THU0573

15-YEAR TRENDS AND CORRELATES OF SCHOOL SPORTS ATTENDANCE AMONG CHILDREN AND ADOLESCENTS WITH JIA ENROLLED IN THE GERMAN NATIONAL PAEDIATRIC RHEUMATOLOGIC DATABASE

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Background: Besides leisure-based physical activities (PA), the school-setting is described as one of the most effective areas for providing opportunities for PA, collectively reaching school-aged children vulnerable to sedentary behaviours.¹ In this context, regular participation in school sports can help children and adolescents achieve a part of the recommended amount of daily physical activity and help gain the knowledge and attitudes they need to engage in lifelong active lifestyle.

Objectives: Since adolescents with juvenile idiopathic arthritis (JIA) are less involved in physical and social activities compared to their healthy peers, the objectives were as follows:¹ to describe the extent to which school sports attendance among patients with JIA changed over time, and² to determine correlates associated with exemption from school sports.

Methods: Data of school-aged children and adolescents with JIA recorded in the National Paediatric Rheumatologic Database (NPRD) in the years 2000 to 2015 were considered for the analyses. Whether school sports participation had changed between 2000 and 2015 was determined using linear mixed models. Data from 2015 were inspected to analyse correlates of school sports absenteeism.

Results: During the observation period, participation rates in school sports were determined in 23,016 patients. The proportion of patients who participated always steadily increased from 31% in 2000 to 64% in 2015 ($\beta=0.017$, 95% confidence interval (CI) 0.015, 0.020), whereas the exemption rate simultaneously decreased from 44% in 2000 to 16% in 2015 [$\beta=-0.009$, 95% CI -0.011, -0.007]. In 2015, data from 5879 patients (mean age 13.1±3.3 years, disease duration 5.9±4.0 years, persistent oligoarthritis 37%) were available for evaluation. Fully exemption was associated with functional limitations, disease activity and any use of DMARDs, intra-articular glucocorticoid injection or physiotherapy.

Conclusions: School sports attendance among children and adolescents with JIA has increased significantly over the last 15 years. Possible explanations may

include improved functional ability, probably due to earlier and more frequent use of DMARDs. Considering the impact of JIA on daily life, the sedentary habits that come with it, and the potentially favourable effect of PA, it is important to promote an active lifestyle in children with JIA. In order to encourage patients to attend more frequently, it will be necessary to provide comprehensive information among teachers, parents and physicians regarding opportunities and risks of school sports.

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THU0574

LONG TERM PHARMACOVIGILANCE OF BIOLOGICS FOR JUVENILE IDIOPATHIC ARTHRITIS: THE BIKER-REGISTRY

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Background: Long-term surveillance of biologics drugs is particularly important in paediatric patients (pts)

Objectives: To evaluate long-term rates of serious adverse events (AE) and AEs of special interest (AESI) in clinical practice in pts with juvenile idiopathic arthritis (JIA)

Methods: Safety data from pts registered in the BIKER registry were analysed. Rates of 25 AESI were analysed from first dose through 70 days after last dose and compared by Wald test

