Sleep Quality in Children With Juvenile Rheumatoid Arthritis

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Children with juvenile rheumatoid arthritis (JRA) report poor sleep quality, daytime sleepiness, fatigue, anxiety, and altered mood. Sleep disturbances in school-aged children are an issue of serious concern. Children are at an age when sleep is of primary importance to physical and intellectual growth, and sleep disturbances that begin in childhood may persist into adulthood. In this article we will review what is currently known about sleep in children with JRA, the influence of medications on sleep quality, the potential impact of poor sleep quality on daily life issues, and complementary/alternative modalities that may be effective in reducing sleep disturbances. **KEY WORDS:** *behavior, children, complementary and alternative therapies, juvenile rheumatoid arthritis, performance, sleep, sleep disturbances* *Holist Nurs Pract* 2003;17(4):193–200

Nearly 300,000 children in the United States have been diagnosed with arthritis, and juvenile rheumatoid arthritis (JRA) is the most prevalent form of connective tissue disease.[1] Recent findings show that sleep is disrupted in children with JRA.[2–5] They experience difficulty falling asleep, frequent night awakenings, early morning awakening, and excessive daytime sleepiness. While we know that sleep is disturbed in children with JRA, we do not know the severity of these sleep disturbances, nor do we know the extent to which sleep disturbances influence daytime sleepiness, performance, and behavioral emotional functioning.

Sleep disturbances and insufficient sleep in healthy children are typically associated with changes in behavior that include irritability, decreased attention span, distractibility, impulsivity, hyperactivity, excessive daytime sleepiness, chronic fatigue, decrements in daytime alertness and performance, and an increase in school absenteeism.[6,7] Sleep disturbances in the school-aged child can lead to difficulty concentrating in school, and subsequently result in secondary behavior problems in the classroom. Children may be labeled as "hyperactive" or "ADHD" when the primary underlying problem is poor sleep.[8] A report of the National Commission on Sleep Disorders Research notes that "the relative paucity of research on mechanisms, treatments, and prevention is disturbing"[8(p94)] particularly given the prevalence of sleep disturbances in children (see Fig 1).

Sleep disturbances in school-aged children are an issue of serious concern. Children are at an age when sleep is of primary importance to physical and intellectual growth and development, and sleep disturbances that begin in childhood may persist into adolescence and adulthood.[8] In this article we will review what is currently known about sleep in children with JRA, the influence of medications used in the treatment of JRA on sleep quality, the potential impact of poor sleep quality on daily life issues, and complementary/alternative strategies that may be effective in reducing sleep disturbances.

BIOLOGICAL BASIS OF SLEEP DISTURBANCES WITHIN RA PATHOLOGY

JRA is an incurable disease characterized by episodic exacerbations and remissions. During periods of

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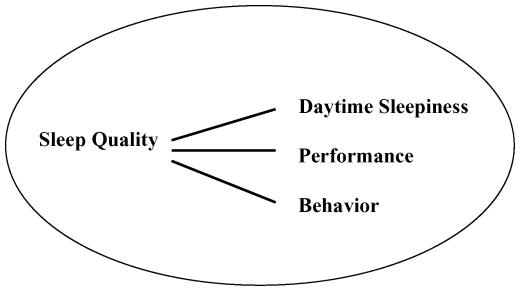

FIGURE 1. Evidence suggests that sleep quality is a predictor of daytime sleepiness, performance, and behavioral emotional functioning in children.

disease exacerbation, children with JRA fatigue easily and experience joint inflammation and swelling, accompanied by acute joint pain and tenderness, morning stiffness and gelling after inactivity, and limited mobility. They may display increased irritability, regression to more infantile patterns of behavior, loss of appetite, weight loss, and failure to grow.[9] Muscle weakness, functional disability, and other debilitating symptoms of the disease often inhibit these children from actively engaging in their environment and interacting with playmates/classmates. Some children, particularly those who experience systemic onset of the disease, have persistently active disease that is associated with joint destruction and profound growth delay. Growth in general may be slowed in children with JRA, joints may grow unevenly, and asymmetrical patterns of growth in long bones may occur resulting in gait disturbances.[9] Other growth anomalies that may occur in children with prolonged active disease include a significant reduction in height,[10] premature fusion of the epiphyses and growth disturbances of the hip joint,[11] and maldevelopment of the mandible resulting in retrognathia, malocclusion, and/or asymmetries in the jaw.[12]

