AB1006

DRUG SURVIVAL OF SYSTEMIC TREATMENTS IN JUVENILE IDIOPATHIC ARTHRITIS

L. Trives Folguera¹, I. Monteagudo¹, B. Serrano Benavente¹, L. R. Caballero Motta¹, A. M. Anzola¹, K. López Gloria¹, J. C. Nieto¹. ¹Gregorio Marañón Hospital, Madrid, Spain

Background: Juvenile idiopathic arthritis (JIA) comprises a group of inflammatory diseases that frequently requires systemic treatments. There are some studies that evaluate the systemic drug survival in adults with JIA; but there is scarce data about the drug survival in paediatric population.

Objectives: Our main objective was to study the drug survival of biologic therapies and synthetic DMARD in a monocentric cohort and the related factors influencing on it.

Methods: Patients with JIA visited in the last 12 years were included. We carried out a retrospective, longitudinal study and collected data on treatment (start date, tapering and stop the treatment date; causes of finish and combined treatment or not). We also collected demographic data with date of birth, sex, symptoms onset data and JIA subcategory. We studied time to relapse since the drug suspension. The drug survival for each kind of treatment was analyzed with Kaplan-Meier curves.

Results: We included 158 patients with JIA. Demographic data are shown in table 1. One hundred and thirty (82.3%) patients started methotrexate (MTX) with a half-life of 34.8 months; 79 (51.5%) patients started biologic therapy with half-life of 29 months and 14 (17.7%) patients started a second biologic with a half-life of 5 months. Time to first tapering of MTX was 12 months, for the first biologic was 10.5 months and for the second biologic was 15 months. The main cause of suspension was remission for each group. Treatment according to different JIA subcategories is shown in table 2. In 45 patients (28.5%) systemic treatment was stopped and 11 (24.4%) had a disease flare in a mean time of 36 months. Taking into account only patients who flared, the mean time was 15.6 months.

Table 1. Demographics features

	Total (n:158)
Sex (female)	96 (60,76%)
Starting age (median y RI)	4,9 (2,6-9,8)
AAN positives	91 (57,6%)
JIA oligo persistent	66 (41,77%)
JIA oligo extended	16 (10,13%)
JIA enthesitis	14 (8,86%)
JIA psoriasis	9 (5,7%)
JIA systemic	18 (11,39%)
JIA poli FR-	29 (18,35%)
JIA poli FR+	4 (2,53%)
JIA undifferentiated	2 (1,27%)

Table 2. Treatment according to JIA subcategories

	Group 1 (Systemic JIA n=18 (%))	Group 2 (Oligoarticular JIA n=82 (%))	Group 3 (Polyarticular JIA n=33 (%))	Group 4 (Juvenil SpA n=23 (%))
Synthetic DMARD (n:130)	9 (50%)	71 (86,6%)	33 (100%)	17 (74%)
Biologic Therapy (n:79)	6 (33,3%)	34 (41,46%)	22 (75%)	17 (74%)
No systemic treatment (n:21)	7 (38,9%)	10 (12,2%)	0	4 (17,4%)

Conclusion: The drug survival for systemic therapies in children with JIA is more than 2 years, without significant differences between synthetic DMARDs and biologics. Remission is the main cause for ending treatment. Biologic drug survival was significantly shorter between systemic JIA and the other subcategories. Only one fourth of patients had a flared after stopping the systemic treatment.

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AB1007

SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: ARE DIFFERENT CLINICAL PATTERNS ASSOCIATED WITH S100A8/S100A9 SERUM LEVELS?

M. G. Villarreal¹, S. Bonaldi¹, L. Perez¹, M. Katsikas¹. ¹Service of Immunology & Rheumatology. Hospital de Pediatría J. P. Garrahan, Buenos Aires, Argentina

Background: Systemic juvenile idiopathic arthritis (SJIA) is a category of Juvenile Idiopathic Arthritis (JIA). Different clinical patterns (articular/systemic/both

of them combined) have been recognized, possibly identifying distinct sub-populations. Serum biomarkers that reflect disease activity include S100A8/S100A9 (S100A8/9), however to date patterns of SJIA and their association with S100A8/9 has not been tested.

