AB1008 AGE DEPENDENT SAFETY AND EFFICACY OF COLCHICINE TREATMENT FOR FAMILIAL MEDITERRANEAN FEVER IN CHILDREN

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Background: Colchicine has been found to be highly effective for the treatment of familial Mediterranean fever (FMF). However, it is FDA-approved only for children older than 4 years owing to the lack of studies in younger children.

Objectives: Our tertiary pediatric rheumatology department routinely uses colchicine even in very young children with FMF. The aim of the study was to evaluate its safety and efficacy in children with FMF <4 years old.

Methods: The departmental database was searched for all children diagnosed with FMF between 2010-2018. Those who started treatment with colchicine before age 4 years were identified and matched by MEFV variant to children who started treatment at age 4-8 years. Drug efficacy was assessed by the improvement in the frequency and duration of attacks. Adverse events were assessed according to the Rheumatology Common Toxicity Criteria ver. 2.0.

Results: The cohort included 89 patients with FMF: 41 first treated before age 4 years, and 48 first treated at age 4-8 years. Rates of complete response to colchicine were 61% in the younger group and 60.4% in the older group. Corresponding rates of partial remission were 24.4% and 29.2% ($p=0.77$). The most frequent adverse event was diarrhea, with a prevalence of 24.4% in the younger group and 22.9% in the older group ($p=0.87$). There were no significant between-group differences in other adverse events.

Conclusion: Colchicine is equally effective and safe for use in patients with FMF under 4 years old, with no difference in response from older pediatric patients.

Abstract AB1008 Table 1. Clinical parameters at disease onset in younger and older patients with FMF

Clinical parameter	Age <4 yr (n=41)	Age 4-8 yr (n=48)	P value
Age at symptom onset (yr), mean±SD	1.70 ±0.86	3.45 ±1.40	<0.001
Fever*	39 (95.1%)	42 (87.5%)	0.27
Erysipelas-like rash	5 (12.2%)	7 (14.6%)	0.74
Arthralgia	20 (48.8%)	36 (75.0%)	0.011
Arthritis	6 (14.6%)	7 (14.6%)	0.99
Abdominal pain	27 (65.9%)	35 (72.9%)	0.47
Chest pain	5 (12.2%)	8 (16.7%)	0.55
Orchitis	1 (2.4%)	1 (2.1%)	1.00
Protracted febrile myalgia	0 (0%)	2 (4.2%)	0.49
Frequency of attacks (per month), median (IQR)	2.0 (1.00-4.00)	1.00 (1.00-2.00) [†]	0.041
Duration of attacks (days), median (IQR)	2.0 (1.5-3.00) [‡]	2.0 (1.0-3.0) [§]	0.39
Initial colchicine dose (mg/kg), median (IQR)	0.038 (0.034-0.046)	0.036 (0.031-0.050)	0.60

*Defined as >38°C rectally or >37.5°C orally

[†]Data available for 45 patients.

[‡]Data available for 38 patients.

[§]Data available for 43 patients.

IQR=interquartile range

Values are n(%) unless otherwise indicated.

Abstract AB1008 Table 2. Safety of colchicine in younger and older children with FMF

Variable	Age <4 yr (n=41)	Age 4-8 yr (n=48)	P value
Durable colchicine dose (mg/kg)	0.053 (0.039-0.066)	0.050 (0.040-0.060)	0.33
Primary outcome			
No AEs	30 (73.2%)	33 (68.8%)	0.24 [§]
RCTC score, %	7 (17.1%)	5 (10.0%)	
1	4 (9.8%)	9 (16.0%)	
2	0	1 (4.0%)	
3	0	0	
4	0	0	
Secondary outcomes			
Lowered dose due to AEs	5 (12.2%)	8 (16.7%)	0.55

Colchicine failure due to AEs	1 (2.4%)	0 (0.0%)	0.46
Reported adverse events			
Diarrhea	10 (24.4%)	11 (22.9%)	0.87
Abdominal pain	3 (7.3%)	2 (4.2%)	0.65
Anorexia/nausea	0 (0%)	1 (2.1%)	1.00
Elevated transaminase levels	4 (11.8%) [†]	10 (23.3%) [‡]	0.19
Leukopenia	0 (0%)	2 (4.4%)	0.50
Total	14 (34%)	19 (39.6%)	0.59

AEs – adverse events

* RCTC- Rheumatology Common Toxicity Criteria, version 2.0 for AE severity: 0- no, 1- mild, 2- moderate, 3- severe, 4- life-threatening

Values are n (%) unless otherwise indicated.

[§] Due to statistical limitations, Statistic analysis (Fisher's exact test) was performed between No AEs & RCTC score 1 and RCTC score 2-4 in the respected age groups.

[†]Data available for 34 patients.

[‡]Data available for 43 patients.