Growth hormone (GH) plays a critical role in growth, and lower levels of serum GH have been reported in ANA-positive (antinuclear antibody) JRA subjects compared with healthy controls.[13] The decline in serum GH is thought to be associated with inflammatory activity, and diminished levels of GH may play a significant role in delayed/stunted growth observed in children with rheumatological diseases.[13] The secretion of GH appears to be modulated by sleep, and approximately 80% of GH is secreted in 1 to 2 large pulses during the first episodes of slow wave sleep (stages 3 and 4).[14,15] A recent finding that JRA children display a higher arousal index and spend less time in slow wave sleep than do healthy controls is an area of concern since frequent arousals from slow wave sleep could potentially interfere with the timing and secretion of this essential hormone.[5] Periods of disease remission and proper management of the disease with pharmacological agents may provide an opportunity for JRA children to "catch up" on their skeletal growth. The quality of sleep that children with JRA achieve during these periods of remission are likely to play a critical role in this phase of "catching up," and yet this has never been evaluated.

The underlying cause of sleep fragmentation in RA remains uncertain. Current data are inadequate to draw conclusions about whether sleep disturbances result from underlying mechanisms related to the inflammatory process or are the result of increased pain.[16] Nocturnal pain is associated with insomnia in adults with RA, specifically with delays in sleep onset and interference with both the depth and continuity of specific sleep states.[17]

SLEEP DISTURBANCES IN CHILDREN WITH JRA

Sleep in arthritic adults is characterized by marked disturbances including frequent movement of the extremities, night awakenings, apnea, and arousals from sleep.[17–21] The behavioral manifestations of such sleep disturbances include excessive daytime sleepiness and fatigue, coupled with decrements in mood and performance.[22] Given that so much is known about sleep in adults with arthritis, it is surprising that so little is known about the quality of sleep in children who have arthritis. Much of what we know about sleep in these children is based on parental and self-report and isolated reports of sleep using physiological measures such as actigraphy and polysomnography.

Self-report and actigraphy

Recent findings reveal that children with JRA and their parents report significantly more instances of night awakening, parasomnias, sleep anxiety, sleep-disordered breathing, early morning awakening, and daytime sleepiness than do healthy controls.[2–4] Amos et al[2] found that children with greater disease severity (eg, greater number of joints affected) had higher scores on the daytime sleepiness indices, and

daytime sleepiness was significantly correlated with parental reports of pain and degree of interference of JRA in the child's life. In another study it was reported that pain in children with JRA was positively correlated with their reports of sleep disturbances.[3] Thus, survey findings suggest that pain is associated with sleep disturbances and daytime sleepiness in this population of children.

Actigraphy is becoming an increasingly popular way of measuring/monitoring daily patterns of activity and sleep, and provides a reliable and valid assessment of sleep quality in pediatric and adult subjects.[23,24] In one recent study,[25] sleep was assessed in 14 children with JRA and 16 age-matched and sex-matched healthy control children by asking them to (1) wear a wrist actigraph continuously for 8 days on their nondominant wrist (Mini-Motionlogger, Ambulatory Monitoring Inc, Ardsley, NY), and (2) complete a brief sleep survey in which they responded to questions about their sleep over the previous 2 weeks. Parents completed the Child Sleep Habits Questionnaire (CSHQ),[26] a survey in which they recalled their child's sleep behavior over the previous 2 weeks, and the Child Behavior Checklist (CBCL),[27] a tool that measures multiple dimensions of the child's behavior including competence in activities, social behaviors, and school performance. Results from this study revealed that, compared with healthy children, children with JRA were more than twice as likely to report sleep disturbances (eg, difficulty initiating sleep, difficulty maintaining sleep, early morning awakening). Two children with JRA reported falling asleep in an afternoon class within 2 weeks of the survey, while no one in the control group reported this incident. Seventy-nine percent of the children with JRA reported having nightmares or bad dreams during nocturnal sleep, compared with 38% of the control group. Fifty-four percent of the JRA group reported feeling nervous and tense and 69% reported worrying too much about things, compared with 31% and 25% of the control group respectively. Parental reports revealed that, compared to healthy children, JRA participants displayed significantly more disrupted sleep, a higher frequency of parasomnias (eg, sleep walking, sleep talking, night terrors), and higher "total" and "internalizing behavior" (eg, withdrawn, somatic complaints, and anxious/depressed) scores. Findings from wrist actigraphy indicated that JRA children display a trend toward increased wakefulness during the night and shorter sleep episodes compared to healthy children (see Fig 2); however, differences between the 2 groups did not reach statistical significance.[25]