Objectives: To evaluate S100A8/9 levels in a cohort of patients with SJIA. To determinate S100A8/9 inactive vs inactive visits. To distinguish patterns on SJIA and their association with S100A8/9. To compare serum levels of S100A8/9 with other JIA categories and autoinflammatory diseases.

Methods: An unicenter, observational, cross sectional study was conducted. Patients with SJIA according ILAR whom S100A8/9 was measured as part of standard care were enrolled. Consecutive visits were included. Variables recorded were: clinical (systemic: fever, serositis, adenopathy, hepatomegaly, splenomegaly and arthritis); biochemical (S100A8/9, hemoglobin, platelet, erythrocytopenia, c-reactive protein, ferritin). Activity measures: Juvenile Arthritis Disease Activity Score (JADAS -10) and physician visual analogue scale (phy VAS). Visits were divided into active/inactive. Active visit was defined as at least one clinical feature.(systemic and/or arthritis). Inactive visit no clinical symptoms neither JADAS-10> 1 and phy VAS: 0. SJIA patterns were defined as: "articular pattern": those patients with arthritis without systemic features, "systemic pattern": any systemic feature without arthritis, "mixed pattern": both articular and systemic. Levels of S100A8/9 were tested using Calprotectin Elisa Kit. For comparisons others JIA: enthesitis related arthritis (ERA), polyarticular and autoinflammatory diseases who had at least one S100A8/9 determination were included. Descriptive statistics, Mann-Whitney U test and ANOVA were used as appropriate.

Results: Forty-two patients with SJIA were included (25 F). Age at evaluation 13 (1-16.5) years. Clinical features at study baseline: arthritis 57 %, rash 19%, fever 15 %, adenopathies 6%, splenomegaly 4%, hepatomegaly 1.5%. Laboratory features (median): hemoglobin 12.2 gr/dl, platelet 314000 cel/mm3, erythrocytopenia 12.5 mm/h, c-reactive protein 0.7 mg/dl, ferritin 235 ng/ml. JADAS -10 ≥ 1: 62%. Number of active patients were 29 (69%). Scheduled Medical visits were 129 (active 65%, inactive 35%). Active visits were divided according patterns into: articular 54%, mixed 35%, systemic 11%.

Serum Levels of S100A8/9 according to SJIA patterns.

SJIA	Overall	Active	Articular	Systemic	Mixed	Inactive
Visits	129	84	46	9	29	45
S100A8/9 ng/ml	7590	16788	10750	5200	25000	3103
Median (range)	(300-2625)	(300-26250)	(300-26250)	(850-12250)	(3290-2625)	(1140-1010)

S100A8/9 analysis revealed significant differences among active vs inactive medical visits (p: 0.00001). ANOVA test among SJIA patterns showed, F:86.48, (p:0.00001). Mixed pattern was distinctive to others. S100A8/9 (medians ng/ml) in comparable diseases were: ERA: 4320, polyarticular: 4120, autoinflammatory: 6532. SJIA had the higher S100A8/9. SJIA was different than others comparable diseases (F: 11,62,p: 0.00001). Comparisons among SJIA patterns and others disease found that systemic and articular pattern did not show differences (F:2.78, p:0.067)

Conclusion: S100A8/9 was higher in SJIA compared to others diseases. It reflected disease activity. Mixed pattern evidenced to be different to others (systemic/articular). Mixed pattern was the unique that showed significative difference compared to other diseases. SJIA is probably not a single disease, but not only clinical patterns and biomarkers as S100A8/9, if not, genetic variants and their expression would be able to identify homogeneous groups towards tailored treatments.

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AB1008

METABOLIC DISORDERS IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

I. Chyzeuskaya^{1,2}, A. Vishnevskaya¹, I. Arher¹, T. Matsushko¹. ¹4th City Children's Clinical Hospital, Minsk, Belarus; ²Belarusian Medical Academy of Postgraduate Education, Minsk, Belarus

Background: Systemic lupus erythematosus (SLE) is the most common pathology from the group of systemic diseases of the connective tissue. Currently, the problem of deadly complications in patients with SLE is progressively shifting towards vascular catastrophes, such as strokes and heart attacks. If a few years ago, patients mainly died at a young age from renal failure as a complication of lupus nephritis, now thromboses of various localization are in first place.

