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Original article

Sleep and fatigue and the relationship to pain, disease activity and quality of life in juvenile idiopathic arthritis and juvenile dermatomyositis

Yonatan Butbul Aviel[1], Robyn Stremler[2], Susanne M. Benseler[3], Bonnie Cameron[3], Ronald M. Laxer[3,4], Sylvia Ota[5], Rayfel Schneider[3], Lynn Spiegel[3], Jennifer N. Stinson[2,6,7], Shirley M. L. Tse[3] and Brian M. Feldman[8,9]

Abstract

Objectives. To determine and compare the prevalence of disturbed sleep in JIA and JDM and the relationship of sleep disturbance to pain, function, disease activity and medications.

Methods. One hundred fifty-five patients (115 JIA, 40 JDM) were randomly sampled and were mailed questionnaires. Sleep disturbance was assessed by the sleep self-report (SSR) and the children's sleep habits questionnaire (CSHQ). Fatigue, pain and function were assessed by the paediatric quality of life inventory (PedsQL) and disease activity by visual analogue scales (VASs). Joint counts were self-reported.

Results. Eighty-one per cent responded, of whom 44% reported disturbed sleep (CSHQ > 41); there were no differences between disease groups. Poor reported sleep (SSR) was highly correlated with PedsQL fatigue ($r = 0.56$, $P < 0.0001$). Fatigue was highly negatively correlated with quality of life ($r = -0.77$, $P < 0.0001$). The worst pain intensity in the last week was correlated to sleep disturbance ($r = 0.32$, $P = 0.0005$). Fatigue was associated with prednisone and DMARD use.

Conclusions. Sleep disturbance and fatigue are prevalent among children with different rheumatic diseases. Sleep disturbance and fatigue are strongly associated with increased pain and decreased quality of life. Strategies aimed at improving sleep and reducing fatigue should be studied as possible ways of improving quality of life for children with rheumatic illness.

Key words: Juvenile idiopathic arthritis, Dermatomyositis, Sleep, Fatigue, Pain.

Introduction

JIA is one of the most common rheumatic diseases in childhood, affecting at least 1 in 1000 children [1]. Findings suggest that fatigue is common [2] and that sleep is disrupted in children with JIA [3, 4].

Sleep in adequate amount and quality is essential for normal child development. Sleep disturbances collectively refer to impairments in the ability to initiate or maintain sleep, and can be measured by parent or child self-report and by objective measures such as actigraphy and polysomnography [5]. Sleep disorders may affect a child's daytime function, resulting in behavioural problems such as attention deficit, aggressiveness, hyperactivity, chronic fatigue, decrements in daytime alertness and performance, and an increase in school absenteeism [6, 7]. Sleep disturbances have also been associated with children's quality of life—negatively impacting children's physical and emotional well-being [8, 9].

Sleep disorders are common in adult patients with musculoskeletal diseases including RA, FM and OA [10–12]. In patients with RA there is evidence for severe sleep

[1]Department of Pediatrics, Technion Institution, Pediatric Department Rheumatology Unit, Technion Faculty of Medicine, Meyer Children's Hospital of Haifa, Haifa, Israel, [2]Lawrence S. Bloomberg, Faculty of Nursing, [3]Department of Pediatrics, [4]Department of Medicine, Division of Rheumatology, The Hospital for Sick Children, University of Toronto, [5]Child Health Evaluative Sciences, [6]Department of Anesthesia, [7]Department of Pain Medicine and Nursing, The Hospital for Sick Children, [8]Department of Pediatrics, Health Policy Management & Evaluation and [9]Dalla Lana School of Public Health, Division of Rheumatology, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada.

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Correspondence to: Brian Feldman, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G1X8, Canada.
E-mail: brian.feldman@sickkids.ca

fragmentation with frequent awaking and arousal. The behavioural manifestations of such sleep disturbances in adults include excessive daytime sleepiness and fatigue, coupled with decreases in mood and performance [13]. Although it is generally assumed that joint pain may induce sleep abnormalities, the cause of frequent awaking and arousals in patients with RA is controversial.

