THU0582

A SYSTEMATIC REVIEW OF EMPLOYMENT OUTCOMES OF ADULTS WITH CHILDHOOD-ONSET SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES

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Background: Childhood-onset systemic autoimmune rheumatic diseases (ChildCRD) include: systemic lupus erythematosus (SLE), Sjogren's syndrome, systemic sclerosis, inflammatory myositis, and chronic systemic vasculitides (Takayasu arteritis, polyarteritis nodosa, anti-neutrophil cytoplasmic antibodies (ANCA) associated systemic vasculitides). These conditions had mortality rates of up to 50%, but most patients now live into adulthood. Employment is an important milestone in adulthood: it has direct effects on one's socioeconomic status and access to health insurance, which could in turn affect disease outcomes.

Objectives: To perform a systematic review of the employment outcomes of ChildCRD individuals. To identify gaps of knowledge and methodological issues in this field so as to inform future studies.

Methods: ChildCRD patients have disease-onset <18 years old and adulthood outcomes reported at ≥18 years old. We developed a search strategy for employment outcomes of ChildCRD with an academic librarian; this was iteratively refined and finalised after peer-review by other librarians. We included English language articles published from Jan 1990 Oct 2017 in MEDLINE, EMBASE, and Scopus. Case reports, case series, editorials, letters, or short reports were excluded. We supplemented our search by hand-searching references in review articles. Information on outcomes, prognostic factors, and study designs was recorded. Studies were graded independently by 2 reviewers (after prior training for agreement) using the Quality in Prognosis Studies (QUIPS) risk-of-bias tool which examines quality in 6 study domains. Authors were contacted as necessary for further information or clarification.

Results: Of 2109 studies, we identified 3 publications (G1) studying SLE patients. None studied other ChildCRD. Two papers were from a single study and studied both SLE and juvenile arthritis; we only used SLE patients' information. Three additional manuscripts (G2) studied childhood- and adult-onset patients but did not report outcomes separately. All G1 publications were from North America (2 Canada, 1 USA). 193 patients in 2 studies were examined; 1 study had longitudinal (non-inception) design. Only G1 studies have data for report. Patients' disease durations were a mean of 7.6–15 years and the mean ages at study were 23–29 years. Half of the patients were employed. Lower disease activity, better physical function, and higher education were associated with longitudinal employment in 1 study; greater independence and social support were associated with employment in another. One study showed psychosocial and work context factors to be associated with absenteeism, disease activity with job disruptions, and fatigue and work context factors with lost productivity. Of QUIPS-graded G1 publications, study populations and confounding were at moderate-high risk-of-bias. Study outcomes, prognostic factors, and statistical analyses were at low-moderate risks-of-bias. Attrition was low in the longitudinal study.

Conclusions: Currently, there is minimal information on employment outcomes in ChildCRD adults except for few studies on SLE; information about other ChildCRD is needed. Study populations and confounding are at moderate-high risks-of-bias, limiting the generalizability. More information on employment outcomes, the specific aspects of employment, disease and non-disease related prognostic factors affecting employment are needed.

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THU0583

PAIN INTERFERENCE ASSOCIATED FACTORS IN A COHORT OF FINNISH YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Pain is one of the most distressing and persisting features of JIA and frequently interferes with everyday life.

Objectives: This study was conducted to find out the factors associated with pain interference in young adults (aged 18 to 30 years) with JIA.

Methods: 195 adult patients with JIA were eligible for the study. Associations between patients reported outcome data and pain interference were examined. Sociodemographic and clinical data were analysed. Pain interference was measured by a single item from the RAND 36 questionnaire. Five response categories were coded into different groups: patients reporting "extremely" and "quite a bit" or "moderate" were classified having significant pain interference; "a little bit" as having minor pain interference; and "not at all" as having no pain interference. Functional disability was measured by HAQ, depressive symptoms were measured by Beck Depression Inventory-II, self-esteem was assessed by Rosenberg Self-

Esteem Scale, and anxiety was assessed by PASS-20. Leisure time physical activity (LTPA) metabolic equivalent (MET) score was calculated.

