Sleep and Its Relationship to Pain, Dysfunction, and Disease Activity in Juvenile Rheumatoid Arthritis

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ABSTRACT. ***Objective.*** To determine what sleep abnormalities may exist in children with juvenile rheumatoid arthritis (JRA), and their relationship to pain, dysfunction, and disease activity.

Methods. Twenty-five children with active JRA (11 pauciarticular, 9 polyarticular, 5 systemic) had their sleep assessed by parallel, validated patient and parent questionnaires (Sleep Self-Report, SSR, and Children's Sleep Habits Questionnaire, CSHQ). Disease activity was assessed by parent and physician global assessments (on a 5 point scale: 0 = no disease activity to 4 = very severe disease), erythrocyte sedimentation rate (ESR), and numbers of swollen and limited joints. Functional assessment was based on parental completion of the Juvenile Arthritis Functional Assessment Report (JAFAR). Pain was assessed by the average pain visual analog scale of the Varni Pediatric Pain Questionnaire. Results were compared to those from 45 healthy age and sex matched controls by Mann-Whitney U tests, and correlated with variables of JRA disease activity, function, and pain using Spearman correlations.

Results. Patients with JRA had higher total score on the CSHQ ($p < 0.0001$), as well as subscales assessing night wakings, parasomnias, sleep anxiety, sleep-disordered breathing, and morning wakening/daytime sleepiness ($p < 0.0001$-0.05). There were no correlations between CSHQ scores and JRA disease activity or pain variables, but the total score on the SSR did correlate with pain ($r = 0.56$, $p = 0.005$).

Conclusion. We conclude that sleep abnormalities are common in children with JRA, and are multidimensional. (J Rheumatol 2002;29:169–73)

Key Indexing Terms:
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Disturbed sleep has been well documented in adults with rheumatoid arthritis (RA). These patients report frequent night wakenings and daytime somnolence[1-3]. These subjective self-reports have been corroborated by polysomnographic studies that show numerous awakenings from sleep, increased sleep fragmentation, and reduced sleep efficiency compared to controls[1,4,5]. These findings have also been correlated with actigraphy, a mode of ambulatory monitoring of movement[6]. Furthermore, the abnormalities have also correlated with measures of quality of life, health status, and health satisfaction[1,7]. Primary sleep disorders, such as periodic leg movement disorder and obstructive sleep apnea, also appear to be more prevalent in these patients[1].

Only a few studies have examined sleep in children with juvenile rheumatoid arthritis (JRA), and they have yielded somewhat conflicting results. One questionnaire study demonstrated that these children had more night-wakenings and daytime somnolence than controls[8], and the degree of daytime somnolence correlated with physician and parent assessments of disease activity, pain, and degree of interference of JRA with the child's life. Another study of 16 children with JRA, using polysomnography, also demonstrated sleep fragmentation and resultant daytime sleepiness, but no correlation was found between sleep abnormalities and disease activity[9]. Neither of these studies examined the possible association between JRA and behaviorally based sleep problems, such as bedtime resistance. Furthermore, no studies have questioned the children themselves about their sleep, a dimension that may be important to assess, especially in older children. Thus, further study is warranted to investigate the previous findings, and to examine other aspects of sleep in children with arthritis. We tested the following hypotheses: (1) disturbed sleep, characterized by

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night wakenings and restless sleep, is more frequent in patients with JRA; (2) bedtime resistance and anxiety about sleep are increased in JRA; and (3) these abnormalities would lead to increased daytime sleepiness. Furthermore, we theorized that the degree of sleep abnormality would correlate with objective measures of disease activity and reported levels of pain, and that children would report more problems with sleep than their parents.