Disclosure of Interests: None declared

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AB1009 CLINICAL FEATURES PREDICTIVE OF RENAL AND GASTROINTESTINAL INVOLVEMENT IN PATIENTS WITH HENOC-SCHÖNLEIN PURPURA

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Background: Henoch-Schönlein purpura (HSP), the most common form of vasculitis in children, predominantly involves the small vessels of the skin, the gastrointestinal (GI) tract, joints, and kidneys. GI involvement is the most severe short-term complication, in contrast, renal disease is the most troublesome long-term complication. Meanwhile, although the disease course of HSP is usually benign in children, recurrence still occurs in a subset of patients. Studies documenting the incidence and predictive factors of recurrent HSP, and biomarkers of the various manifestations of HSP are limited.

Objectives: We aimed to delineate characteristics and biomarkers of HSP patients with GI or renal involvement, and hoped to clarify the incidence and predictive markers of recurrent HSP

Methods: We retrospectively reviewed the medical records of 40 patients admitted in one tertiary medical center in Taipei, Taiwan over a 5-year period with a diagnosis of Henoch-Schönlein purpura. Incidence and risk factors for GI involvement, renal involvement, and recurrent HSP were analyzed. The Mann-Whitney U test and Fisher exact test were utilized for statistical assessment.

Results: From January 1, 2005 to December 31, 2010, 40 HSP patients aged < 18 years were identified. The mean onset age was 8.35±3.3 years. Among them, 45% (18/40) of the patients were male. Ten patients had more than 2 HSP episodes (recurrence rate 25%). Renal involvement was noted in 17.5% (7/40) of the patients, and it was found to occur more frequently in children with later onset age (with renal involvement: 11.43±4.33 years; without renal involvement: 7.73±2.72 years; $p=0.03$). Recurrent HSP was found to occur more frequently in patients with renal involvement, though without statistical significance (odds ratio: 6; 95% confidence interval; 1.05-34.14; $p=0.051$). Renal involvement was not associated with GI involvement ($p=0.69$). GI involvement was noted in 47.5% (19/40) of the patients, and it was found to occur more frequently in patients with higher segmented neutrophil percentage as assessed by complete blood count (with GI involvement: 74.16±13.31%; without GI involvement: 63.14±11.11%; $p=0.0056$). GI involvement was not associated with relapse of HSP. Fourteen patients (35%) had arthritis or arthralgia, and it was found to occur more frequently in children with earlier onset age (with arthralgia/arthritis: 7.26±2.55 years; without arthralgia/arthritis: 10.39±3.63 years; $p=0.01$).

Conclusion: HSP patients with GI involvement had higher segmented neutrophil percentage, consistent with previous studies proposing neutrophil-lymphocyte ratio as a biomarker for GI involvement. Patients with renal involvement had a later age of onset, and the relapse rate was higher in this subpopulation but not statistically significant.

Table 1. Clinical manifestations

	Hb	Nt	Pla	Crea	Brb	AST	ALT	Fe	Tg	Fb	INR
sJIA	10.1	2.736	116930	0.85	2.77	141.8	257.9	9508.7	297.7	237.9	1.24
SLE	7.4	1.403	59983	1.53	9.77	274.3	133.2	5736	433	192.3	2.06

Table 2. Analytical measures. Hb=haemoglobin(g/dl), Nt=neutrophils ($10^3/\text{mm}^2$), Pla=platelets ($10^3/\text{mm}^2$), Cr=creatinine (mg/dl), Brb=bilirubin (mg/dl), AST (UI/L), ALT (UI/L), Fe=ferritine (ng/ml), Tg=triglycerides (mg/dl), Fb=fibrinogen (mg/dl), INR (International Normalized Ratio).

	Hypotension	Fever	Rash	Adenopathy	Splenomegaly	Hepatomegaly	Haemorrhage
sJIA	1 (10%)	7 (70%)	7 (70%)	3 (30%)	4 (40%)	1 (10%)	0
SLE	0	4 (66.7%)	1 (16.7%)	3 (50%)	5 (83.3%)	4 (66.7%)	3 (50%)

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AB1010 MACROPHAGE ACTIVATION SYNDROME: A CASE SERIES OF 16 PATIENTS

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Background: Macrophage activation syndrome (MAS) is a severe complication of several rheumatologic diseases, being of special relevance systemic lupus erythematosus (SLE) and systemic juvenile idiopathic arthritis (sJIA). Its characterized by an excessive activation of the immune system due to various mechanisms, including hyperactivation of macrophages and a failure in downregulation activity by NK and cytotoxic lymphocytes. There are various criteria for its diagnosis, highlighting secondary lymphohistiocytosis syndrome (HLH) criteria from 2004 and provisional secondary MAS criteria for JIA proposed by Ravelli in 2016¹.