Little is known about the quality of sleep in children with rheumatic diseases. Studies suggest that sleep is disrupted in children with JIA [3, 4]. Children with JIA and their parents report significantly more instances of night awaking, parasomnia, sleep anxiety, sleep-disordered breathing, early morning awaking and day-time sleepiness than do healthy children [14]. The cause of sleep disturbance in patients with JIA has yet to be elucidated; Bloom [14] and Lewin and Dahl [15] hypothesize a bi-directional interplay between pain and sleep disturbance. Currently there are no data about sleep disturbance in children with JDM. The aims of this study were to describe and compare sleep disturbance in the most common subtypes of JIA and in JDM, to explore possible associations of sleep disturbance with fatigue, disease activity, pain and health-related quality of life (HRQL), and to measure the influence of different medications on sleep.

Patients and methods

We used a cross-sectional, mailed survey design. The research was approved by The Hospital for Sick Children Research Ethics Board (approval number 1000010691).

Study population

A random, representative sample, balanced for disease subtype, was drawn from the population of all patients diagnosed with JIA (by the ILAR criteria) [16] currently followed at The Hospital for Sick Children. For feasibility reasons, we limited the onset subtypes of JIA that we sampled to oligoarticular, polyarticular (RF negative) and systemic. We used a computer-generated list of random numbers in order to draw the sample. Eligible children were between the ages of 8 and 16 years so that they were able to answer the study questionnaires.

One hundred and fifteen patients with JIA (oligoarticular, $n = 40$; polyarticular, $n = 40$; and systemic, $n = 35$) were randomly selected. Forty patients with probable or definite JDM [17, 18] between the ages of 8 and 16 years were randomly selected using the same strategy. Patients with concomitant chronic inflammatory diseases (e.g. IBD, active atopic dermatitis, etc.) were excluded.

Procedure

In order to achieve a high response rate we used components of the Tailored Design Method [19] that comprises several contacts with the families. A pre-notice letter was sent a week before the questionnaire mail out. One week later a questionnaire with a cover letter was sent; 2 weeks after the questionnaire a thank you/reminder postcard was sent. For those who did not respond after 2 weeks, a fourth reminder letter was sent with a replacement questionnaire; finally, 2 weeks later telephone contact was made with those who had not yet answered the survey.

Questionnaires

We developed a questionnaire that captured demographic and disease-related information and comorbidities, e.g. age, disease type, medication (including dose and frequency) as well as questions regarding family history of sleep disturbance and other conditions affecting the patient associated with sleep disturbance (i.e. attention deficit hyperactivity disorder, FM and psychiatric illness).

Evaluation of sleep and fatigue

Sleep was assessed by two questionnaires, the parent-reported children's sleep habits questionnaire (CSHQ) [20] and the child-reported sleep self-report (SSR) [21]. The CSHQ is a retrospective, 45-item parent questionnaire that has been used in a number of studies to examine sleep behaviour in children and has established validity and reliability. Thirty-five items on the CSHQ are grouped into eight subscales related to a number of key sleep domains:

- bedtime resistance (six items);
- sleep onset delay (one item);
- sleep duration (three items);
- sleep anxiety (four items);
- night awakening (three items);
- parasomnia (seven items);
- sleep-disordered breathing (three items); and
- day-time sleepiness (eight items).

The total score consists of 33 items, rather than 35, because two of the items on the bedtime resistance and sleep anxiety subscales are the same. Parents are asked to recall sleep behaviours occurring over a typical recent week. Items are rated on a 3-point scale for frequency of the sleep behaviour: usually = 5–7 times/week; sometimes = 2–4 times/week; and rarely = 0–1 times/week. A cutoff total CSHQ score of 41—as has been previously suggested—was chosen as the cutoff to define a patient as having sleep disturbance.

The SSR is a 26-item, 1-week retrospective survey designed to be administered to or self-administered by elementary school-aged children (generally ages 7–12 years). The SSR was designed to assess sleep domains like those of the CSHQ, and, in its development, items were selected to be approximately similar to items on the CSHQ. Though designed to parallel the CSHQ, the SSR addresses domains with fewer and less-complex questions in order to be understandable to children. Items are rated on the same 3-point scale as the CSHQ, with higher scores indicating more disturbed sleep. Some items are reverse scored so that a higher score in any given item consistently indicates more disturbed sleep or more problematic sleep behaviour. The SSR yields a total score only.

