Sleep quality in infants with atopic dermatitis: a community-based, birth cohort study

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Summary

Background: **Sleep disturbance has been reported in both pre-school and older children with atopic dermatitis (AD). There have been no studies examining whether sleep disturbance occurs at the onset of the AD, or develops later.**

Objective: **To evaluate sleep characteristics in infants with AD.**

Methods: **A cross-sectional survey based on interviews with parents of infants aged 1 year. AD was diagnosed by showing the parents 3 pictures of typical AD. AD was considered as mild if the rash was a single occurrence or there was only 1 lesion and severe if there were 2 or 3 recurrent or persistent lesions. The infant's sleep behavior was evaluated through information on sleep onset, sleep duration, number of night wakings and the caregivers' perception of problematic sleep behaviors.**

Results: **Of the total sample, 96.2% (4085 of 4245) provided complete AD information and 148 infants (3.6%) had at least one AD skin lesion. Sleep duration was significantly reduced in infants with severe AD when compared to no-AD infants (542+67 vs 569+62 minutes, p 0.02). The percentage of infants who had night waking with parent intervention required to calm them down "often or always" was significantly higher in mild AD infants than in normal infants (61.7 vs 49.8%, p 0.02). No significant differences were noted between infants with or without AD for other infant sleep behavior.**

Conclusion: **In AD patients, sleep disturbances can occur early following the onset of the disease. We suggest that clinical assessment of AD infants should take these aspects into consideration.** ***(Asian Pac J Allergy Immunol 2012;30:26-31)***

Key words: *atopic dermatitis, eczema, sleep, night waking, infant*

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Introduction

Atopic dermatitis (AD) is a common inflammatory skin disorder in children and is characterized by pruritus, eczematous lesions, dryness and thickening of the skin. The prevalence rate of AD is 10-30% in children[1, 2] and the disease most often begins in the first year of life.[3,4] The chronic and recurrent nature of the disease, combined with the absence of a curative treatment, causes a negative impact on the quality of life of both the child and the parents. One of the burdens is sleep disturbances, which has been found to affect 47-60% of patients,[5,6] and usually involves delay in sleep onset,[7] frequent night waking,[7,8] and a decrease in sleep duration.[7-9] Previous studies have indicated that pruritus and scratching are important factors in the development of sleep disturbance in AD children. Physicians are usually aware of pruritus (scratching and clawing at the skin or rubbing against hard objects) in older children with AD, but may not pay much attention to similar symptoms in infants as they do not typically manifest in this age group, perhaps because young infants do not have the physical coordination to scratch or rub against things no matter how itchy they are. However, in the literature, there is evidence

that the symptoms of pruritus may develop in infancy.[10]

Sleep disturbances affect not only the child but also the entire family. For instance, parents caring for children with AD have reported disruptions to parental sleep.[11] Although there have been many studies on the impact of AD on sleep, most have dealt mainly with pre-school or older children, who may have suffered from AD for a long period of time. Although sleep quality has been used as one of the parameters in assessing quality of life in infants with AD,[12,13] it has not been thoroughly investigated and there are no studies examining whether sleep disturbances occur soon after the onset of the disease or develop later. To attempt to shed some light on this time of onset, the purpose of this study was to evaluate sleep characteristics in infants with AD. Greater information concerning the influence of this disease on infant sleep patterns would be helpful in the development of effective intervention strategies.

Methods

Study population

The data for this study were collected as part of the larger "Prospective Cohort Study of Thai Children (PCTC)". The PCTC is an observational community-based study begun in the year 2000 and designed to follow a large group of individuals from the 3rd trimester of pregnancy to age 24 years. For the study, a birth cohort born over a one-year period was chosen from each of the 4 regions in Thailand, plus one from Bangkok, the capital city. The times of initial recruitment varied among the regions and were as follows: (1) Panomtuan district in Kanchanaburi province in the west, October, 2000, (2) The-pa district in Songkhla province in the south, November, 2000, (3) Kranuan district in Khon-Kaen province in the north-east, January 2001, and (4) Meuang district in Nan province in the north, March 2001. The method of recruiting the study sample from Bangkok differed from the other 4 districts because of the very large number of births occurring per year. Only births from 3 selected hospitals, 1 private and 2 public, with parents willing to participate in the study, were recruited commencing in September 2001. The total sample size recruited from these 5 regions was 4,245 infants.