Results: Pain intensity scores were higher in patients expressing significant pain interference (mean 5.3, SD 2.1) and minor pain interference (mean 2.8, SD 2.09); p for linearity <0.001, thus the mean pain intensity for the whole study group was quite low (mean 2.3, SD 2.3). Of the 195 patients 98 (50.3%) reported no pain interference, 59 (30.3%) reported minor pain interference, and 39 (20%) reported significant pain interference. We found that pain interference was associated with older age ($p=0.029$), female gender ($p=0.028$) and receiving antirheumatic treatment ($p=0.032$), analgesics ($p<0.001$), antidepressants ($p=0.008$), and opioids ($p<0.001$). Also cohabiting ($p=0.003$), LTPA MET ($p=0.032$), smoking (0.006), being more disabled ($p<0.001$), having fewer leisure time activities ($p<0.001$) or having co-morbidities ($p=0.006$), and headache ($p<0.001$) were associated with having pain interference. Higher anxiety scores were associated with more pain interference ($p<0.001$). When controlling for gender, age, depression, LTPA MET, disability, life situation, disease remission, analgesics, antidepressants, and pain intensity, all subscales in PASS-20 were significantly associated with higher pain interference levels: cognitive anxiety ($p=0.004$), escape/avoidance ($p<0.001$), fear ($p=0.001$), psychological anxiety ($p=0.016$).

Conclusions: Half of the JIA patients reported pain interference, and they also expressed higher pain scores. Age, gender, using antirheumatic drugs, antidepressants, analgesics or opioids, cohabiting, lower LTPA MET score, disability, smoking, co-morbidities, lack of activities, and suffering anxiety were most significantly related to pain interference. Our study highlights the need to develop better strategies for pain-relieving interventions and for supporting patients' health-behaviour in order to achieve better pain outcome in young adults with JIA.

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THU0584

VITAMIN D STATUS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AND ITS ASSOCIATION WITH DISEASE ACTIVITY AND PROGRESSION – RESULTS FROM THE INCEPTION COHORT ICON

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Background: Vitamin D has been shown to have immunomodulatory properties in addition to its well-established role in the maintenance of mineral homeostasis and bone health. Conflicting data have been available regarding vitamin D status in children and adolescents with juvenile idiopathic arthritis (JIA) and its influence on the disease.

Objectives: To determine 25–0 hour-vitamin D3 (25-OHD) levels in patients with JIA, and to evaluate whether 25-OHD levels are associated with disease activity and disease course.

Methods: Serum 25-OHD levels were determined in a pair of serum samples from patients with JIA who were enrolled in the JIA inception cohort study ICON and prospectively followed for three years. The frequencies of 25-OHD deficiency (defined as <20 ng/ml) and 25-OHD sufficiency (≥30 ng/ml) were determined and compared with those of the age-, sex- and ethnicity-matched general population (KIGGS study). The association of 25-OHD levels and the likelihood for uveitis were analysed by a Cox-proportional hazard model. Logistic regression analysis was used to investigate the predictive value of 25-OHD in terms of disease progression into extended oligoarthritis (OA).

Results: In 360 patients with early JIA (48% OA, 27% rheumatoid-factor negative polyarthritis), 25-OHD levels were determined twice: after a median disease duration of 6.6 and of 13.0 months. The mean 25-OHD level of all JIA samples was insufficient (22.1 ng/ml, SD 7.8), but significantly higher than that of the control population (18.4 ng/ml, SD 10, $p<0.001$). Vitamin D levels decreased with age in patients and controls, but did not differ between males and females.