Fatigue was assessed by the PedsQL multi-dimensional fatigue scale—parent and patient form. This is an 18-item

questionnaire that was designed to measure child and parent perception of fatigue in paediatric patients and comprises the general fatigue scale (six items), sleep/rest fatigue scale (six items) and cognitive fatigue scale (six items). This questionnaire was previously validated in paediatric patients, including those with rheumatologic disease [22, 23].

Evaluation of disease activity and HRQL/functional status

Disease activity was assessed with the following variables:

(i) Parents' global assessment of overall disease activity on a 10-cm visual analogue scale (VAS).
(ii) Number of swollen and painful joints by parents' and patients' self-report joint count—using a pictorial (mannequin) format. This method was previously validated in adult patients with RA and found to have a high correlation with physician assessment [24]. We modified the original mannequin format for use by paediatric patients; to the best of our knowledge, the mannequin has never been tested in this population before. Although a majority of JDM patients have arthritis during the course of their illness [25], the self-assessed joint count is a more important indicator of disease activity for the JIA subjects.
(iii) PedsQL (pediatric quality of life inventory) core modules—parent and patient form. The PedsQL is a modular instrument designed to measure HRQL in children and adolescents aged 2–18 years; the generic core scales are multi-dimensional child self-report and parent proxy-report scales developed as generic measures to be integrated with the PedsQL disease-specific modules [22]. Lower scores denote a poorer quality of life.
(iv) PedsQL rheumatology module—parent and patient form. This is a 22-item questionnaire that was designed to measure paediatric rheumatology-specific HRQL.

Both the PedsQL core and rheumatology modules have been tested in this population and have well-established validity and reliability [22, 23, 26–35].

Evaluation of disease-related pain

To assess pain, parents and patients completed the PedsQL paediatric pain questionnaire [34]. Present pain and worst pain intensity were assessed by a 10-cm VAS. In addition, four developmentally appropriate categories of pain descriptors were provided along with a body outline. The child was instructed to colour the four boxes underneath each descriptive category representing pain intensity and then to colour the body outline with the selected colour/intensity match. On the parents' form, pain was rated using numbers from 1 to 10 according to pain intensity, and parents were requested to place the numbers in the body outline. For simplicity, the body was divided into 34 areas (17 in the front and 17 in the back of the body) and only the number of painful areas was evaluated for our statistical calculations.

Statistical analyses

Continuous scores were described as means and medians as appropriate; categorical scores were described as frequencies. To compare groups, analysis of variance (ANOVA) was used with subsequent pairwise comparisons corrected for multiple comparisons using the Tukey honestly significant difference (HSD) test. Frequencies were compared by chi-square analysis. Correlations were performed using the Pearson's product-moment correlation. General linear modelling using standard regression diagnostics was used to look at predictive relationships. Due to possible confounding between medication use and disease activity, when medications were investigated as independent variables, models were constructed in which diagnosis, present pain, worst pain, number of painful areas, tender joint count, swollen joint count and global assessment were included as co-variates; final models were chosen using a backwards selection process. All analyses were performed using the R statistical language [version 2.7.2, Copyright (C) 2008, The R Foundation for Statistical Computing, ISBN 3-900051-07-0], and DataDesk 6.2.1 (Data Description, Inc., Ithaca, NY, USA).

Results

We had a high response rate; of 155 questionnaires that were mailed, we received 125 (80.6%). The demographic data are summarized in Table 1. The ages and sexes of the respondents did not differ between the groups.

Sleep and fatigue

All groups suffered from moderately severe fatigue, with no real differences between them; 44% reported sleep disturbance (CSHQ score $\geqslant 41$; Table 2). There was no difference in sleep disturbance between the groups—sleep disturbance was as marked in the JDM group as it was in the different JIA subtypes.