MATERIALS AND METHODS

Patients. Twenty-six children with definite JRA by American College of Rheumatology (ACR) criteria were consecutively recruited from the Pediatric Rheumatology Clinic of Hasbro Children's Hospital, Providence, RI, USA. One patient was dropped from the study due to failure to complete the questionnaires. No patient approached for recruitment met the exclusion criteria: presence of another chronic disease (e.g., diabetes mellitus, inflammatory bowel disease) or incidental acute painful condition (e.g., fractured bone). There were no refusals to participate. All children had active disease, defined as at least one joint with either (1) swelling or (2) limited range of motion and tenderness. Eleven had pauciarticular disease, 9 polyarticular, and 5 systemic. There were 20 girls and 5 boys, ages 6-12 years (mean 8.7). Demographic data are further summarized in Table 1.

Controls. Forty-five children, age and sex matched, obtained from a regional survey of sleep habits in normal children from the same geographic area were used as controls. Subjects were not specifically matched for socioeconomic status (SES) or race. However, a retrospective review of census tract data allowed us to make the following comparisons: 24% of the patients with JRA were from areas of high SES, 48% from middle SES, 19% from low SES, and 9% below poverty level. Controls were all from the same school district, which is roughly 2/3 high SES and 1/3 middle SES. Other independent data show that the area has 5% below poverty level, and is 95% Caucasian.

Evaluation of JRA disease activity and functional status. JRA activity was assessed with the following variables, recently designated by the ACR as the preferred core set of assessment variables to determine improvement in JRA-related clinical trials[9]. These include: (1) parent and (2) physician global assessments of overall JRA disease activity on a scale of 0-4 (0 = no disease activity, 4 = very severe disease); (3) erythrocyte sedimentation rate, measured in the clinical pathology laboratory by standard methods; total numbers of (4) swollen, and (5) limited joints; and (6) functional limitations due to arthritis as determined by score on the Juvenile Arthritis Functional Assessment Report (JAFAR), a 23-item parent-completed questionnaire[10].

Table 1. Demographic data on the JRA subjects (n = 25).

Sex:	
M	5
F	20
Disease subtype:	
Polyarticular	11
Pauciarticular	9
Systemic	5
Age, yrs, mean (range)	8.7 (6–12)
Race:	
Caucasian	23
Hispanic	1
Mixed race	1
Disease duration, yrs, mean (range)	3.1 (0.2–5.5)
Medications	
None	3
NSAID*	20
Methotrexate	9
Sulfasalazine	2
Cyclophosphamide	1
Intra-articular steroids within previous 6 mos.	2

* NSAID: nonsteroidal antiinflammatory drugs, including: naproxen, aspirin, tolmetin, or indomethacin.

Evaluation of JRA-related pain. To assess pain, parents completed the average-pain visual analog scale of the Varni Pediatric Pain Questionnaire[11]. This is a 100 mm scale anchored on one end by the statements Not hurting, no discomfort, no pain, and on the other, Hurting a whole lot, very uncomfortable, severe pain. Parents marked the point on the scale between these statements that reflected the average level of pain they estimate their child had over the week prior to the visit.

Evaluation of sleep. Sleep was assessed by 2 questionnaires, the Children's Sleep Habits Questionnaire (CSHQ)[12,13], a parent report, and the Sleep-Self-Report (SSR)[14], a child report. The CSHQ is a retrospective, 45-item parent questionnaire that has been used in a number of studies to examine sleep behavior in children, and appears to have adequate validity and reliability. Parents are asked to recall sleep behaviors occurring over a typical recent week. Items are rated on a 3-point scale for frequency of the sleep behavior: usually = 5-7 times/week; sometimes, 2-4 times/week; and rarely, 0-1 time/week. Scores are adjusted so that a higher score was indicative of more disturbed sleep. In addition to a total score, 33 items of the CSHQ were grouped into the following 8 subscales: (1) bedtime resistance, (2) sleep onset delay, (3) sleep duration, (4) sleep anxiety, (5) sleep-disordered breathing, (6) night wakenings, (7) parasomnias, and (8) morning wakening/daytime sleepiness.

