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THU0545

CHARACTERISING A MOUSE MODEL OF TEMPOROMANDIBULAR JOINT (TMJ) ARTHRITIS TO STUDY OROFACIAL PAIN AND INFLAMMATION

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Background: The temporomandibular joints (TMJ) encompass the jawbones (mandibular condyle) and the skull region (temporal bone)¹. Dysfunctions in these joints and surrounding muscles result in a condition known as TMJ disorder (TMD), which include mastication-related pain. 16%–59% of patients reported painful symptoms while 33%–86% of these patients showed clinical signs¹. Currently, the etiology of TMD is unknown, although lavage samples from patients showed signs of synovitis, which may lead to the development of degenerative disorders, such as TMJ arthritis². There are only a few murine models available, as the most commonly used animal model is TMJ arthritis in rats.

Objectives: We aimed to characterise a mouse model of TMJ arthritis by mimicking the formation of synovitis using zymosan. We sought to characterise the development of orofacial pain by performing various behavioural measurements and measure joint inflammation.

Methods: All *in vivo* procedures were carried out according to the UK Home Office Animals (Scientific Procedure) Act 1986. Male CD1 mice (6–8 weeks) were anaesthetised transiently using 2% isoflurane. Zymosan (10, 30, or 100 µg; 10 µl), or saline was administered unilaterally into the TMJ as previously described³. Spontaneous pain behaviours were observed by counting the number of unilateral cheek wipes. All studies were terminated by cervical dislocation and the tissue was collected for *ex vivo* analyses. Mean ± SEM was calculated and data were analysed by unpaired Student's T-test or 2-way repeated measures ANOVA with Bonferroni's *post hoc* test. *p* < 0.05 was accepted as statistically significant.

Results: A dose response study showed that 30 µg, but not 10 µg and 100 µg of zymosan, resulted in a maximal wiping response at 2 hours, which was maintained at 4 hours (table 1; ****p* < 0.001 zymosan ipsi vs saline ipsi; ## *p* < 0.01 zymosan ipsi vs contra). Hind paw scratching was negligible. Hence, 30 µg was used for subsequent experiments. Increased neutrophils (measured by MPO assay) was observed in zymosan-treated joints (table 1 ***p* < 0.01 saline ipsi vs zymosan ipsi), while a similar trend was also observed in 3-nitrotyrosine protein expression, a marker of protein nitrosylation (*p* = 0.053). Preliminary studies are being undertaken to characterise other inflammatory markers in addition to the development of *in vivo* orofacial mechanical hyperalgesia using the Von Frey filaments.

Table 1 A summary of zymosan-mediated spontaneous orofacial pain behaviours and inflammation.

	Saline (n=4)				Zymosan							
					10 µg (n=6)		30 µg (n=5)		100 µg (n=6)			
	Ipsi	Contra	Ipsi	Contra	Ipsi	Contra	Ipsi	Contra	Ipsi	Contra	Ipsi	Contra
Unilateral cheek wipe (no. of events)	5.0 ±1.0	5.5 ±1.9	5.7 ±2.6	6.0 ±1.2	22.0 ±4.4	8.2 ±2.6	5.3 ±3.3	3.1 ±1.2				
					*** ##							
Unilateral hind paw scratching (no. of events)	0.5 ±0.5	0.0 ±0.0	1.0 ±0.7	4.5 ±2.6	3.4 ±0.8	2.1 ±1.0	0.4 ±0.2	0.4 ±0.2				
MPO (U/mg of protein)	0.01 ± 0.003		N/A		0.08 ± 0.01 **		N/A					
3-nitrotyrosine/GAPDH	2.3 ± 0.4				3.8 ± 0.5							

Conclusions: We have established a mouse model of TMJ arthritis, which showed significant orofacial pain responses *in vivo*. Our data highlights an inflammatory profile typical of zymosan and shows a potential use for this model to investigate novel TMD treatments.