Disease activity

Disease activity was mostly low to moderate and the number of active (swollen or painful) joints was low (Table 3). As expected, the polyarticular-onset JIA group had a higher parent-reported painful joint count than the other groups.

Pain and HRQL

Pain was low to moderate in the studied subjects; 33% of the children reported no pain at the time of assessment (Table 4). Self-reported pain was somewhat higher in the polyarticular-onset JIA group. HRQL scores demonstrated moderate impairments in all groups; the polyarticular-onset JIA group appeared to be more affected than the others.

Factors influencing sleep disturbance and fatigue

Comorbidity and sleep

Very few subjects had comorbid illnesses or a family history of sleep disorder (Table 1). Sleep scores as measured by the CSHQ and SSR did not differ significantly between

Table 1 Demographic and clinical data for the JIA and JDM subjects ($n = 125$)

	Oligoarticular ($n = 31$)	Polyarticular ($n = 33$)	Systemic ($n = 28$)	JDM ($n = 33$)	Summary ($n = 125$)	*P*-value
Female : male	22 : 9	25 : 8	14 : 14	20 : 13	81 : 44	0.16
Mean (S.D.) age (median), years	12.5 (0.4) (12.5)	12.9 (0.4) (13.5)	12.7 (0.4) (13.2)	12.6 (0.4) (12.7)	12.7 (2.3) (12.8)	0.94
Family history of a sleep disorder (*n*)	3	2	4	1	10	0.64
Anxiety or psychiatric co-morbidity (*n*)	2	0	3	1	6	0.31
Attention deficit hyperactivity disorder comorbidity (*n*)	2	2	1	0	5	0.62
FM comorbidity (*n*)	0	0	1	0	1	0.58

Table 2 PedsQL multi-dimensional fatigue scale, children's CSHQ and SSR

	Oligoarticular ($n = 31$)	Polyarticular ($n = 33$)	Systemic ($n = 28$)	JDM ($n = 33$)	Summary ($n = 125$)	*P*-value
Parent report						
PedsQL multi-dimensional fatigue scale, mean (S.D.)	78.1 (3.5)	72 (3.3)	77.6 (3.5)	76.6 (3.3)	76 (18.7)	0.56
CSHQs, mean (S.D.)	39.6 (1.3)	42 (1.3)	40.6 (1.3)	41.1 (1.3)	40.9 (7)	0.60
Abnormal CSHQ ($\geqslant 41$), %	43	47	36	50	44	0.72
Patient report						
PedsQL™ multidimensional fatigue scale, mean (S.D.)	80.1 (3.2)	72 (3)	76.3 (3.2)	78.1 (3)	76.7 (17.1)	0.23
SSR, mean (S.D.)	36.6 (7)	36 (4.3)	34.6 (4.5)	37 (5.7)	36 (5.4)	0.36

Table 3 Reported number of painful and swollen joints and disease activity

	Oligoarticular ($n = 31$)	Polyarticular ($n = 33$)	Systemic ($n = 28$)	JDM ($n = 33$)	Summary ($n = 125$)	*P*-value
Parent report						
Swollen joints, mean (S.D.) (median)	0.2 (0.3) (0)	1.0 (0.3) (0)	1.4 (0.4) (0)	0.3 (0.3) (0)	0.7 (2.0) (0)	0.05
Painful joints, mean (S.D.) (median)	1.1 (2.4) (0)	3.1 (3.2) (2)	1.7 (2.8) (0)	1.1 (2.9) (0)	1.8 (2.9) (0)	0.016*
Disease activity, mean (S.D.), cm	0.8 (1.7)	1.8 (1.8)	2.0 (2.7)	1.3 (2.2)	1.5 (2.2)	0.2
Patient report						
Swollen joints, mean (S.D.) (median)	0.3 (0.4) (0)	0.8 (0.4) (0)	1.3 (0.4) (0)	0.3 (0.4) (0)	0.6 (.1) (0)	0.2
Painful joints, mean (S.D.) (median)	1.2 (0.5) (0)	2.2 (0.4) (1)	2.4 (0.5) (0.5)	1.1 (0.4) (0)	1.7 (2.6) (0)	0.1

*Polyarticular subtype significantly differs from oligoarticular and JDM but not from systemic subgroups.

those who had any of the measured comorbid illnesses or a family history of sleep disorder and those who did not.

