forms of JIA are respectively 9 and 11%. For the control group, 10 (40%) children had diabetes and 15 (60%) had IBD.

Levels of anti-*P. gingivalis* anti-*Prevotella Intermedia* antibodies were higher in AJI group compared at control groups ($P < 0.01$, $P < 0.05$). These difference are mainly related to oligoarthritis and ERA subsets for both *P. gingivalis* and *Prevotella Intermedia*.

Figure 1. Relative titer of antibodies to *P. gingivalis* and anti *Prevotella intermedia*.*: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$. *P. gingivalis* (control vs oligoarthritis $p = 0.0032$, control vs ERA $p = 0.0092$). *Prevotella intermedia* (control vs oligoarthritis $p = 0.0194$, control vs ERA $p = 0.0039$).

Conclusion: We confirmed high level of anti-*P. gingivalis* and anti-*Prevotella intermedia* antibodies in JIA compared to other inflammatory disorders. For the first time, we observed that this high level was mainly in oligoarthritis and ERA. Further investigations are required to investigate involvement of oral dysbiosis in AJI pathogenesis. As observed in RA, it could be a new way to integrate in JIA therapy management.

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POS0069

INCREASED T CELL RESPONSES, METABOLIC ACTIVITY AND FIBROBLAST INVASIVE CAPACITY IN CHILDREN WITH DOWN'S SYNDROME-ASSOCIATED ARTHRITIS COMPARED TO JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) was thought to be the most common inflammatory arthritis in children (Shih *et al.*, 2019). However an aggressive,

erosive arthritis of little-known immunologic mechanism occurs 20 times more frequently in children with Down's syndrome (Foley *et al.*, 2019).

Objectives: This study was undertaken to characterize immune cell responses and synovial fibroblast invasiveness in children with Down's syndrome-associated arthritis (DA).

Methods: Multiparametric flow cytometric analysis was used to examine peripheral blood T cell, B cell and monocyte populations. In addition, T cell cytokine responses and their metabolic profile in children with DA, JIA, Down's Syndrome (trisomy 21 [T21]), and in healthy controls were assessed. The function of DA primary synovial fibroblasts (FLS) was assessed in response to stimulation with pro-inflammatory mediators alone and in combination (TNF- α , IL-17a, IFN- γ , GM-CSF). The two major energy pathways glycolysis (ECAR) and oxidative phosphorylation (OCR) were quantified by the Seahorse XFe96 Analyser. Migration, adhesion, invasion and cytokine/chemokine secretion were quantified by wound repair scratch assays, Transwell collagen invasion chambers, adhesion binding assays, and ELISAs.

Results: T cell frequencies were higher in DA compared to JIA and T21 in contrast to B cell frequencies which were decreased. T cell responses in DA were characterized by increased frequencies of CD4⁺ and CD8⁺ TNF- α , IFN- γ and GM-CSF producing T cells. The frequency of T peripheral helper (Tph) cells were elevated in children with DA compared to all other groups. In parallel, an increase in their metabolic profile evident by higher phosphorylation of mTOR pathway components AKT, mTOR and S6. Comparison of DA and JIA FLS demonstrated that DA FLS display a more invasive/migratory capacity and are more metabolically active. Based on the increased cytokine responses in DA T cells, we next examined the effect T cell derived cytokines TNF- α , IL-17a, IFN- γ and GM-CSF alone and in combination on DA FLS function. TNF- α , IL-17a and IFN- γ induced IL-6, RANTES and MCP-1 secretion, with no effect observed for GM-CSF. Furthermore, TNF- α and IL-17a induced DA FLS migration and PBMC adhesion to DA FLS. Finally IL17a and IFN- γ potentiated the effect of TNF- α on IL-6 and MCP-1 secretion compared to stimulations alone.

Conclusion: DA is a more common and aggressive form of arthritis compared to JIA. It is characterized by increased T cell responses and a more invasive FLS phenotype compared to that of JIA, with T cell derived cytokine alone and in combination further inducing DA FLS pathogenic mechanisms. These effects mirror the increased erosive disease observed clinically.

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POS0070

POPULATION PHARMACOKINETICS OF INFLIXIMAB IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Higher dosage regimes for Infliximab (IFX) have been described to be effective in partial- or non-responding adults and children with rheumatic disease and appear to be safe (1,2). To optimize IFX treatment in juvenile idiopathic arthritis (JIA) patients, therapeutic drug monitoring (TDM) might be beneficial. To support routine TDM of IFX and dose regimen optimization in JIA patients, more in-depth knowledge of the pharmacokinetic (PK) variability of IFX is needed. Ultimately, as soon as the optimal therapeutic drug ranges will be known, PK model-based simulation can be used to individualize drug dosing recommendations. Individual dosages may be adjusted by taking specific patient characteristics into account that explain inter-patient variability in pharmacokinetics (PK). Inter-patient variability can be quantified and investigated by the population approach.

Objectives: Our hypothesis is that optimizing dosage and frequency of IFX administration for individual patients will improve treatment outcome. In this current study, the population PK for IFX are described for JIA patients.

Methods: Data including IFX trough concentrations and anti-IFX antibodies of 27 JIA patients on IFX maintenance treatment were retrieved from electronic charts. Three population pharmacokinetic models from literature were validated for our dataset using nonlinear-mixed effects modeling program NONMEM (3,4,5). A novel population pharmacokinetic model was developed based on our study data.