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THURSDAY, 14 JUNE 2018

Paediatric rheumatology

THU0546

CHILDREN WITH PSORIASIS ALSO SHOW ENTHESOPATHY SIGNS RELATED TO SKIN DISEASE ACTIVITY

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Background: Many recent evidences shows the role of enthesopathy in psoriatic disease and the high prevalence of musculoskeletal widespread pain in patients with psoriasis and psoriatic arthritis. It may be very difficult to distinguish between inflammatory disease activity and fibromyalgia. Limited data are available about the prevalence of rheumatological findings in children with psoriasis.

Objectives: To determine the prevalence of musculoskeletal pain complaints, enthesitis and tender points in a population of children and adolescents with psoriasis and correlate it to the skin disease activity and quality of life.

Methods: 26 children and adolescents with psoriasis were included in this cross sectional study and assigned a written informed consent. Patients and parents were interviewed about musculoskeletal complaints, personal and familiar history of rheumatic diseases. A paediatric rheumatologist performed the physical examination, which included evaluation of active joint count, palpation of entheses and tender points of fibromyalgia. A paediatric dermatologist performed PASI score and BSA to assess skin disease activity. Nails involvement were assessed by NAPS. The functional capacity was assessed by CHAQ. The quality of life was assessed by CDLQI.

Results: Participants were 69% female, with a mean age of 10.1 ± 3.0 years at observation. The median of age at the beginning of skin disease was 3 (0.5–12) years. PASI median was 4 (0.6–30.2), BSA 6 (2–39) and NAPS 12.3–36. A severe PASI above 5 were present in 38.5%. Complaints of any kind of musculoskeletal recurrent pain were seen in 46.1% of the patients and lumbar pain in 15.4%. Pain, limit on motion or joint oedema were seen in 26.9% whereas tenderness on palpation of any site of enthesitis was found in 30.7% and tenderness on palpation of sacroiliac joint was found in 19.2% of the patients. The median of fibromyalgia tender points was 5 (0–16). The presence of enthesitis was associated to the skin disease activity scores of PASI (*p* < 0.006), BSA (*p* < 0.016) and nail index NAPS (*p* < 0.05) (figure 1). As expected, the presence of enthesitis was associated to the number of tender points (*p* < 0.001). For those with a severe PASI > 5, we found a higher number of tender points (Med 0 versus 10; *p* < 0.03), a worst functional capacity by CHAQ (Med 0 versus 0.12; *p* < 0.03) and worst quality of life by CDLQI (Med 1 versus 9; *p* < 0.05).

Conclusions: High prevalence of musculoskeletal pain symptoms, enthesitis and fibromyalgia tender points was observed in this sample of children and adolescents with psoriasis. Differently from adults, we do not expect to have age-related degenerative changes in entheses in this population, what reinforce the inflammatory origin of these rheumatologic findings. Otherwise, the association with the severity of psoriasis increases the need for vigilance against the appearance of psoriatic spondyloarthropathy in this group.

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Rheumatoid arthritis – biological DMARDs

THU0547

REAL-WORLD EFFECTIVENESS OF EARLY AGGRESSIVE TREATMENT WITH BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS FOR THE TREATMENT OF NEWLY DIAGNOSED POLYARTICULAR FORM OF JUVENILE IDIOPATHIC ARTHRITIS

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Background: Limited evidence from randomised clinical trial suggested early aggressive treatment with biological disease modifying antirheumatic drugs (DMARDs) maybe a better treatment strategy in children with polyarticular form of Juvenile idiopathic arthritis (pJIA).¹ Three consensus treatment plans (CTP) were recommended for treating children with newly onset of pJIA.² The real-world effectiveness is unknown.

Objectives: Evaluate the comparative effectiveness of early combination CTP vs. the step-up CTP, in treating children with newly diagnosed pJIA, utilising electronic health records (EHR) data collected from routine clinical care.