Relationship between disease activity and sleep and fatigue

For the group as a whole, there was no correlation between disease activity (as measured by the VAS) and the severity of the sleep disturbance (as measured by the CSHQ) ($r = -0.03$, $P = 0.8$). The number of tender joints as reported by parents correlated modestly with the CSHQ ($r = 0.27$, $P = 0.002$); the relationship was similar when reported by children themselves. Parent-reported swollen joint count correlated less well with the CSHQ ($r = 0.15$, $P = 0.09$). Fatigue was worse (as measured by the parent-reported PedsQL fatigue scale) as disease activity increased ($r = -0.21$, $P = 0.03$) and as tender joint count ($r = -0.35$, $P \leqslant 0.0001$) and swollen joint count ($r = -0.23$, $P = 0.01$) increased. Similar results were seen when patients reported for themselves.

Relationship between pain and sleep and fatigue

Pain and fatigue were correlated. For example, parent rating of worst pain was moderately correlated with fatigue as reported by the PedsQL ($r = -0.51$, $P < 0.0001$). Worst pain was modestly correlated with sleep disturbance as measured by the CSHQ ($r = 0.23$, $P = 0.01$). Likewise, patient-reported sleep disturbance (SSR) correlated moderately with pain and fatigue (number of painful areas $r = 0.11$, $P = 0.22$; worst pain $r = 0.32$, $P = 0.0003$; present pain $r = 0.32$, $P = 0.0003$; and PedsQL fatigue $r = -0.45$, $P < 0.0001$).

The effect of sleep disturbance and fatigue on quality of life

Disturbed sleep (parent and self-report) and increased fatigue were both strongly related to HRQL—both generic, as measured by the PedsQL core module, and specific, as measured by the PedsQL rheumatology module.

TABLE 4 PedsQL pediatric pain questionnaire and HRQL in JIA and JDM subjects [mean (S.D.)]

	Oligoarticular (n = 31)	Polyarticular (n = 33)	Systemic (n = 28)	JDM (n = 33)	Summary (n = 125)	*P*-value
Parent report						
Number of painful areas	1.4 (0.5)	2.9 (0.5)	1.9 (0.6)	1.8 (0.5)	2 (3)	0.20
Current pain (worst pain in the last week)	1.2 (0.3) [1 (0.4)]	1.6 (0.3) [2.2 (0.4)]	1.1 (0.3) [1.6 (0.5)]	1 (0.3) [1.5 (0.4)]	1.3 (1.8) [1.6(2.4)]	0.56 (0.30)
PedsQL core modules	84.4 (3.2)	72.6 (3)	77.3 (3)	77.8 (3)	77.9 (17.4)	0.06
PedsQL rheumatology module	85.8 (14.2)	72 (18.6)	82 (16.3)	85.8 (14.2)	81.2 (16.8)	0.003*
Patient report						
Number of painful areas	1.3 (0.8)	4.8 (0.8)	2.3 (0.9)	2.8 (0.9)	2.8 (4.8)	0.02*
Current pain (worst pain in the last week)	1 (0.4) [1.5(0.5)]	1.9 (0.4) [2.6 (0.5)]	1.1 (0.4) [1.7(.5)]	1.4 (0.3) [2 (0.5)]	1.5 (2.1) [2(2.6)]	0.35 (0.37)
PedsQL core modules	86.1 (3.3)	76.3 (3)	80 (3.3)	80 (3)	80 (17.4)	0.18
PedsQL rheumatology module	85.5 (2.6)	78.4 (2.5)	84.3 (2.2)	86.2 (2.4)	83.6 (14.4)	0.10

*Subjects with polyarticular JIA have lower HRQL scores and a higher number of painful areas compared with all other groups.