Objectives: The purpose of the study was to determine the state of lipid peroxidation and antioxidant protection, the main indicators of the lipid spectrum and the state of hemostasis in children with SLE.

Methods: 25 children with SLE and 20 healthy children were examined in the rheumatology department of the 4th city children's clinical hospital in Minsk. The lipid spectrum, lipid peroxidation (LPO) and serum ACL, ACW were determined in the Central Research Laboratory of the Belarusian Medical Academy of Postgraduate Education.

Results: In children with SLE a significant increase in the content of total cholesterol (5.56 ± 0.36 mmol/l) and a decrease in HDL-cholesterol levels (0.94 ± 0.18 mmol/l) were found in comparison with the control group (3.71 ± 0.69 mmol/L and 1.29 ± 0.33 mmol/l, respectively).

A significant ($p < 0.05$) decrease in the concentration of ApoA ($85.1 [59.8; 94.9]$ mg/dl), ApoE ($2.1 [1.2; 3; 7]$ mg/dl) and an increase in ApoB ($59.8 [51.9; 67.8]$ mg/dl) in children with SLE were found compared with the control group ($127.2 [122.1; 132.3]$ mg/dl, $3, 2 [2.3; 5.9]$ mg/dl and $32.1 [19.9; 50.8]$ mg/dl, respectively). ApoB / ApoA > 1 was established in 7 (28%) children with SLE.

The study found a significant ($p < 0.05$) increase in the level of intermediate (DK233, DK278) and final (MDA) LPO products in the blood serum of children with SLE in comparison with the control group, which indicates the activation of LPO processes in these patients. During the correlation analysis, a positive correlation was established between the levels of DK233, DK278 in blood serum and CRP ($r_s = 0.87$, $p < 0.001$). When studying the main indicators of the blood lipid spectrum in children with SLE, a significant increase in the serum concentration of total lipids ($p < 0.01$) and triglycerides ($p < 0.001$) was revealed when compared with the control group.

When determining indicators of coagulation hemostasis, in children with SLE, a predominance of hypercoagulation was detected, accompanied by a significant increase in serum fibrinogen level (5.08 ± 0.14 g/l) and an increase in platelet level ($479.57 \pm 8.01 \times 10^9/l$) in peripheral blood compared with the control group (3.24 ± 0.07 g / l and $294.23 \pm 5.39 \times 10^9/l$, respectively). These indicators correlated with serum CRP concentration ($r_s = 0.62$; $p < 0.01$) and ESR level ($r_s = 0.73$; $p < 0.01$). A relationship was established between elevated serum levels of fibrinogen and disease activity indicators ($r_s = 0.74$; $p < 0.01$).

Conclusion: The atherogenic orientation of the blood lipid spectrum, characterized by hyperlipidemia, hypertriglyceridemia, hypercholesterolemia and dyslipoproteinemia in the form of a decrease in HDL-cholesterol and an increase in LDL-cholesterol, as well as an increase in ApoB/ApoA ratio > 1 and a decrease in ApoE, the activation of LPO processes and a significant decrease in ACW and ACL in the serum of children with SLE are cardiovascular events risk factors (pulmonary thromboembolism, myocardial infarction and brain).

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AB1009

THE EFFICACY OF TOCILIZUMAB ON THE TREATMENT OF TAKAYASU ARTERITIS IN CHINESE CHILDREN

C. Wang¹, H. Song¹, Z. Yu¹, M. Quan¹. ¹Peking Union Medical College Hospital, Beijing, China

Background: Takayasu arteritis (TA) is the most prevalent large-vessel vasculitis in children. Patients with TA have a high morbidity and mortality. It remains a therapeutic challenge because corticosteroids monotherapy can rarely cure TAK and the relapse rate is high during GC tapering.

Objectives: The aim of this study is to investigate the efficacy and safety of tocilizumab (TCZ) in Chinese children with Takayasu arteritis (TAK).

Methods: We retrospectively studied 6 TAK children treated with TCZ in our hospital from July 2017 to October 2018. The demographic and clinical data, laboratory examination results and vascular imaging data were collected.