The SSR is a 26-item, one-week retrospective survey designed to be administered to or self-administered by elementary school-aged children (generally ages 7-12). The SSR was designed to assess sleep domains like those of the CSHQ, and items were selected to approximate similar items on the CSHQ. Though designed to parallel the CSHQ, the SSR tends to address domains with fewer questions, and less-complex questions in order to be understandable to children. For example, daytime sleepiness/morning waking is assessed in the CSHQ with 7 questions that address more detailed information such as whether the child awakens with an alarm clock or whether the child awakens in a negative mood. The same domain of the SSR is only 3 questions long, and is more general in nature with questions such as, Do you feel sleepy during the day? The child, in the clinic, completed the SSR at the time of recruitment. Children and parents were instructed not to allow parental help in completing the SSR. Items are rated on the same 3-point scale as the CSHQ, with higher scores indicating more disturbed sleep. The SSR yields a total score only.

Statistical analyses. Scores from the 8 sleep domain subscales and total score on the CSHQ were compared between the patients with JRA and the controls by Mann-Whitney U test. Correlations between the JRA-related variables and the CSHQ and SSR total and subscale scores were determined by Spearman correlations. Correlations between scores on analogous questions on the CSHQ and the SSR were also determined by Spearman correlations.

RESULTS

Evaluation of JRA disease activity, functional status, and pain. A summary of averages and ranges of results for the JRA-related variables are presented in Table 2.

Evaluation of sleep and statistical analyses. Mean subscale and total CSHQ scores for the JRA and control groups are presented in Table 3. When evaluated by Mann-Whitney U test, total CSHQ scores were significantly higher in the patients with JRA ($p < 0.0001$). Significant differences were also found in several subscales. Highly significant differ-

Table 2. JRA-related variables.

	Potential Range	Mean	Range
ESR, mm/h	1–150	24.6	2–88
JAFAR score	0–46	5	1–18
MD global score	0–4	2.1	1–4
Parent global score	0–4	1.6	0–4
Limited joints, No.	0–60	8.2	1–35
Swollen joints, No.	0–60	8.7	1–30
Pain, mm on scale	0–100	33.4	4–100

ences were seen on the night wakening and parasomnia subscales (both $p < 0.0001$). Significant differences were also seen in scores on the sleep anxiety ($p = 0.05$), sleep-disordered breathing ($p = 0.04$), and morning wakening/daytime sleepiness ($p = 0.007$) subscale scores. There were no direct correlations between total CSHQ or CSHQ subscale scores and arthritis activity or pain (Pearson correlation coefficients = 0.008-0.393, p = NS for all), though there was an apparent trend in correlation between the CSHQ sleep anxiety subscale score and the JAFAR functional assessment report completed by the parents ($p = 0.058$) (Table 4).

Total score on the SSR correlated highly with average pain ($\rho = 0.56$, $p = 0.005$), but not with other arthritis-related variables.

Finally, we compared scores on analogous items from the CSHQ and SSR. The strongest consistent correlations were between questions related to sleep anxiety ($\rho = 0.451$-0.748, $p = 0.03$-0.0001). There were also some significant correlations between items on night-wakings (specifically a question on whether pain awakens the child during the night ($\rho = 0.475$, $p = 0.02$) and an item on whether the child moves to someone else's bed during the night ($\rho = 0.623$, $p = 0.001$). Results on 2 questions related to daytime somnolence also correlated (regarding the child seeming tired during the daytime, and regarding the child's sleeping too much ($\rho = 0.685$, 0.460; $p < 0.0001$ and 0.03, respectively).

Table 4. Correlation of JRA disease-related variables with total score on the Childrens' Sleep Habits Questionnaire.

Variable	Spearman Correlation Coefficient	Significance (p value)
ESR (mm/h)	0.102	0.628
JAFAR	0.253	0.222
Physician global	0.008	0.969
Parent global	0.258	0.212
Limited joint count	–0.184	0.380
Active joint count	–0.100	0.633
Average pain VAS	0.262	0.207

JAFAR: Juvenile Arthritis Functional Assessment Report.
VAS: visual analog scale.

