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FRI0467

DRUG SURVIVAL AND SAFETY OF BIOLOGICAL THERAPIES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Biological treatment (BT) has changed perspectives of JIA patients. Increasing data from real life experience have been reported.

Objectives: To compare drug survival, safety and efficacy of BT in patients with Juvenile Idiopathic Arthritis (JIA).

Methods: A retrospective observational study was conducted on JIA patients followed in a referral hospital and who had received at least one BT between 1999 and 2019.

Results: 218 BT in 130 JIA patients were analyzed. 67.7% were women with a median age at diagnosis of 8 years old IQR (3-13) and a median age at the beginning of the BT of 15 years old IQR(7.8-21). 21.5% of the patients had uveitis during follow-up. BT were indicated due to: arthritis(73.9%), uveitis(10.1%), arthritis and uveitis(2.7%), systemic activity(8.3%) and macrophage activation syndrome (1.8%). There were 130 BT started in 1st line, 55 in 2nd line, 20 in 3rd line, 10 in 4th line and 3 in 5th line.

The 1st line BT most frequently indicated was Etanercept(ETN) up to 40%, followed by 30% Adalimumab(ADA) and 16.2% Infliximab(INF). The median duration of the 1st line was 51 months IQR (14-109,3). However, 53.8% of the 1st line BT were switched: 28.3% due to adverse events, 25.7% due to 1st failure and 25.7% due to 2nd failure. The BT that were discontinued were: INF (76.2%) and Anakinra (ANAK) (75%) due to adverse events and ETN (59.6%) due to 1st and 2nd failure. 55 patients started a 2nd BT: 43.6% received ADA and 20% Tocilizumab (TCZ) with a median duration of 43 months IQR (12-90). 22 of 55 BT required a change: 75% of ETN and 59% of INF prescribed in 2nd line were discontinued. The causes were: 40% 1st failure, 28% 2nd failure and 12% remission. In 1st line 87.6% of patients received TNF inhibitors, 74% maintained the target in 2nd line. In 3rd line TCZ was the most frequent BT. 71.5% of patients continue on BT. BT was withdrawn in 20 of 130 patients due to remission (40%), adverse events (30%), and pregnancy (10%).

In the analysis by decades, 80 BT (36.7%) were started from 1999 to 2008 and 138 BT (63.3%) from 2009 to 2019. In the 1st decade ETN and INF were the most frequently prescribed and in the 2nd decade, ADA and TCZ ($p < 0.0001$). The 1st BT in the 2nd decade were indicated sooner compared to the 1st decade (1st decade: mean 119.5months SD(109.2); 2nd decade: mean 53.9 months SD(99.7); $p < 0.0001$). In 1st line BT, the BT prescribed in the 2nd decade had a shorter duration than those in the 1st decade (1st decade: mean 84.1 months SD(71.8); 2nd decade: mean 51.7 months SD(5); $p < 0.0001$).

In the survival analysis, TCZ and ADA were the BT with the highest survival ($p=0.001$). Of the 31 patients that started TCZ, 61.3% continue on TCZ, with a median duration of 46 months IQR(25-99) and 36/68(52,9%) still on ADA with a median duration of 61,5 months IQR(30.5-98).

Conclusion: 42.3% of patients required more than one BT. Since the onset of the BT there has been a change in prescription, probably related to the emerge of new targets and the evidence provided by clinical trials and guidelines. TCZ and ADA were the BT with the highest survival rate. On the other hand, INF and ANAK were the ones with the lowest survival rate. The most common causes of BT change in 1st line were adverse events in relation to INF and ANAK. In 2nd line there was a high rate of change in those patients who maintained TNFi, related to 1st failure.

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FRI0468

SYSTEMIC AND CUTANEOUS POLYARTERITIS NODOSA IN COLOMBIAN PEDIATRIC PATIENTS: CUTANEOUS POLYARTERITIS IS NOT SO BENIGN

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Background: Polyarteritis nodosa (PAN) is the third most frequent vasculitis in pediatrics. Cutaneous PAN (CPAN) being more common than Systemic PAN (SPAN). CPAN is frequently described as a benign disease. In children, PAN onset is frequent between 9 and 11 years of age, with no sex differences, and its clinical features may be nonspecific.

Objectives: To characterize pediatric patients who were diagnosed with CPAN and SPAN and to compare their clinical features, treatments, and outcome.