Polysomnography

The timing and duration of specific stages of EEG sleep, often referred to as sleep architecture, is an important physiological indicator of sleep quality. Abnormal changes in sleep architecture may be associated with impaired daytime functioning with excessive daytime sleepiness and poor performance. To our knowledge there is only one published study evaluating sleep architecture in children with JRA. Zamir et al[5] used polysomnography to evaluate nocturnal sleep in 16 school-aged children with JRA and 9 healthy age-matched controls. The most striking finding in this study was the extent of sleep fragmentation in children with JRA. JRA participants displayed an average of 23 arousals/awakenings per hour, compared to 12 arousals/awakenings per hour in healthy controls (arousal: >1.5 second alpha frequency EEG; awakening: >15 second waking EEG). Nine JRA children displayed more than 20 arousals per hour; no one in the healthy control group displayed more than 20 arousals per hour. Leg movements were associated with 19.4% of the arousals/awakenings in JRA subjects and 4.5% in healthy controls. Less than 0.1% of the arousals were associated with respiratory events (eg, apneas and hypopneas) in either JRA or control groups.

Compared with healthy participants, children diagnosed with JRA spent significantly less time in stages 2 and 3 non-rapid eye movement (NREM) and rapid eye movement (REM) sleep, and displayed significantly more shifts from deeper to lighter stages of sleep than did their healthy counterparts. The restorative functions of sleep have been linked to deep or slow wave sleep, and frequent shifts from deep to light sleep could potentially interfere with that restorative function.[28] The intrusion of a waking alpha EEG pattern into slow wave sleep is present in some individuals diagnosed with chronic pain syndromes as well as in adults with RA.[21,29] In this sample an average of 15% of NREM sleep was staged as alpha-delta sleep in 93% of the JRA subjects and in 33% of the controls. Twenty-five percent of the children participating in the Zamir et al[5] study were diagnosed with pauciarticular (<5 joints affected) arthritis and 75% with polyarticular (>5