This study was approved by the National Ethics Committee of the Ministry of Public Health of Thailand. All families were clearly informed of all the study procedures and possible risks before signing the consent form.

Data collection

As scheduled by the PCTC, well-trained data collectors made visits and interviewed the primary caregivers of all eligible infants at their homes when the infants were 1 year of age or within 2 weeks after that date. The questionnaires used in the study were tested on a sample of parents. The data collectors who conducted the survey were all trained to explain and ask questions in a uniform manner to ensure consistency and quality of findings. The information obtained included parental demographic data, the infant's feeding pattern, the presence of AD and the infant's sleep behavior.

The questions used for identifying atopic dermatitis were modified from the ISAAC questionnaire[14] and 3 pictures of a typical manifestation of AD on the face, trunk and legs were shown to the primary caregivers. They were asked whether the infant had had any rashes on his/her body that looked like the rashes in the pictures in the past 6 months and, if yes, whether the rash had been a single occurrence, recurrent or persistent for several weeks. AD was considered as mild severity if the rash was single occurrence or there was not more than 1 lesion and severe if the rash had shown 2 or 3 lesions and had been recurrent or persistent for several weeks.

A number of aspects of the infant's sleep behavior over the 2 weeks prior to the interview were examined, notably sleep onset (approximate time on average needed to get the infant to fall asleep after going to bed), sleep duration (the total time that the infant slept on average each night), and nap duration (the total time that the infant slept on average each day). The caregivers' perceptions of problematic sleep behaviors were also investigated using specific questions examining crying at sleep onset, difficulty falling asleep, and night waking that required the caregivers' intervention. (For the complete list of major interview questions see appendix 1). The caregivers were also asked to complete a 3 day sleep-wake record for the number of night wakings and number of naps per day.

"Nighttime" was defined as 6.00 pm. to 6.00 am the next day, and "Daytime" was defined as 6.00 am. to 6.00 pm. The reason for using these definitions was that some of the study families were from a low socioeconomic background and to assess the time precisely, especially in the late night, may have been difficult in some households, so we tried by using these criteria.

Table 1. Characteristics of the infants (n =4085)

	Number of cases	%
Sex		
Male	2032	49.7
Female	2053	51.3
Feeding		
Breast	1318	32.3
Bottle	1876	45.9
Mixed	818	20.0
Missing	73	1.8
Maternal education		
Primary school	2144	52.5
Secondary school	1154	28.2
College or university	747	18.3
Missing	40	1.0
Severity of atopic dermatitis		
No atopic dermatitis	3937	96.4
Mild	115	2.8
Severe	33	0.8

Statistical analysis

Statistical analysis was performed using SPSS software, version 16. Analysis was restricted to infants who had complete information for AD at 1 year of age. Descriptive statistical methods (mean +S.D., median, and frequency) were applied. The mean number of night wakings and the mean number of naps were calculated from a 3-day sleep record. Log transformation was used for the variable "sleep onset" to normalize the distribution of the data. Analyses of the difference in frequencies across groups (sex, infant feeding, maternal education, and parental perception of sleep-related problematic behaviors) were performed with the Chi squared test. The continuous variables (duration of sleep onset, nighttime sleep or nap duration, number of naps and night wakings) were compared with the t-test. All sleep variables were adjusted for sex, types of feeding and maternal education using regression analysis. Statistical significance was defined by $P < 0.05$.

Results

Participants

Of the total sample, 96.2% (4085 of 4245) provided complete AD information for further analysis. Table 1 shows the infants' characteristics. Of the total sample, 3.6% (148 of 4085) had had at least one AD skin lesion on their face or trunk or a leg. The frequency of area of involvement was 1.6% for face, 1.2% for trunk, and 2.2% for leg.

Infant sleep characteristics and atopic dermatits

Of the total infants, the mean morning wakeup time was 6.23 AM (SD= 42 minutes), and the mean night bedtime was 20.20 PM (SD=23 minutes). Table 2 shows the sleep characteristics of the infants according to the severity of AD, adjusted for sex, type of feeding, and maternal education. The average infant sleep onset was significantly shorter in infants with mild AD, and sleep duration was significantly reduced in infants with severe AD when compared to infants with no AD. No significant difference was noted between infants with or without AD regarding nap duration, number of night wakings and number of naps. For the parental reports of sleep-related problematic behavior, the percentage of infants who had night waking "often or always" requiring the parents to calm them down before they could get back to sleep was significantly higher in mild AD infants compared to infants without AD. No significant differences were noted between infants with or without AD for other sleep-related problematic behavior, such as crying at sleep onset and difficulty falling asleep.