An insufficient mean 25-OHD level was found in 40% of JIA patients and in 25% in both samples each, sufficient levels in 13% and 7%, respectively. There were no significant differences in 25-OHD levels among the JIA categories. Disease activity, measured by the cJADAS-10, was inversely correlated with the first 25-OHD level ($\beta=-0.20$, 95% CI $-0.37, -0.03$, $p=0.018$), especially in 141 DMARD-naïve patients ($\beta=-0.26$, 95% CI $-0.44, -0.01$, $p=0.041$). Up to the 3-year-follow-up, 17% (61/360) developed uveitis, and 30% (52/173) of OA patients an extended OA. While 20% (17/87) of those with 25-OHD deficiency at both measurements were affected by uveitis, this applied to only 9% (2/23) in those with sufficient levels. Multivariable regression analysis revealed that the 25-OHD level was significantly associated with the risk to develop uveitis (Hazard ratio 0.95, 95% CI 0.91, 0.99, $p=0.008$). Twelve out of 29 (41%) patients with OA and two deficient

vitamin D levels, but only 2 of 14 (14%) with two sufficient 25-OHD levels developed extended OA during the first 3 years ($p=0.034$).

Conclusions: Overall, vitamin D levels were higher in JIA patients than in matched controls. JIA patients with higher disease activity had lower 25-OHD levels. In particular, complicated courses with uveitis or the development of polyarthritis seem to be associated with lower 25-OHD levels. Further studies are needed to substantiate these results.

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THU0585

PERSONALISED TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS – FUTURE OR FICTION? PRELIMINARY RESULTS OF USING S100A8A9, S100A12 AND VASCULAR ENDOTHELIAL CADHERIN AS DIAGNOSTIC AND PROGNOSTIC BIOMARKERS

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Background: Serological biomarkers with ability to predict outcome and therapeutic response of patients might be helpful in introducing the concept of treat-to-target into management of juvenile idiopathic arthritis (JIA). Among others, calprotectin (S100A8A9) and calgranulin C (S100A12) are considered to be valuable markers of disease activity and risk factors for flare after withdrawal of treatment. Vascular endothelial cadherin (VE-cadherin) is a marker of endothelial permeability which has been postulated to predict response to methotrexate therapy in rheumatoid arthritis (RA) patients.

Objectives: The aim of the study was to assess the clinical significance of measuring serum concentrations of S100A8A9, S100A12 and VE-cadherin in patients with freshly diagnosed JIA and those with exacerbated course of the disease.

Methods: Serum levels of the listed biomarkers were determined in 30 patients diagnosed with JIA and 21 age- and sex-matched healthy controls. In the study group blood samples were obtained in two time points in order to evaluate dynamics of concentrations of markers.

Results: S100A8A9 and S100A12 serum concentrations at baseline were positively correlated with ESR at second time point ($r=0.378$ and 0.425 , $p=0.0397$ and 0.0193 , respectively). S100A12 had equal correlation with CRP at second time point ($r=0.391$, $p=0.0329$). Patients freshly diagnosed with JIA had higher levels of S100A12 (8.49 ± 4.92 ng/ml vs. 5.49 ± 2.21 ng/ml, $p=0.007$) and VE-cadherin (5.31 ± 1.13 ng/ml vs. 3.50 ± 0.58 ng/ml, $p<0.001$) when compared to healthy controls. VE-cadherin level was elevated in JIA patients at second time point as well (4.10 ± 0.93 ng/ml, $p=0.0194$). Patients who underwent arthrocentesis at baseline had higher concentrations of S100A12 at second time point (6.69 ± 3.56 ng/ml vs. 3.84 ± 2.58 ng/ml, $p=0.0168$). Levels of markers were independent of sex and age.