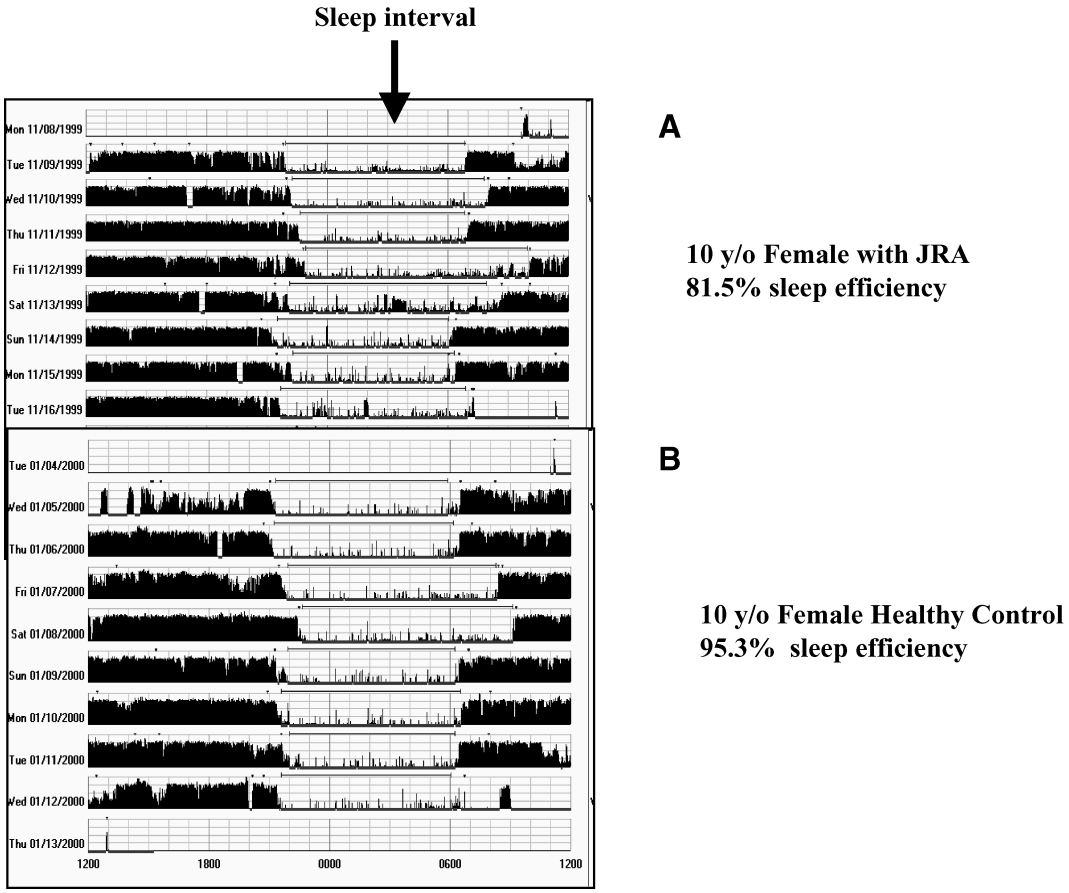

FIGURE 2. Actigraph output of 2 children, one with JRA (A) and one healthy child (B). Black areas indicate movement. While some movement typically occurs with sleep, note increased activity during the sleep interval in the child with JRA.

joints affected) arthritis. Group data were presented without distinguishing between individuals who were in arthritic flare and those who were in remission, and subjects spent only one night in the laboratory and did not have a night to adapt to the laboratory environment.

Zamir et al[5] also noted that JRA children reported significantly longer afternoon naps than did healthy controls, sleeping more than an hour longer. Multiple sleep latency tests (MSLTs) were performed to evaluate daytime sleepiness in 7 of the JRA subjects. MSLTs are polysomnographic EEG recordings that have been widely used in adult and pediatric populations to assess daytime sleepiness. MSLTs are performed at 2-hour intervals (eg, typically starting at 8:30 AM and ending at 4:30 PM) to assess physiological sleepiness. Participants are asked to lie down quietly on their bed for 20 minutes in a darkened room, to keep their eyes closed, and attempt to fall asleep.[30] Zamir et al[5] noted an average sleep latency (length of time to fall asleep) of 10.3 ± 2.6 minutes—sleep latency less than 10 minutes in school-aged children is generally indicative of daytime sleepiness.[31] Thus, findings from polysomnography confirm that nighttime sleep is fragmented in children with JRA, and this fragmentation may lead to some degree of daytime sleepiness.

RA MEDICATIONS AND EFFECT ON SLEEP

Pharmacological agents used to treat JRA are critical to controlling/suppressing inflammatory activity. While much is known about the impact of pharmacological agents on sleep in adults with RA, the influence of such agents on sleep in children has not been evaluated. In adults, NSAIDs are known to be disruptive to sleep. Aspirin and ibuprofen increase the number of awakenings and percentage of time spent awake at night, and thus decrease sleep efficiency. Also, ibuprofen delays the onset of deeper stages of sleep.[32] These same agents are likely to influence the quality and quantity of sleep in children. Nonsteroidal anti-inflammatory agents (eg, ibuprofen, naproxen) are routinely used as a first-line approach to managing