Methods: A descriptive study was conducted in two centers from Medellín - Colombia, using retrospective data from January 2010 to December 2019. Patients under 18 years of age classified as PAN according to EULAR/PRINTO/PRES(1) criteria were included. CPAN patients were defined according to EULAR/PRES definition (2). Data from medical records were registered, and were expressed in median and ranges and mean and standard deviation (SD) according to their distribution. A univariate analysis was carried out by comparing signs, symptoms, and treatment between CPAN and SPAN, and a p -value $< 0,05$ was considered as significant.

Results: Twenty patients were included. The median age at diagnosis was ten years. 60% were boys. The median follow-up period was 27 months. CPAN was diagnosed in 11 (55%) and SPAN in 9 patients (45%). The most frequent symptoms were cutaneous manifestations (95%), fever (60%) and Calf Pain (55%). Mucosal ulcers were described in four patients; 3 of them were defined as CPAN. Lingual necrosis was present in two CPAN, and peripheral nervous system involvement was found in one SPAN and two CPAN patients in skin affected with lesions; even though, no significant statistical differences between CPAN and SPAN were found in constitutional, cutaneous, muscle-skeletal symptoms, and acute phase reactants. Arteriographic anomalies as hepatic and renal microaneurysms, carotid aneurysms without aortic involvement, and renal infarction were found in one patient each. Skin Biopsy was performed in 18 patients, being compatible with PAN in 16. All PAN patients (CPAN and SPAN) required treatment with glucocorticoids. None of the patients died during the follow-up period.

Conclusion: In this Colombian pediatric cohort of PAN patients, the disease was more common in boys than girls, and CPAN was more frequent than SPAN, as already been described. As is evident in this cohort, although CPAN has been considered a benign disease, these patients may be severely ill, requiring glucocorticoid treatment. Pediatric CPAN patients should be strictly followed with particular attention to identify systemic involvement, considering that constitutional, cutaneous, and muscle-skeletal features may be very similar between CPAN and SPAN.

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FRI0469

TO DISTINGUISH BETWEEN DISEASE FLARE AND ACTIVE INFECTION IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: SLE is the autoimmune disease involving multiple systems. Infections might mimic SLE flare, leading to confusion over the diagnosis and appropriate treatment. To distinguishing acute infection from active flare always remains a clinical challenge.

Objectives: We aim to explore the potential parameters in identifying active infection and disease activity in pediatric SLE.

Methods: We reviewed the medical charts of the pediatric SLE patient in National Taiwan University Hospital from August 2015 to September 2019, and 50 SLE patients presented 185 episodes of suspicious activity or infection and received CRP, ESR, and Procalcitonin measurement were included. Time matched other laboratory parameters and clinical assessments were also collected. Episodes were divided into 4 groups: infected-active, infected-inactive, noninfected-active, and noninfected-inactive. Association of parameters with outcomes were predicted by generalized estimating equation. The receiver operating curve and the area under the curve were used to evaluate the diagnostic performance. We also used multinomial logistic regression model for nominal outcome, by setting noninfected-inactive group as the reference category.

Results: There were 7 males (14%) and 43 females (86%), with the mean ages 13.9 ± 4.4 years old. Most of the patients had renal (72%) or mucocutaneous (72%) involvement. The most common infection site was respiratory system (56%). Multivariate GEE analysis showed Damage index(DI), SLEDAI-2k, neutrophil-to-lymphocyte ratio (NLR), hemoglobin, platelet, RDW-to-platelet ratio (RPR), and C3 are independent parameters for predicting SLE activity flare. Combination of these seven parameters resulted in a model with calculated AUC of 0.8964 and with sensitivity of 82.2 % and specificity of 90.9%. Multivariate GEE analysis showed DI, fever, CRP, Procalcitonin, lymphocyte percentage, NLR, hemoglobin, and renal score in SLEDAI-2k are independent parameters for predicting acute infection. These eight parameters resulted in a model with calculated AUC of 0.7886 and with sensitivity of 63.5% and specificity of 89.2%. We select a total of 10 variables (DI, SLEDAI-2k, Fever, Procalcitonin, lymphocyte percentage, NLR, hemoglobin, platelet, RPR, C3) to establish multinomial logistic regression, then predict four groups with accuracy of 70.13% for infected-active, 10% for infected-inactive, 59.57% for noninfected-active, and 84.62% for noninfected-inactive.

Conclusion: The proposed predictive calculator could be a useful tool for differentiation between activity flares and acute infections in pediatric SLE. Obtaining and combination of several parameters is effective and helpful to make appropriate judgement and treatment decisions for SLE patients.