The parent's PedsQL core module was negatively correlated with the CSHQ ($r = -0.56$, $P \leqslant 0.0001$), and the child's PedsQL core module was negatively correlated with the SSR ($r = -0.42$, $P \leqslant 0.0001$). The parent's PedsQL rheumatology module was negatively correlated with the CSHQ ($r = -0.49$, $P \leqslant 0.0001$), and the child's PedsQL rheumatology module was negatively correlated with the SSR ($r = -0.36$, $P \leqslant 0.0001$). Greater fatigue, as measured by the PedsQL fatigue scale, was highly correlated with worsened HRQL as measured by the PedsQL core module—both parent and child reported ($r > 0.70$, $P \leqslant 0.0001$).

The influence of medications on sleep and fatigue

A number of subjects, in each of the diagnostic categories, were being treated with anti-rheumatic medications at the time of the study (Table 5). Additionally, two subjects were treated concomitantly with fluoxetine and one with risperidone; additional analyses with these medications were not done due to the small numbers.

Subjects treated with NSAIDs had a lower CSHQ score than those not treated (mean 37.3 *vs* 41.5) when adjusted for present pain ($F_{1,113} = 6.9$, $P = 0.01$). The CSHQ did not differ between those subjects taking DMARDs, biologics or prednisone (even when prednisone dose was considered) and those not taking these medications. The SSR was not different among those taking or not taking NSAIDS, DMARDs, biologics or prednisone when adjusted for diagnosis.

Fatigue (as scored by the parents on the PedsQL fatigue scale) was worse in those subjects taking DMARDs—no matter what the diagnosis—when compared with those subjects not taking DMARDs (mean 70.5 *vs* 79.4, $F_{1,112} = 6.8$, $P = 0.01$); however, this relationship was no longer statistically significant in models that included parent ratings of worst pain. The same findings were seen when child-rated fatigue was examined.

Discussion

We found that sleep is disturbed in almost half of our patients with both JIA and JDM, and that there are important relationships between disturbed sleep, fatigue, pain, disease activity and HRQL. From these cross-sectional data, we cannot determine whether disturbed sleep causes higher pain and poorer quality of life, or whether pain and disease activity lead to poor; however, we believe that it is likely a vicious cycle [15], and that attention to improving sleep may lead to reduced pain and is worthy of study.

Healthy children also frequently suffer from sleep disturbance; our findings may not be specific for rheumatic disease. For example, 23% of healthy American elementary school children are expected to score $\geqslant$41 on the CSHQ [20], whereas about 10% are considered to have sleep disturbance when considering together the scores of the CSHQ, SSR and teacher reports of daytime sleepiness [36]. Our subjects had a somewhat higher frequency of disordered sleep and higher average CSHQ scores than community school children studied in North

Table 5 Medication use

Diagnosis	NSAID ($n = 115$), n (%)	DMARD[a] ($n = 115$), n (%)	Biologic ($n = 115$), n (%)	Prednisone ($n = 113$), n (%)	None ($n = 115$), n (%)
JDM ($n = 29$)	0	16 (55)	1 (3)	6 (21)	12 (41)
Oligoarticular JIA ($n = 28$)	6 (21)	4 (14)	0	2 (7)	15 (54)
Polyarticular JIA ($n = 30$)	10 (33)	13 (43)	7 (23)	6 (21)	5 (17)
Systemic JIA ($n = 28$)	8 (29)	11 (39)	7 (25)	6 (21)	8 (29)

Shown is the number of subjects within a diagnosis group who were taking any medication within the broad grouping at the time of the study. Percentages refer to the proportion within disease subgroups and may add up to >100%. Not all subjects answered the medication questions; the number answering is listed next to the medication category. NSAID, DMARD (mostly MTX in this sample, includes IVIG taken by JDM and systemic JIA subjects), biologic (mostly anti-TNF agents in this sample). [a]MTX ($n = 36$), AZA ($n = 1$), tacrolimus ($n = 1$), LEF ($n = 6$).

America [37–39] and higher average SSR scores than seen in community school children in North America and England [39, 40]. Nevertheless, the relationships between poor sleep, pain and quality of life that we saw may not be specific to children with rheumatic diseases, and may be a general phenomenon in children [41–43].