Methods: This inception cohort is derived from data captured in a single institute EHR from January 2009 to July 2017. Eligible patients are 2–16 years of age, newly (<6 m) diagnosed with pJIA and treated on DMARD. The first clinical encounter initiate DMARDs is identified as the baseline. The primary end point is clinical Juvenile Arthritis Disease Activity Score (cJADAS) 6 months after the treatment.

Results: Out of 1834 pJIA patients captured in EHR, 432 are eligible for the study. Most patients (362, 84%) initiated DMARD within 6 month of diagnosis: 105 (29%) on early combination and 257 (71%) on step-up plan. Three months following the initial DMARD assignment, 98 (93%) and 244 (95%) remained on the initial early combination and step-up plan respectively, thus are used in this study. Patients on early combination had significantly higher cJADAS score at the baseline (15.5±6.6 vs. 12.5±5.9; Student P value<0.01), and higher rate of RF (18% vs. 7%, Chisq p<0.01). After 6 months of treatment, their cJADAS scores are more comparable (mean ±SD of 6.9±5.4 in early combination, and 7.1±6.1 in step-up; Student T p=0.7). After statistically adjusting for treatment selection bias, causal inference methods suggest lower cJADAS is expected had the patient been treated on early combination than on the step-up plan, mean and 95% confidence interval of averaged treatment effect is 2.90 (0.89, 4.91).

Conclusions: The early combination approach improves clinical outcomes at 6 months more effectively than the step-up strategy in children with newly onset pJIA.

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Diagnostics and imaging procedures

THU0548

STANDARDISED PROCEDURES FOR ULTRASOUND IMAGING IN PAEDIATRIC RHEUMATOLOGY: PROGRESS OF EULAR/PRES TASK FORCE

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Background: Musculoskeletal ultrasound (MSUS) is dependent on sensitivity of the machine used and the skills of the operator. Additional specificities are unique features of the growing skeleton, which include age-related variation of the thickness of the articular cartilage (due to incomplete ossification) and the presence of physiologically detected vascularisation even in healthy children.

Objectives: EULAR/PreS task force objective was to develop EULAR/PreS Standardised Procedures for Ultrasound Imaging in Paediatric Rheumatology through a consensus process among rheumatologists, paediatric rheumatologists, and radiologists highly experienced in the performance, teaching and research in paediatric MSUS in rheumatic diseases.

Methods: In the first phase we performed a systematic literature review (SLR) on guidelines for MSUS for children endorsed by international societies and articles on how to perform MSUS scanning in children. Based on the SLR results, project conveners formulated a Delphi survey by selecting the items to be included (i.e. musculoskeletal anatomic structures evaluable by US, scanning technique, and their lesions/abnormalities detectable by US at the principal joint areas). The Delphi survey was distributed among a broad panel of experts in MSUS, selected for their high experience in the performance, teaching and research in MSUS in children. Based on the Delphi results the main anatomical structures (for definitions, photo and video recordings) were selected to be analysed in the final phase organised as an exercise on live healthy children models. The meeting involved: 16 project participants (13 paediatric US experts, fellow, as well as, AHP and PARE representatives), 16 healthy children models (representing four different age groups) accompanied by their parents (who had signed informed consent to participate), 4 photo/imaging technicians, 2 expert technicians in US machines.

Results: Structures from 8 musculoskeletal areas (i.e. shoulder, elbow, wrist and hand, hip, knee, ankle and foot) in 4 age groups of children were selected. Detailed scanning procedures (i.e. patient position, probe placement, scanning method and bony/other landmarks) were defined. We recorded the reference photo (live and US image) and video (procedure video clip and US video record) of the scanning procedures. As a result, we obtained photo and video image library with a detailed description of the standardised US procedures in children which can be used as EULAR/PreS web-based educational application.

Conclusions: This task force has produced a consensus-based comprehensive and practical framework on standardised procedures for MSUS imaging in paediatric rheumatology.

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