Discussion

We performed this study to investigate sleep characteristics in AD infants. The strengths of this study relate to the large cohort of infants and a study design that was different from previous studies. The significant differences between this and earlier studies were first that our study was community-based, birth cohort as part of a much larger study involving sampling of a very large population and secondly that because of this initial very large sample we were able to compare our results with a control group of normal infants, while all previous reports were confined to children with AD who had been referred for specialty care. It is difficult to extrapolate the results of such small groups to the larger population due to potential bias in the referral pattern of more severe cases. Another strength of our study is that comparison of sleep characteristics within similar age groups should provide a higher degree of accuracy than studies involving children with a wide age range because sleep physiology changes with age.

In our study, we identified AD infants who had had a skin lesion within the previous 6 months and collected detailed sleep data for the previous 2 weeks

Table 2. Sleep characteristics according to severity of atopic dermatitis (n=4085)

Sleep characteristic	Atopic dermatitis			Difference Between groups 1 and 2	Difference Between groups 1 and 3
	None n=3937 (group1)	Mild n=115 (group2)	Severe n=33 (group3)	Adjusted *p* value*	Adjusted *p* value*
Sleep characteristic, mean± SD					
Sleep onset, ln min	2.9±0.8	2.8±0.8	2.8±0.8	0.02	0.26
Sleep duration, min	569±62	579±52	542±67	0.10	0.02
Nap duration, min	183±79	172±75	159±69	0.22	0.13
Mean number of night wakings	2.7±1.3	2.5±1.2	2.6±1.5	0.07	0.26
Mean number of naps	2.1±0.6	2.0±0.5	2.2±0.8	0.07	0.59
Parental reports of infant sleep behavior, n %					
Crying at sleep onset				0.78	0.89
Never	954 (24.4)	21 (18.3)	5 (15.1)		
Sometimes	1656 (42.4)	56 (48.7)	17 (51.5)		
Often	699 (17.9)	21 (18.3)	6 (18.2)		
Always	597 (15.3)	17 (14.8)	5 (15.1)		
Difficulty falling asleep				0.10	0.65
Sometimes	1568 (40.1)	36 (31.3)	12 (36.4)		
Often	1860 (47.6)	64 (55.6)	16 (48.5)		
Always	477 (12.2)	15 (13.0)	5 (15.1)		
Night waking requiring the parents to calm down the baby				0.02	0.32
Never/sometimes	1961 (50.2)	44 (38.3)	12 (36.4)		
Often	1154 (29.5)	40 (34.8)	13 (39.4)		
Always	790 (20.2)	31 (26.9)	8 (24.2)		

Mild: 1 lesion or single occurrence Severe: 2 or 3 lesions and recurrent or persistent

*adjusted for sex, type of feeding, maternal education Total may vary because of missing values

with a 3-day sleep record. We used this time frame because AD is a chronic disease which may flare up or subside periodically and also because the physiology of sleep characteristics is known to change with age and thus the time frame of any study examining this condition should not be too long. We did not ask the parents for information on current skin lesions or scratching behavior because we hypothesized that sleep disturbances can occur at any time during the course of the disease, a hypothesis supported by at least one previous study which found that children with AD in clinical remission could develop sleep disturbances not related to scratching.[15]

Our study demonstrates the substantial impact of infantile AD on sleep characteristics. We found sleep duration was significantly reduced in infants with severe AD, a finding which provides objective confirmation of the occurrence of infant sleep loss very soon following the onset of the disease. We could not directly compare our findings with other studies because no other study has been performed on first year AD infants. However, despite the difference in study age groups, our findings were similar to several studies involving pre-school and older children in terms of a decrease in sleep duration in AD children. A previous study by Stores et al.[8] who performed a home polysomnographic study in 20 school-age children with AD, provided objective confirmation of disruption of sleep by awakening associated with scratching episodes resulting in an overall reduction in sleep efficiency. In another study, Shani-Adir et al.[9] investigated 57 AD patients and 37 healthy children aged 3-10 years and found that the AD group demonstrated significantly worse sleep quality compared with the controls, including reduced sleep duration, parasomnia, sleep disordered breathing and daytime

sleepiness. The same study also found an association between sensory hypersensitivity and lower sleeping quality. Additionally, a study performed by Hon et al.[5] on 133 children with AD, aged 5-16 years also demonstrated sleep disturbances affecting 47% of the patients, which was more common in children younger than 10 years.