Likely because of the small numbers, we did not find the expected relationships between comorbid personal illnesses, or family illnesses, thought to adversely affect sleep. FM [44–46], attention-deficit hyperactivity disorder [39, 47], anxiety or other psychiatric disorder [48, 49] and a family history of sleep disorder [50] have all been associated with poor sleep in previous studies; there were so few subjects with each of these problems in our sample that we were likely underpowered to detect potentially important relationships. Moreover, we did not ask about other potential sleep predictors such as disease duration, functional ability (outside that measured by the PedsQL), socioeconomic status, housing status and education. Given the anonymous nature of our data collection, we were unable to get this information from clinic charts.

Our cohort appears to be generalizable to other JIA and JDM patients. This is a prevalence sample of patients, and our subjects should therefore be representative of patients seen at any one point in clinical practice rather than seen at diagnosis or at any other extreme point in the disease. Our equal sex ratio among the patients with systemic JIA and the predominance of female subjects in the other groups are similar to previous series [51, 52]. Our cohort consists only of patients between the ages of 8 and 16 years, which must be considered when assessing our findings. Our average parents' global assessment of overall disease activity was higher among patients with systemic JIA and polyarticular JIA when compared with patients with oligoarticular JIA, and this is similar to previous reports [22, 51, 53, 54]; our overall disease activity was low, again similar to other series [2, 55]. Our average VAS pain was similar to previous reports assessing adolescents with JIA [2, 56]. Whereas we collected little self-report data regarding the severity of our JDM subjects, we feel the random sampling process, high response rate and relatively large number of JDM respondents ensured a high likelihood of representativeness.

Few studies have examined sleep in children with JIA. Our finding of a high prevalence of sleep disturbance is similar to a previous report of 74 subjects with limb pain (25 with JIA); in that study 40 (54%) patients had insomnia [8]. Similarly, a study of 21 children with active polyarticular arthritis demonstrated increased sleep fragmentation compared with controls and a strong correlation between alpha activity and pain [57]. Previously a few small studies have demonstrated that sleep is interrupted among patients with JIA; this included poor sleep quality, parasomnia, daytime sleepiness, sleep fragmentation, increased cyclic alternating patterns and sleep disordered breathing [4, 14, 58]. Similar to our finding, Zamir *et al*. [4] demonstrated that the sleep abnormality in JIA patients was associated with pain. Other studies have failed to show an association between sleep disturbance and disease activity; however, in one study there was a high correlation between SSR and average pain [14], and in another, total sleep time and arousals were associated with symptoms of fatigue [59]. Laplant *et al*. [8] have similarly shown that an impaired PedsQL score is related to insomnia.

Since our research was directed towards comparison of sleep and fatigue *within* the major subtypes of JIA, and the comparison between JIA and JDM, we did not include healthy control subjects. We are satisfied that it has been adequately proven that sleep is poorer in children with JIA than in the general population of children, as demonstrated in the discussion above.

To our knowledge, this is the first study to systematically address the problem of poor sleep in JDM. The fact that sleep abnormalities were equivalent to those seen in our JIA subjects suggests that, in general, chronic inflammatory diseases—and perhaps their associated treatments—may have similar effects on sleep.

Much more is known about sleep in adults with RA. One of the largest studies evaluated 8676 patients with RA and a comparison group of 1364 subjects without FM and without inflammatory disorders. In that study the investigators found that sleep disturbance is increased in RA, and 25–42% of the variability in sleep disturbance can be attributed to RA. There was a significant positive correlation between pain, mood, disease activity and sleep disturbance [60].

Several studies have shown that pain is more prevalent in JIA than had been previously recognized. Sherry *et al*. [61] found that 86% of 293 children with arthritis reported pain during a routine clinic visit. Schanberg *et al*. [62] demonstrated, using a daily paper diary, that school-aged children with chronic arthritis report pain on an average of 73% of days. More recently, Stinson *et al*. developed and validated an electronic multi-dimensional pain diary for youth with JIA. On average, participants reported mild pain intensity, pain unpleasantness and pain interference over the course of the 2-week study period (they recorded pain three times per day for 14 days). During this 2-week period, 17.1% reported pain on every entry [56]. Surprisingly, pain was as high in our JDM subjects—a finding that has not been widely reported.