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FRI0470 CARDIORESPIRATORY FITNESS IN JUVENILE IDIOPATHIC ARTHRITIS IN 6 – 17-YEAR-OLD CHILDREN- CROSS-SECTIONAL STUDY

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Background: Children with juvenile idiopathic arthritis (JIA) have been found to have reduced cardiorespiratory fitness and lower physical activity. Poor cardiorespiratory fitness is associated with a risk of cardiometabolic diseases.

Objectives: The aim of this study was to study the levels of cardiorespiratory fitness, respiratory function and hemodynamic responses during and after maximal cycle ergometer exercise test in children with JIA aged 6-17 years and compare the results with healthy controls.

Methods: Study group in this analysis consisted of 43 patients with JIA who were treated in Department of Pediatrics in Kuopio University Hospital, Finland and 40 healthy age- and sex matched controls. Maximal exercise tests were carried out with an electromagnetic cycle ergometer using a pediatric saddle module. Maximal workload per kilogram ($W_{\max}/kg$) was used as a measure of cardiorespiratory fitness and was presented relative to bodyweight. In addition the peak values of VO_2 per kilogram ($VO_{2\max}/kg$) were used as a measure of highest amount of oxygen that an individual can consume during exercise. Values of $VO_{2\max}$ were collected from respiratory gases measured directly from breath by breath method and was presented relative to body weight.

Physical activity and sedentary behavior (minutes per day) was assessed by the PANIC (Physical activity and nutrition in children -study) Physical Activity Questionnaire which the participants filled.

Results: Statistical analyses were performed for 43 children with JIA and 40 controls. Mean age in JIA group was 12.09 years (95%CI 11.04-13.14), and 11.72 years (95%CI 10.52-12.93) in controls ($p=0.572$). Mean body mass index for age (BMI) was $22.58 kg/m^2$ (95%CI 21.54-23.62) in JIA and $18.95 kg/m^2$ (95%CI 17.73-20.16) in controls ($p<0.05$). In JIA group BMI was 19.18 % higher compared to controls. Mean physical activity in JIA group was 94.11 minutes per day (95% CI 81.09-107.13), and 122.54 minutes per day (95% CI 102.84-142.24) in controls, thus JIA group was 23.20 % less physically active than controls ($p=0.015$).

Mean $W_{\max}/kg$ was $2.65 W/kg$ (95% CI 2.49-2.82) in JIA and $3.01 W/kg$ (95%CI 2.86-3.15) in controls thus $W_{\max}/kg$ in JIA was $0.36 W/kg$ (11.8 %) lower than in controls, ($p = 0.002$). $VO_{2\max}/kg$ was 37.00 (95%CI 33.96-40.84) ml/kg/min in JIA and 43.30 (95%CI 40.79-45.82) ml/kg/min in controls thus in JIA group mean $VO_{2\max}/kg$ was $6.3 ml/kg/min$ (14.4 %) lower than in controls ($p=0.001$).

Conclusion: Children with JIA were found to have significantly lower cardiorespiratory fitness. In addition, BMI in JIA patients was higher compared to healthy age- and sex-matched controls. Impaired cardiorespiratory fitness and higher BMI may predispose children with JIA to cardiometabolic comorbidities later in life. In addition to disease-control, more attention should be paid to maintaining good cardiorespiratory fitness and normal BMI in these patients already before adulthood.

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FRI0471 ADVERSE FACTORS OF COMORBID DISEASES DEVELOPMENT AT DIFFERENT VARIANTS OF JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: It is known that rheumatic diseases are the pathogenetic basis for the formation of many comorbid conditions, the most important of that are cardiovascular pathology, atherosclerosis, osteoporosis, chronic kidney disease and amyloidosis, chronic obstructive pulmonary disease. The start of the disease at an early age, the long-term duration of JIA, the use of basic immunosuppressive therapy lead to the possibility of the onset of the first signs of comorbid conditions in childhood.

Objectives: To study risk factors for the formation of damage of internal organs and systems in children with non-systemic JIA.

Methods: The case histories of 121 patients aged 7-18 years (mean age 11.0 ± 0.3 years) with polyarticular (67.7%), oligoarticular (14.88%) and uveitis-associated (17.35%) JIA were studied, mainly of females (73.5%). The age of the start of the disease was 5.9 ± 0.4 years, the duration of JIA at the time of analysis reached 67.1 ± 4.3 months. All children received basic methotrexate therapy (plus folic acid), short courses of NSAIDs. There are studied changes in the cardiovascular system (ECG, ultrasound, 6-minute walk test),