When we specifically examined parental views of infant sleep characteristics, we found a higher incidence of problematic night waking in infants with AD than without AD, however this finding was statistically significant only in the mild AD group, but not in the severe AD group. The possible explanation for this finding is that the number of severe AD cases in our study was too small, especially when categorized into three groups, to find a difference if such existed. The findings of problematic night waking, notably night waking requiring the parents to calm down the baby, are, however, consistent with a previous study by Reid et al.[16] who found that the families of affected preschool children are likely to also exhibit disturbed sleep patterns, as they must interrupt their sleep to comfort or treat the symptoms of their children. Chamlin et al.[17] who performed a study on parents of children ranging in age from birth to 6 years with AD, found that most parents (>60%) reported that their child's dermatitis affected how well both they and their child slept. Additionally, Moore et al.[11] found that caring for a child with chronic atopic eczema was associated with an increased number of times that the caregiver's sleep was disturbed by the child and the number of times the parent got up to attend to the child. Another recent study on the parents of 45 AD children aged from 3-84 months reported that infant sleep quality was one of the greatest problems, including staying awake at night and disturbed sleep in higher percentages when compared to no AD children.[13]

One of the significant findings in our study was that sleep onset in the AD infants was faster than in the control infants, a finding which was opposite to that of previous studies. We cannot explain this finding with certainly, but it may be related to confounding factors which were not examined in our study. For example, previous studies have found that various practices were performed at bedtime among infants during the first year of life including such things as the use of sleep aids, soothing techniques, and parenting styles[18,19] which would likely affect sleep onset. Another possible cause of more rapid sleep onset is the use of a sedating antihistamine, but no data regarding drug use was collected in our study so we cannot assess this possibility.

Studies in older AD children have found that sleep disturbances due to itching and scratching interfere with the onset and maintenance of sleep and that such events usually occur when the dermatitis is flaring up. No studies have been undertaken specifically looking at infantile AD, and whether related sleep disturbances are associated with itching or scratching and further studies are needed.

In addition to the itching and scratching that are the main causes of disturbed sleep in AD children, the origins of disordered sleep in allergic patients may also be traced to altered inflammatory processes. A variety of cytokines are elevated in patients with an allergy, which are implicated in sleep regulation. Recently, Bender et al.[20] found that decreased sleep efficiency in AD patients was associated with not only disease severity or scratching but also elevated level of interleukin-6.

Poor sleep has well documented deleterious effects. A recent study reports that individuals with AD slept more poorly and had more waking episodes which were then associated with increased daytime drowsiness.[16,21] Sleep disturbances have also been reported to have negative effects on attention and emotion.[22] As in the first year of life infants take much more time for sleep compared to older children, sleep loss during this period may have a much greater influence on later development and long term effects. To evaluate such potential consequences, further studies are needed.

Limitation

The ISAAC questionnaire is mostly used to identify atopic dermatitis in population-based studies, but in our survey we did not use the complete form of this questionnaire because it includes multiple questions but no assessment of clinical signs. We reduced the number of questions and simplified the ones used and added some pictures of AD to accurately identify the disease. With this method, we believed that the occurrence of the disease could be more accurately assessed than by using a questionnaire alone. However, this method has not been reported and validated previously. The Severity Scoring of Atopic Dermatitis (SCORAD) index is the standard assessment tool for AD severity,[23] but in our study we could not employ the SCORAD as it requires an

expert to administer it and no such expert was available. Instead, we used the number of lesions and their persistence to classify the severity of the condition, which was simple to perform in a large cohort of infants. Another limitation in this study was the lack of information about AD status in the 2 weeks prior to the day the questionnaire was completed, daytime sleep behavior and what if any medications were used for AD. More information and improved research approaches are crucial to better understanding of the effect of AD on sleep.

Conclusion

This study demonstrated that in AD patients, sleep disturbances, including decreased sleep duration and problematic night waking, can occur at an early stage following the onset of the disease. We suggest that clinical assessment and treatment of AD infants should consider this potential early onset when assessing treatment efficacy.

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