Measured disease activity seems to predict only a portion of children's pain ratings (8—28%) [63–65]; other factors may influence the pain experience. Our findings raise the possibility that pain may influence the quality of sleep, or that poor quality sleep may influence the perception of pain and increase a child's pain ratings. Several previous studies—in other conditions—have also demonstrated an association between poor sleep quality and chronic widespread pain [9, 45, 46, 66, 67]. As in our study, those investigators were unable to determine whether the sleep disturbance preceded or was a consequence of chronic pain. However, induced periods of night-time mini-arousal have been shown to induce symptoms of chronic widespread pain, while removal of these arousal periods are associated with resolution of pain [68]. Furthermore, sleep deprivation studies have shown in healthy volunteers that poor sleep lowers pressure pain thresholds [69]. Recently Davies *et al*. [70] demonstrated in 1061 patients with chronic widespread pain that improvement in restorative sleep was associated with the resolution of symptoms of pain. It appears reasonable that poor sleep may have, in part, caused pain in our subjects. We think it most likely that, in fact, the relationship between pain, poor sleep and fatigue may be a vicious cycle—with a significant influence on quality of life [58].

In our cohort, fatigue was related to DMARD therapy (which consisted mostly of MTX). Fatigue is listed as one of the adverse effects of MTX in its product monograph; however, the relationship between fatigue and MTX in rheumatic and other diseases does not appear to have been widely studied. Husted *et al*. [71] have recently shown, in 499 patients with PsA, that among other variables, MTX therapy was associated with fatigue [71]. It is unclear from our study whether MTX causes fatigue or whether this relationship is a result of confounding—possibly by severity of disease.

Our results would suggest that fatigue is strongly associated with poorer quality of life. This relationship has been widely studied in other conditions, e.g. lymphoma [72], vasculitis [73], chronic insomnia [74], multiple sclerosis [75], IBD [76] and a variety of chronic illnesses of childhood [77]. Fatigue may be an appropriate therapeutic target for improving quality of life.

When interpreting our results, limitations due to our design must be considered. We used a cross-sectional design; despite correlations between disease, pain, fatigue and poor sleep, we cannot make definitive causal statements. We sampled a relatively small number of patients in each disease subtype; however, our sampling process and high response rate ensured that our subjects were representative, and the strong relationships were highly statistically significant. It is possible that due to the small numbers we missed relationships of smaller magnitude. In addition, we measured disease activity using parent- and patient-reported subjective measures, and the joint mannequin technique that we used has only been validated for adult patients. This may have led to imprecision and weakened the reported relationships; it is possible that the relationships between disease activity and sleep disturbance are stronger than what we report. Given the nature of our data collection, medication use was self-reported. It is possible that subjects underreported their use of medications due to poor understanding, and that we missed other important correlations with sleep. Conversely, our results may more closely represent what patients are actually taking than what is prescribed. Finally, we did not include a healthy control population, as we felt that the differences in sleep between JIA patients and healthy controls had been adequately demonstrated and we were interested in comparisons with a disease control group.

In summary, sleep disturbance and fatigue are an important problem in JIA and JDM patients. Sleep disturbance and fatigue are both correlated to disease activity. Increased pain is associated with more sleep disturbance and more fatigue, and these appear to negatively influence quality of life. From our data we hypothesize that increased disease activity leads to poorer sleep, which then adversely affects pain and quality of life. Further study focusing on mechanisms of impaired sleep is warranted to clarify these relationships. It is likely that a better understanding of the role of disordered sleep in childhood rheumatic disease will lead to therapeutic strategies that will improve pain and quality of life.

Rheumatology key messages

- Sleep disturbance and fatigue are prevalent among children with different rheumatic diseases.
- Sleep disturbance and fatigue are associated with increased pain and decreased quality of life.
- Strategies for improving sleep/fatigue should be studied for children with rheumatic illness.

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