Abstract THU0585 – Table 1. General characteristics of the study group

No. of patients (%)	30 (100.0%)
Age at diagnosis of JIA±standard deviation	9.6±4.8 years
Female (%)	23 (76.7%)
Oligoarticular JIA (%)	24 (80.0%)
Enthesitis-related JIA (%)	2 (6.7%)
Polyarticular RF-negative JIA (%)	3 (10.0%)
Polyarticular RF-positive JIA (%)	1 (3.3%)
Freshly-diagnosed JIA at 1st time point (%)	10 (33.3%)
Exacerbated course of the disease at 1st time point (%)	15 (50.0%)
Minimal disease activity at 1st time point (%)	5 (16.7%)
Arthrocentesis performed at 1st time point (%)	16 (53.3%)
Duration of period between time points±standard deviation	99.1±27.7 days
Exacerbated course of the disease at 2nd time point (%)	9 (30.0%)

Abstract THU0585 – Table 2. Serum concentrations of assessed biomarkers (values presented as mean±standard deviation)

Marker	Study group – 1st time point (n=30)	Study group – 2nd time point (n=30)	Control group (n=21)
S100A8A9 [ug/ml]	2.56±2.15	1.69±1.42	1.47±0.68
S100A12 [ng/ml]	9.08±5.25	5.36±3.41	5.49±2.21
VE-Cadherin [ng/ml]	4.85±0.93	4.10±0.93	3.50±0.58

Conclusions: Presented study group needs to be expanded with more patients, especially with minimal disease activity, in order to validate demonstrated preliminary results. VE-cadherin may be considered as a future diagnostic biomarker, however its specificity requires detailed assessment. S100A8A9 and S100A12 merit further evaluation as potential prognostic biomarkers for more aggressive course of the disease.

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THU0586

METHOTREXATE DRUG SURVIVAL AND ADVERSE EFFECTS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Methotrexate is usually the first-line disease modifying anti-rheumatic drug (DMARD) for patients with juvenile idiopathic arthritis (JIA), due to its efficacy, the low-cost and favourable safety profile in patients. However, one of the most reported adverse effects of interest (AEIs) of methotrexate is nausea.

Objectives: The objectives of this analysis were to (i) calculate methotrexate monotherapy drug survival, (ii) describe AEIs over the first two years of treatment, and (iii) investigate factors associated with occurrence of AEIs among children with JIA.

Methods: Patients with all forms of JIA starting methotrexate monotherapy from both the UK BSPAR Etanercept Cohort Study (BSPAR-ETN) and Biologics for Children with Rheumatic Diseases study (BCRD) were included. Patient characteristics and anti-rheumatic therapy details were collected at treatment start. Follow-up data were collected at six months, one year, and annually thereafter, on changes to anti-rheumatic therapy and any adverse events. AEIs were grouped into gastrointestinal-related (nausea, vomiting, abdominal pain), raised liver enzymes, leukopenia, drug hypersensitivity (injection site reaction), rash, needle phobia, and any other event leading to permanent discontinuation of methotrexate. All person time was included from methotrexate start date until first methotrexate stop date, start of biologic therapy, last patient follow-up date, or 30-June-2017 (study cut-off date), whichever came first. Survival analysis was used to assess time on methotrexate monotherapy and time to first AEI on methotrexate monotherapy. Multivariable logistic regression was used to assess baseline characteristics associated with experiencing an AEI, and a gastrointestinal-related AEI only.

Results: Of 505 patients starting methotrexate between 01-January-2010 and 30-June-2015 (to allow at least two years of follow-up for all children), median time on monotherapy was 1.5 years (IQR 0.7, 2.3). At two years, 274 (54%) patients were no longer on methotrexate monotherapy. Reasons included: inefficacy ($n=174$; 64%) mostly due to start of biologic therapy ($n=161$), adverse events ($n=54$; 20%), remission ($n=24$; 9%), and patient/family decision ($n=9$; 3%). Within the first two years of methotrexate monotherapy, 181 (36%) patients experienced at least one AEI; the most common were gastrointestinal problems ($n=116$; 53%) and liver enzyme abnormalities ($n=42$; 19%). No clinical factors were associated with occurrence of any AEI, nor a gastrointestinal-related AEI.

Conclusions: After two years, over half of the patients were no longer on methotrexate monotherapy, whilst one-third experienced at least one AEI, most commonly gastrointestinal-related problems. Further research focussing on identifying which children will respond and/or experience an AEI with methotrexate is crucial, such that AEIs can be minimised or prevented and treatment benefit maximised.

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