JRA, and for maintenance once acute inflammation is under control. Selective cyclooxygenase-2 inhibitors (COX-2 inhibitors; eg, celecoxib, rofecoxib), a new class of drugs being used in the initial treatment of JRA, are similar to NSAIDs in their anti-inflammatory effect and have the advantage of producing fewer gastrointestinal disturbances.[33] We were unable to find any studies of the impact of COX-2 inhibitors on sleep in either adults or children. When acute disease persists, children are started on a more aggressive protocol that involves the use of disease-modifying antirheumatic drugs (DMARDS; eg, methotrexate, sulfasalazine, hydroxychloroquine) or biologic response modifiers such as tumor necrosis factor inhibitors (eg, etanercept). Intraarticular systemic corticosteroids may be employed as an interim measure to manage severe symptoms.[33] DMARDs are known to be irritating to the gastrointestinal system, which in turn can be disruptive to sleep,[16] and corticosteroids contribute to severe insomnia.[29]

The trend to treat persistent disease aggressively has resulted in minimizing joint erosion and subsequent disability. Furthermore, the use of new drug therapies, particularly the biologic and immunosuppressive agents, has produced dramatic improvements in children suffering from JRA. There is, however, growing concern that little has been done to assess the impact of chronic administration of these potent drugs in children. Children on these medications are potentially at risk for developing secondary infections, malignancies, or other autoimmune diseases.[33] Isolated cases have already been reported in the literature of children developing secondary varicella infections following treatment with etanercept,[33] as well as non-Hodgkin's lymphoma[34] and Hodgkins lymphoma[35–37] following treatment with low-dose methotrexate. The paucity of information and lack of follow-up in children on these drugs is an issue of serious concern, and underscores the need to design longitudinal studies that will evaluate short-term and long-term consequences on specific health indices, including sleep, in children.

EFFECT OF SLEEP DISTURBANCES ON DAILY LIVES OF CHILDREN

Mastery of their environment and the need to become increasingly independent are 2 key developmental tasks for school-aged children. Socializing with other children and actively engaging in school and other activities are important arenas for fostering and developing the social skills and self-confidence that children need to successfully accomplish these tasks. Social interchanges with peers are often filled with social pressures and social tensions specific to their world, and such interactions provide the opportunity to develop effective coping skills. Chronic illnesses such as JRA may limit the child's ability to actively engage in their world, and thus may interfere with successfully accomplishing these important developmental milestones.[38]

JRA is associated with major alterations in the physical, mental, and social worlds of the children who live with it—alterations that result from behavioral symptoms brought about by the chronic and often progressive nature of the disease. Children with JRA are vulnerable not only to delays in growth and development, but also to cognitive and social delays. The fatigue and irritability that they often experience coupled with muscle weakness, joint inflammation and swelling, acute joint pain and tenderness, morning stiffness, limited mobility, loss of appetite, weight loss, and failure to grow often inhibit them from actively engaging in their environment and interacting with playmates/classmates.[9] Managing the symptoms associated with illness is a significant stressor for up to 20% of the children who suffer from chronic illness.[39,40] Estimates suggest that children with JRA lose up to one third of their free time focusing on the management of daily symptoms of the disease.[41] The intensity, constellation, and pattern of symptoms, coupled with personal characteristics of the child and family, lead to a wide range of individualized responses to JRA, from mild anxiety and distress to severe distress. Stress, mood, and general adaptation to disease have been described as predictors of how children experience their disease.[42] Reports of increased pain in children with JRA have been linked to greater emotional distress in the child, greater emotional distress in the mother, and greater family disharmony.[43]

Sleep quality may be an important predictor of symptom severity, school performance, and how well children with JRA adjust to living with this chronic illness. For example, disrupted sleep may negatively influence the child's mood, behavior, performance, and parental-child interactions as well as other aspects of family function—an area that remains to be explored in children with JRA.[44] Furthermore, sleep disturbances that begin in childhood may persist into adolescence and adulthood.[8] The idea that certain