	ETA	ADA	GOL	INF	ABA	TOC	ANA	CAN
Patients,n	2481	845	67	69	98	295	57	45
Exposure, years	5376.0[KM1]	1333.6	71.7[KM2]	98.6	109.3	434.8	96.6	71.3
AE all*	1878 (34.9)	748 (56.1)	214(298)	100(101)	61 (55.8)	452(104)	39 (40.4)	94(131)
SAE	252 (4.7)	78 (5.8)	10 (13.9)	14 (14.2)	6 (5.4)	75 (17.3)	9 (9.3)	17 (23.8)
AESi all	320 (6.0)	143 (10.7)	16 (22.3)	23 (23.3)	10 (9.1)	96 (22.1)	7 (7.2)	14 (19.6)
Uveitis	106 (2.0)	70 (5.2)	5 (7.0)	9 (9.1)	2 (1.8)	2 (0.5)	0	0
	RR2.01 [1.52–2.67]; p<0.0001	RR2.64 [1.98–3.54] p<0.0001	RR2.78 [1.13–7.14] p=0.025	3.68 [1.89–7.19] p=0.0001				
Infection	90 (1.7)	32 (2.4)	6 (8.4)	3 (3.0)	1 (0.9)	18 (4.1)	4 (4.1)	1 (1.4)
	RR0.57 [0.41–0.78]; p=0.0005		RR4.21 [1.86–9.51] p=0.0005			RR2.17 [1.32–3.54] p=0.002		
Cytopenia	30 (0.6)	1 (0.1)	0	1 (1.0)	0	22 (5.1)	2 (2.1)	6 (8.4)
	RR0.39 [0.23–0.64] p=0.0002					RR9.07 [5.3–15.3] p<0.0001		RR11.34 [4.89–26.3] p<0.0001
Hepatic event	17 (0.3)	6 (0.4)	0	1 (1.0)	1 (0.9)	13 (3.0)	0	1 (1.4)
	RR0.32 [0.17–0.60] p=0.0004					RR8.25 [4.23–16.0] p<0.0001		
Anaphylaxis	3 (0.1)	3 (0.2)	1 (1.4)	5 (5.1)	2 (1.8)	15 (3.5)	0	1 (1.4)
	RR0.05 [0.01–0.15] p<0.0001			RR15.1[5.79–39.5] p<0.0001		RR16.49 [8.06–33.7] p<0.0001		
Autoimmuno-pathy	8 (0.1)	10 (0.7)	1 (1.4)	1 (1.0)	2 (1.8)	3 (0.7)	0	0
	RR0.19 [0.08–0.45] p=0.0001				5.97 [1.41–25.3] p=0.015			
CED	19 (0.4)	2 (0.1)	0	2 (2.0)	0	0	0	0
				RR7.21 [1.69–30.7] p=0.008				
Depression	12 (0.2)	2 (0.1)	0	0	1 (0.9)	1 (0.2)	0	1 (1.4)
MAS	2 (0.0)	0	0	0	0	6 (1.4)	1 (1.0)	3 (4.2)
	RR0.08 [0.02–0.38] p=0.001					RR16.49 [5.32–51.13] p<0.0001		RR 35.3 [9.56–130] p<0.0001
Malignancy	6 (0.1)	0	0	1 (1.0)	0	1 (0.2)	0	0
Hypertension	4 (0.1)	4 (0.3)	0	0	0	0	0	0
		RR4.69 [1.17–18.8] p=0.02						

Results: A total of 3975 courses of biologics with a total exposure of 7592 PY were identified with Etanercept (5376PY) followed by Adalimumab (1334PY), Tocilizumab (435PY), Abatacept (109PY), Infliximab (99PY), Anakinra (96 PY), Canakinumab (71PY) and Golimumab (67PY). Differences in JIA category distribution and concomitant treatment were noted. A total of 3586 AE (47.2/100PY), 461 (6.1) SAE and 629 (8.3) AESI were reported. The most common AESI were uveitis (194 (2.6)) followed by medically important infections (155 (2.0)), cytopenias (62 (0.8)), hepatic events 39 (0.5), anaphylaxis (28 (0.4)), other autoimmune-pathies (25 (0.3)), chronic inflammatory bowel disease (23 (0.3)), depression (17 (0.2)), macrophage activation syndrome (12 (0.2)), malignancies (8 (0.1)) and pregnancies (8 (0.1)). There were marked differences in the rate of AESI with different biologics. Uveitis was most common in TNF-antibody treated cohorts, infections upon GOL, TOC, ANA, cytopenias upon TOC, CAN, hepatic events upon TOC, anaphylaxis upon INF, TOC, CED upon ETA, INF (table 1). One case of latent TB but no further opportunistic infections were reported. There was a single death due to sepsis.

[KM1]Vorn 2481

[KM2]Vorn 67?

Conclusions: Surveillance of pharmacotherapy as provided by BIKER is an import approach especially for long term treatment of children. Overall, tolerance is acceptable. Differences between several biologics were noted and should be considered in daily patient care

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ANAKINRA FOR FIRST LINE STEROID FREE TREATMENT IN SYSTEMIC ONSET JUVENILE IDIOPATHIC ARTHRITIS

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Background: Systemic juvenile idiopathic arthritis (sJIA) is characterised by arthritis accompanied or preceded by systemic autoinflammation. High-dose steroids has been the mainstay of therapy with proven effectiveness but also with side-effects. In many patients a chronic course with destructive arthritis long-term cannot be prevented.

Objectives: In patients naïve for steroids, a steroid-free treatment may allow reconstitution of an impaired NK-cell function and probably remission of sJIA.

Methods: First experience with first line Anakinra without steroids in 9 consecutive patients is reported.

Results: All patients presented with ongoing spiking fever and rash and further features of sJIA, high CRP, S100 and IL18 (table 1). Daily sq. injections of Anakinra 2 mg/kg for 3 months resulted in complete remission in 4 and partial response in two children presenting with an oligoarticular involvement. One patient with typical sJIA and very high S100 (MRP8/9) levels did not respond to Anakinra nor to Canakinumab. Two patients presented with polyarthritis. One had no response, the other showed a minor response but improved on steroids and was later treated with tocilizumab. One of the oligoarticular patients with an initial partial response had a flare upon anakinra captured by increased dosing (4 mg/kg) but finally developed macrophage activation syndrome. Anakinra was discontinued after 3 months in 3 of the 4 responders. Two remained in drug free remission while the remainder flared several months later and retreatment was instituted. The patients with polyarticular involvement first received corticosteroids and were later both treated successfully with the IL-6 inhibitor.