Results: Six pediatric patients with critical or refractory TAK treated with TCZ were analyzed, including 3 males and 3 females. The diagnosis age was ranging in age from 2 to 13 years (median age: 7 years). Three patients were initially treated with TCZ and Mycophenolate Mofetil (MMF) as the first-line regimen without corticosteroid or with a quite rapid GC taper duration, two of which had life-threatening coronary arteries involved and heart failure. The other three patients were switched to TCZ from conventional disease modifying anti-rheumatic drugs (DMARDs) or other biologics due to being refractory to them and recurrent relapses. Four patients were given TCZ at 4 weeks regular intervals for 10 to 22 months, while two patients withdrew TCZ because of disease deterioration and unbearable abdominal or chest pain after the second dose. After 6 months follow-up, four patients experienced significant clinical and biological improvement with angiographically progression in one patient. A corticosteroid-sparing effect is obvious. Drug-related side effects occur in 1 patient manifesting as a mild elevated liver function. Neither neutropenia nor infection was observed.

Conclusion: Our study shows a clinical, biological, and radiological response in patients with refractory TAK treated with TCZ.

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AB1010

CLINICAL SPECTRUM AND IMMUNE ANALYSIS OF PATIENTS WITH CRYOPYRIN-ASSOCIATED AUTOINFLAMMATORY SYNDROME IN TAIWAN

C.-Y. Wu¹, P. S. Chu¹, H. Y. Yang². ¹Linkou Chang Gung Memorial Hospital, Pediatric Allergy, Asthma and Rheumatology, Taoyuan city, Taiwan, Republic of China; ²Linkou Chang Gung Memorial Hospital, Department of Nephrology, Taoyuan city, Taiwan, Republic of China

Background: Cryopyrin-associated periodic syndromes (CAPS) are emerging autoinflammatory diseases with available treatment. No reports have yet been reported from Taiwan.

Objectives: We reviewed cases suspected with CAPS to identify its existence in Taiwan.

Methods: Genomic DNA from one hundred and ten cases with symptom signs suggestive of CAPS(1) between 2016-2019 were sent for NLRP3 gene analysis. Clinical presentations, laboratory data, treatment regimens, as well as inflammation activities were analyzed among those treated in a tertiary medical center in northern Taiwan.

Results: Among the 110 cases sequenced, 16 of them were found to carry missense mutations within the NLRP3 gene. Fourteen cases harbored known pathogenic genetic variants (c.1316C>T; c.1574A>T; and c.907G>C) and two carried novel NLRP3 missense mutations (c.210G>A, c.1371G>T)(2) with unknown pathophysiological roles. Through chart review, chronic urticarial, systemic juvenile idiopathic arthritis, Behcet's disease and refractory Kawasaki disease were most likely diagnosed before genetic analysis were arranged. As compared to chronic infantile neurological, cutaneous and articular syndrome (CINCA) and Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS) was the most frequently observed clinical presentation. Plasma serum amyloid A (SAA) and IL-1b were both significantly elevated among the cases diagnosed with CAPS as compared to the controls ($p < 0.05$). IL-18, on the other hand, showed no significant differences between the groups. While the presence of LPS without ATP significantly increased the level of IL-1b in the PBMC stimulation test, IL-18 were significantly elevated in the confirmed CAPS with or without ATP upon LPS stimulation (all $p < 0.05$). Caspase 1 activity were also tested positive among the cases with CAPS. Furthermore, we compared the immune profiles between those CAPS cases harboring pathogenic mutations with the 2 harboring unreported NLRP3 missense mutations and discovered that the PBMC stimulation test in cases with c.210G>A and c.1371G>T mutation did not differ from the healthy controls.

Conclusion: The number of NLRP3 gene alterations among patients suspected with CAPS in Taiwan is not low. In order to identify potential patients for proper medical intervention in the future, physician awareness, genetic testing as well as functional analysis are important.

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AB1011

LONG TERM FOLLOW-UP OF THE PATIENTS WITH ANTI NUCLEAR ANTIBODY POSITIVITY WHO HAD INITIALLY NO IDENTIFIABLE RHEUMATIC DISEASES

M. Yıldız¹, I. Altun¹, G. Yilmaz¹, A. Aliyeva¹, F. Haslak¹, O. Koker¹, A. Adrovic¹, S. Sahin¹, K. Barut¹, O. Kasapcopur¹. ¹Istanbul University-Cerrahpasa, Pediatric Rheumatology, Istanbul, Turkey