A single item on whether parent and child struggle at bedtime also correlated between reports ($\rho = 0.453$, $p = 0.03$).

DISCUSSION

Children with JRA may suffer many consequences of their disease that negatively impact various normal activities of daily living including self-care, academic performance, participation in physical activities, and social interactions. All children spend at least a third of their time sleeping. Disturbance of that sleep has clearly been demonstrated to impact significantly on mood, cognition, behavior, and school performance. For example, children with obstructive sleep apnea often have significant behavior problems ranging from hyperactivity and aggression to symptoms of depression, and restless legs symptoms in children have been linked to attention deficit disorder-like behavior, and academic problems[15-18]. Most recent studies of behavior in children with JRA show none of the aforementioned problems in higher proportion than controls. However, those studies were limited by small numbers of study subjects and lack of evaluation for attentional/hyperactivity, and it is also

Table 3. CSHQ subscale and total scores in JRA patients versus controls.

	Potential Range	JRA (mean ± SD)	Control (mean ± SD)	Significance
Bedtime resistance	6–18	7.54 ± 2.41	6.76 ± 1.35	p = 0.308
Sleep onset delay	1–3	1.28 ± 0.54	1.23 ± 0.48	p = 0.45
Sleep duration	3–9	3.52 ± 0.82	3.38 ± 0.81	p = 0.275
Sleep-related anxiety	4–12	5.63 ± 1.61	4.89 ± 1.26	p = 0.045*
Night wakings	3–9	4.56 ± 1.29	3.42 ± 0.82	p < 0.0001*
Parasomnias	7–21	10.0 ± 1.85	8.19 ± 1.11	p < 0.0001*
Sleep-disordered breathing	3–9	3.70 ± 1.02	3.25 ± 0.53	p = 0.036*
Morning wakening/daytime sleepiness	8–24	11.88 ± 2.80	9.91 ± 2.68	p = 0.007*
Total score	33–99	45.36 ± 8.01	37.51 ± 6.12	p < 0.0001*

Differences determined by Mann-Whitney U test.
*Statistically significant difference, JRA patients vs controls.

possible that some individual patients still suffer from these problems due to sleep disturbance[19,20].

Our results suggest that patients with JRA have significantly disturbed sleep when compared to otherwise normal children. The differences in multiple sleep domains as well as the total score on the CSHQ suggest that these disturbances are multifactorial, though these factors do all have the common endpoint of leading to sleep fragmentation and/or deprivation. Behavioral factors such as sleep anxiety may be increased in JRA patients due to generalized anxiety on the part of the child and parent related to the effects of having a chronic disease such as difficulties in limit-setting for ill children[21]. Also such problems may appear as a result of the child's anticipation of the other sleep problems.

The observed increase in symptoms of sleep-disordered breathing between children with JRA and controls (suggestive of obstructive sleep apnea) may sometimes be due to direct effects of arthritis such as micrognathia and cervical spine compromise. However, only 10/25 patients with JRA had cervical spine and/or jaw arthritis. Half of these subjects had some report of sleep disordered breathing, but so did 9/15 patients without involvement of these joints. Thus other factors may account for the sleep disordered breathing. Possibly, parents of children with JRA are hypervigilant, and are present to observe more snoring, gasping, etc. than parents of other children. Ideally, it would be helpful to see if other potentially hypervigilant parents (such as parents of children with other chronic diseases) also report more sleep-disordered breathing. However, we did not have such controls in our study. The increased night wakenings in the JRA group are probably also due to multiple problems, but the correlation of the SSR score with pain suggests that pain may be a significant contributor. The increase in parasomnias, including partial arousal parasomnias such as sleep-walking in the JRA group could be a result of sleep fragmentation and deprivation, in turn leading to an increased amount of stages III and IV sleep followed by partial arousals. Finally, our result demonstrating increased trouble awakening in the morning and daytime somnolence in the JRA group is somewhat intuitive given the array of abnormalities related to sleep fragmentation and deprivation seen in these children.