children are at risk for developing long-term complications is supported in the literature. In a study of 433 children treated for JRA in Germany, disease prognosis was different for the 3 subtypes of JRA (eg, pauciarticular, polyarticular, and systemic [acute onset marked by fever, rash, chills]). The most severe limitations (eg, school absences, growth retardation) occurred in children with systemic JRA, while children with pauciarticular JRA had either no disability or slight impairment and missed little school time. The mortality rate for children with pauciarticular JRA was 0%, for children with polyarticular JRA was 1%, and for children with systemic JRA was 13.8%.[45] A follow-up study of 57 (18–53 years) patients who had been treated in Rochester, Minn, from 1960 to 1993 revealed an unusually high mortality rate among adults who had been diagnosed with JRA compared to the mortality rate in the general population. The deaths were all associated with autoimmune disorders.[46] In another study of 43 patients (ages 18–54 years) treated in England for polyarticular JRA, psychological testing revealed that 21% of those individuals were clinically depressed—a rate that increased with degree of disability. Degree of disability was also associated with an increase in the proportion of patients displaying an anxious preoccupation with their disease. Sixty-six percent of the respondents were employed, and 38% noted that their disease did not affect their ability to form relationships with others.[47] In another study of social function in young adults who had been diagnosed with JRA as a child, females had a higher prevalence of persisting disability.[48] Thus, the findings clearly show that some children may be at greater risk for developing long-term functional and psychological complications, and disease severity appears to be a predictor of health outcomes. The impact of chronic sleep disturbances on children's health, on their ability to perform in school as well as engage in activities of daily life, and on how they experience symptoms of the disease are areas that have not been explored. Sleep quality may be an important predictor of short-term and long-term health outcomes in these children.

COMPLEMENTARY/ALTERNATIVE MODALITIES THAT MAY BE EFFECTIVE IN REDUCING SLEEP DISTURBANCES

The use of complementary and alternative approaches has been a topic of heated debate in the effective treatment of rheumatoid diseases, particularly in adults. Although many of these same modalities are being used by children with JRA, little research has been done to evaluate the effectiveness of alternative approaches in children.[49] Parents are often very concerned about having their children on potent pharmacological agents such as methotrexate for prolonged periods of time. Observation of the side effects of the medication (ie, alopecia, stomatitis, gastrointestinal disturbances) is often a source of great distress and ultimately may lead parents to seek other "unconventional" remedies as an alternative or as a supplement to speed the healing process. Whether or not such remedies enhance the healing process or impede remains an unanswered question in children, and an area that needs to be explored.

Southwood et al,[50] surveying 53 children with juvenile arthritis attending youth camps in Australia, New Zealand, and Canada, reported that 70% of the children had used an unconventional remedy for their arthritis. Most commonly reported alternative strategies were use of copper bracelets (68%), diet (43%), and patent medicines (38%). Studies evaluating the effectiveness of these unconventional remedies have not been conducted in children. Massage therapy has proven to be a successful complementary strategy in children. Field et al[51] reported that children with JRA who received a daily 15-minute massage administered by their parents displayed a reduction in pain as well as a reduction in anxiety and the stress hormone cortisol, compared

Table 1. Parental reports of strategies used to ease pain and enhance sleep in their arthritic children*

Warm baths/showers before bedtime
Warm applications (bean bags or thermal packs warmed in the microwave, heating pads)
Waterbed for sleeping
Soothing behaviors: Cuddling, lying in bed/holding the child until sleep onset, reading a bedtime story, co-sleeping (sleeping with the parent), and prayer

*From Labyak et al, unpublished data, 2000.

with a control group of children receiving only relaxation therapy. In recent surveys conducted with 14 families of children with JRA, parents often reported using a variety of approaches to ease their child's pain and enhance sleep (see Table 1) (Labyak et al, unpublished data, 2000). Clearly there is a need to supplement these anecdotal parental reports with sound research, exploring the effectiveness of these alternative strategies and interventions on improving sleep quality in children with arthritis.

CONCLUSIONS

Many children show remarkable resilience in adapting to life with JRA, while others appear to be susceptible to the physical intensity of the symptoms and show physical, emotional, and behavioral manifestations of distress. Increasing symptom severity and the risk for subsequent disability are likely to be greater in children who suffer from the more intense forms of the disease (eg, polyarticular and systemic JRA). Sleep quality may be an important predictor of symptom severity, school performance, and how well these children adjust to living with this chronic illness. Further research is needed to evaluate the short-term and long-term impact of pharmacological agents on sleep and other health indices in children with JRA. Equally important is the need to design interventions that will enhance sleep in children living with chronic diseases such as arthritis, and to evaluate the effectiveness of strategies currently being used by families to comfort and promote sleep in their children.

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