Conclusions: Experience with first line steroid free treatment with Anakinra for sJIA is presented. A complete remission was reached in 4 cases with oligoarticular

involvement. In 3 further cases improvement was observed and 2 had no response including one who also failed Canakinumab. A toddler with a particular response to Anakinra later on developed MAS. One patient did not respond to both IL-1 inhibitors. Thus, steroid free treatment regimen with Anakinra is feasible and resulted into remission in most but not all patients. Aside, unwarranted effects of long lasting steroid application were avoided.

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CARDIOVASCULAR RISK IN LONG-TERM JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Idiopathic Arthritis (JIA) is one of the more common chronic diseases of childhood that often persists into adulthood and can result in significant long-term morbidity, including physical disability. The long-term risk of cardiovascular disease for individuals with Juvenile Idiopathic Arthritis (JIA) remains uncertain.

Objectives: This study aims to determine whether adults with JIA in remission and medium-long duration of the disease have an increased risk of cardiovascular disease.

Methods: This is a cross-sectional study including 25 patients (14 females and 11 males) diagnosed with JIA according to the International League of Associations for Rheumatology criteria ILAR 2001 were compared to 20 age- and sex-matched controls. Remission was determined by JADAS27 <1 and according to Wallace criteria. An extensive clinical analysis including body index mass, lipid profile, HOMA-IR and intra-arterial blood pressure was performed. Intima media thickness of the common carotid artery (CIMT) was measured as a marker of sub-clinical atherosclerosis. Different proinflammatory cytokines (TNF α , IL1b and IL6), molecules involved in the endothelium dysfunction (VEGF and E-Selectin) and adipokines (resistin and visfatin) were analysed on serum by ELISA.

Results: Mean duration of the disease was 13.31 $\pm$ 1.14 years. Mean age was 27.21 $\pm$ 0.68. Time in remission was 3.52 $\pm$ 0.84 years. Metabolic comorbidities such as obesity and metabolic syndrome were more prevalent in our cohort of JIA patients compared to controls. Levels of cholesterol were significantly elevated in patients. However, HOMA-IR values and intra-arterial pressure were not significantly increased in JIA patients. CIMT was higher in JIA patients compared to controls (0.44 $\pm$ 0.009 vs 0.41 $\pm$ 0.017, p=0.078), although it did not reach the statistical significance. Serum levels of cytokines (including TNF α , IL6 and IL1b), adipokines (such as resistin and visfatin), and VEGF were significantly augmented in the cases vs healthy donors. In addition, IMT values significantly correlated with the disease duration (r=0.439, p=0.046) and serum VEGF levels (r=0.498, p=0.030).

Conclusions: In our cohort of JIA patients the increased CIMT was not associated with inflammatory markers, but disease duration. Although patients were in clinical remission, the serum levels of inflammatory cytokines, adipokines and VEGF were elevated, molecules with a relevant role in the onset and progression of endothelial dysfunction and atherosclerosis. These results might suggest that long-term JIA patients could have higher cardiovascular risk, although they are in sustained remission.

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Age, gender	Clinical features	CRP, mg/l	S100 (MRP8/9)	IL18, pg/ml	Initial response	Outcome
11, m	spiking fever, rash, arthralgia	95.6	1910	2483	complete response	remission off treatment
2, m	spiking fever, rash, organomegaly, arthralgia	101.7	14 110	>10 000	complete response	remission off treatment
1, f	spiking fever, rash, organomegaly, oligoarthritis	158.3	820	>5000	partial response	increase of dosage upon flare, discontinued with MAS
8, f	spiking fever, rash, polyarthritis	224.5	4040	>10 000	no response	remission upon Tocilizumab
15, f	spiking fever, rash, polyarthritis	329.6	4780	>10 000	partial response	remission upon Tocilizumab
5, m	spiking fever, rash, organomegaly, arthralgia	20.5	22 650	3820	minor response	improvement with corticosteroids, remission on Tocilizumab
11, w	spiking fever, rash, organomegaly, arthralgia	145.8	20 775	6000	complete response	remission off treatment
4, m	spiking fever, rash, pericarditis, splenomegaly, arthralgia	203.8	3 04 850	>10 000	no response	switch to Canakinumab with no response, remission on steroids
5, m	spiking fever, rash, arthralgia	237.7	1 61 700	2830	complete response, switch to Canakinumab after 7 days	remission off treatment