Objectives: To describe a case series of patients with MAS.

Methods: This is a retrospective case series of 16 patients with MAS secondary to systemic autoimmune diseases diagnosed in Ramón y Cajal University Hospital between April 2009 and September 2018.

Results: The baseline pathology was sJIA in 8 patients (2 cases with 2 episodes) and SLE in the other 6 patients. Mean age at diagnosis was 17.44 years for sJIA and 37.5 years for SLE. Mean time from diagnosis of the baseline disease to MAS episode was 11.31 years, with 3 cases being the initial manifestation of their systemic disease. 43.8% of patients were treated with corticosteroids previously to MAS episode, and 50% were being treated with DMARDS/biologic agents (SLE: 3 patients with hydroxychloroquine and 1 patient with mycophenolate and hydroxychloroquine; sJIA: 2 patients with Anakinra, 1 patient with tocilizumab and 1 patient with etanercept). Clinical and analytical characteristics of the patients are presented in table 1 and table 2, respectively. In SLE group, only 2 patients (33.3%) had high anti-DNA titers during the MAS episode, 5 patients (83.3%) had increased C3 consumption and 4 patients (66.6%) had increased C4 consumption. As severe manifestations, 4 SLE patients presented neurologic abnormalities and 3 patients presented external hemorrhage. Infection was confirmed as a trigger in 3 patients with SLE (50%) and 4 patients with JIA (40%). Prednisone at high doses was prescribed to all patients, cyclosporine in 4 patients (66.6%) with SLE and 9 patients (90%) with sJIA. Additionally, anakinra was prescribed in 4 patients (40%) with sJIA. 4 patients (66.6%) with SLE met secondary HLH criteria and 9 patients (90%) with sJIA met secondary MAS criteria. Bone marrow biopsy was performed in all patients with SLE and in 9 patients with sJIA, demonstrating hemophagocytosis in 5 patients (83.3%) with LES and 5 (50%) patients with sJIA. Only 2 patients in the SLE group died because of MAS.

Abstract AB1010 Table 2. Analytical measures. Hb=haemoglobin(g/dl), Nt=neutrophils ($10^3/\text{mm}^2$), Pla=platelets ($10^3/\text{mm}^2$), Cr=creatinine (mg/dl), Brb=bilirubin (mg/dl), AST (UI/L), ALT (UI/L), Fe=ferritine (ng/ml), Tg=triglycerides (mg/dl), Fb=fibrinogen (mg/dl), INR (International Normalized Ratio).

Conclusion: In our case series rash and fever were more frequent among sJIA patients, the rest of the clinical manifestations were more common in SLE group. Analytical measures were more altered in SLE group except for ferritin and ALT. Mortality was 33.33% in SLE group vs 0% in sJIA group, probably due to early diagnosis and treatment in these patients.

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AB1011 APPLICATION OF AUTOINFLAMMATORY DISEASE DAMAGE INDEX (ADDI) TO AUTOINFLAMMATORY DISEASES IN A TERTIARY REFERRAL HOSPITAL

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Background: Autoinflammatory diseases (AIDs) cause chronic systemic inflammation that can damage multiple organs. Recently, the autoinflammatory disease damage index (ADDI) has been developed and validated in the four most common monogenic AIDs, Cryopyrin-associated Periodic Syndrome (CAPS), Familial Mediterranean Fever (FMF), Mevalonate Kinase Deficiency (MKD) and Tumor Necrosis Factor Receptor-associated Periodic Fever Syndrome (TRAPS). The use of ADDI index could also be of great value in other AIDs.

Objectives: The aim of this study is to assess the application of ADDI in patients with the four most common monogenic diseases and other AIDs. To accomplish this objective a detailed cohort of patients with different AIDs is presented.

Methods: All patients with AIDs followed in the Pediatric Rheumatology Unit comprising the Transitional Care and specialized AIDs outpatient clinics from Hospital Universitari Vall d'Hebron were identified. A cross-sectional, descriptive study was performed applying ADDI by two pediatric rheumatologists (EM, ML). Laboratory test including C-reactive protein (CRP) mg/dl, amyloid protein (AP) mg/L, erythrocyte sedimentation rate (ESR) mm/h and protein/creatinine rate (mg/g Cr) were performed at the moment ADDI was applied. Variables related with disease duration, current treatment and accumulated corticosteroids treatment were assessed. The continuous variables are presented as mean and standard deviation (mean $\pm$ SD) and categorical variables are presented by percentages.

Results: A total of 41 patients with AIDs were included, 61% were female, with a median age of 20 ± 11.9 years at inclusion. Disease duration was 11 ± 8.2 years. AIDs included were 11 patients with FMF (26.8%), TRAPS n=4 (9.8%), MKD n=3 (7.3%), CAPS n= 2 (4.9%), Blau