The added data from the children's self-reports reveal that the total score correlates well with pain, while the parents' reports do not. This may be because pain causes abnormalities such as sleep onset delay and increased night-wakenings, which may go unobserved and thus under-reported by parents. Lack of children reporting certain events to parents likely accounts for most of the discrepancies between the parent and child reports, and highlights the need to take the child's view into account. The strongest correlation seen between the parent and child reports was in the domain of sleep anxiety. This is likely because children primarily look to their parents to assuage their anxieties.

Results of this preliminary study must be interpreted with caution. The main limitation of our investigation is the relatively small number of patients studied. JRA is quite heterogeneous, and thus sleep abnormalities may vary based on such factors as disease subtype or medications used. For example, we suspect that patients with active systemic disease (e.g., high fevers, profound anemia) may have the most disturbed sleep of all JRA patients. We had an insufficient number of patients to analyze our data according to such factors. Nevertheless, based on the demographics in Table 1, we feel that a fairly typical cross-section of JRA patients was studied here. Also, normal sleep variables vary considerably by age; however, we limited the study to ages 6-12 in order to minimize this variability, which is widest in younger children and adolescents. Also, use of age-matched controls should make our comparison to normal children valid. Our JRA patients and controls were of similar racial background. The 2 populations were also both of mostly high and middle SES, though more in the JRA group lived in areas of low or poverty level SES. It is possible that social problems associated with low SES may have contributed to more behavioral sleep problems in our patients with JRA, though these problems clearly were also seen in JRA patients from high or middle SES. It is also difficult to know the clinical significance of statistical differences in questionnaire data. However, it is likely that even small differences were sometimes clinically meaningful. For example, an answer of sometimes on the sleep-disordered breathing question — child gasps for air/stops breathing during sleep — creates only a 1 point difference in score from someone who answers never/almost never, but could be very meaningful as an indicator of obstructive sleep apnea. Perhaps these findings could have been corroborated by more objective tests of sleep such as polysomnography or actigraphy, which we did not include. Nonetheless, other studies have shown that patient reports correlate well with objective measures. In addition, we wanted to study behavioral dimensions of sleep that cannot be measured by objective means.

If our results are corroborated by future study, it is also possible that various therapeutic interventions can be aimed at improving certain sleep disturbances. For example, treatment with low-dose amitryptilline[22] or triazolam[23] have led to improvement in subjective measures of sleep quality and fatigue, as well as arthritis-related variables such as pain, stiffness, and functional disability in adults with arthritis. Therapies that are only directed at pain (such as nonsteroidal antiinflammatory agents) do not seem to ameliorate sleep disturbance in adults with arthritis. However, it is possible that treatments such as cognitive-behavioral therapy (including techniques such as guided imagery and progressive muscle relaxation) can lead to improvement in pain and behavior (such as sleep anxiety) in these patients. Indeed, this therapy leads to improvement in pain and adaptive func-

tioning in children with JRA[24]. Surgical and orthodontic intervention could also correct problems such as micrognathia and associated obstructive sleep apnea. Many patients have a mixture of sleep problems; a multidisciplinary approach is likely to benefit them significantly.

In conclusion, sleep is significantly disturbed in children with JRA. This report corroborates previous findings of increased sleep-fragmentation and effects of sleep deprivation (such as daytime somnolence) in children with arthritis. These factors are likely to significantly impact the child's quality of life. The parents' and the child's view of these problems should be considered. Furthermore, we emphasize that the sleep disturbances in these children are truly multifactorial in cause, including a spectrum from anatomic abnormalities such as micrognathia to behavioral factors such as sleep-related anxiety. This, along with the relative lack of correlation of sleep abnormalities with disease activity and pain, implies that the treatment of sleep abnormalities in children with JRA is not as simple as curing the arthritis. More likely, the treatment of these abnormalities will be complex and will require a multidisciplinary approach.

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