



Sleep in children with asthma: results of the PIAMA study

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ABSTRACT: Children with asthma are thought to have impaired sleep quality and quantity. In this study, we investigated which of the many sleep aspects are associated with asthma.

Our sample consisted of 2529 children (aged 11 years) who participated in the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study. Parents reported about asthma symptoms (wheezing, dyspnoea, prescription of inhaled corticosteroids and asthma diagnosis) and children reported about different aspects of sleep (bedtime, rise time, sleep quality and daytime sleepiness/tiredness). Results were analysed with (logistic) regression analysis.

Children with frequent asthma symptoms significantly more often reported that they felt sleepy or tired during the day (34.4% experienced daytime sleepiness/tiredness at least once a week) than children without asthma symptoms (22.2%) and children with infrequent asthma symptoms (21.9%). This association was not confounded by sex, age of the child, parental educational level or smoking inside the house; the effect was also not modified by sex. There were no associations between asthma and bedtime, time spent in bed or sleep quality.

Children with frequent asthma symptoms experienced daytime sleepiness/tiredness more often than children with infrequent or no asthma symptoms. Otherwise, children with asthma did not differ much from children without asthma with regard to sleep.

KEYWORDS: Childhood asthma, daytime sleepiness/tiredness, dyspnoea, wheezing

Asthma is a chronic inflammatory airway disease and is considered the most prevalent chronic respiratory disorder in childhood [1]. Asthma seems to be a risk factor for disturbed sleep: asthma symptoms often worsen at night [2] and can cause sleep disruptions [1]. Sleep problems in turn have negative consequences for health [3], behaviour [4], cognitive functioning and school performance [5, 6]. As children with asthma generally show more behavioural problems than children without asthma [7], it is important to gain more insight into sleep in childhood asthma.

Research into sleep in children with asthma has yielded contradictory results. On the one hand, several studies have shown that children with asthma wake up more often in the night [1, 8–11] and have worse sleep quality than healthy children [1, 8–10, 12]. On the other hand, other studies did not find that children with asthma have lower sleep quality or more disrupted sleep [13, 14]. Asthma does not seem to influence sleep latency or sleep duration [8–10, 12, 14]. However, asthma appears to be consistently related to sleepiness or tiredness in children [1, 8, 9, 12, 15]. This may have important bearings on daytime

activities and cognitive performance and, hence, school achievements [16].

In addition, it was found that persistent wheezing [17], more severe asthma [12, 16, 18] and uncontrolled asthma [19] were associated with worse sleep. These findings may partly explain the contradictory results described above. It is possible that well-controlled asthma does not affect sleep, but sleep is negatively affected in the case of more serious symptoms or in uncontrolled asthma. As most studies investigated only one or a few sleep aspects (most often night-time awakenings) and used different definitions of asthma, it is difficult to draw firm conclusions about whether asthma affects sleep.

In the present study, we investigated sleep in different groups of children with asthma, based on the frequency of their symptoms. First, to investigate the most essential aspects of sleep, we examined bedtime, a prominent feature of sleep in children. Secondly, we investigated time spent in bed as indicator of sleep duration and sleep latency, frequency of nocturnal awakenings, sleep latency after nocturnal awakenings and feeling fit at rise time as indicators of sleep quality.

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Received:

Jan 31 2012

Accepted after revision:

June 30 2012

First published online:

Aug 16 2012

European Respiratory Journal
Print ISSN 0903-1936
Online ISSN 1399-3003

Sleep duration and sleep quality are considered two different sleep domains [20]. Finally, we assessed daytime sleepiness/tiredness as one of the consequences of insufficient sleep duration and/or unsatisfying sleep quality. By using these different asthma phenotypes and investigating several sleep aspects in the same individuals, we aimed to clarify the contradictory results that are found in the literature on the relationship between childhood asthma and sleep.

We aimed to answer the following two research questions. 1) Are there differences in sleep between children with and without asthma? 2) Are there differences in sleep between children with frequent and infrequent asthma symptoms?

METHODS

Study design and study population

The study population consisted of children born in 1996–1997 who participated in the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study. A detailed description of the study design has been published previously [21]. Briefly, pregnant females were recruited from the general population by means of a validated screening questionnaire on maternal allergy [22], distributed to the females when visiting a pre-natal clinic in the Netherlands. On the basis of this screening, 7862 females (2779 allergic mothers and 5083 nonallergic mothers) were invited to participate in the study. Approximately 50% of the invited pregnant females ($n=4146$) agreed to participate. In the case of multiple births, only one of the children was included in the study. After birth, the baseline study population consisted of 3963 children. Questionnaires were sent to the participating parents during pregnancy, at 3 months, yearly from age 1 to 8 years, and at 11 years of age, around the child's birthday. At the age of 11 years, questionnaires were also completed by the children themselves. The present study reports on the 11-year questionnaires completed by parents and children and includes data on 2529 children for whom data on both asthma and sleep were available.

The study protocol was approved by the medical ethics committees of the participating research institutes, and all parents gave written informed consent.

Measures

Asthma

In all questionnaires from age 1 year onwards, the parents were asked to report whether the child had had an episode of wheezing, an episode of dyspnoea, or a prescription of inhaled corticosteroids for respiratory or lung problems during the last 12 months. In addition, parents were asked about the frequency of attacks during which wheezing or dyspnoea occurred. Additional questions were whether the child was ever-diagnosed with asthma by a doctor and whether the child had had asthma during the previous 12 months. Based on these questions, the following variables were defined and used in the present study. 1) Asthma symptoms were considered to be present when parents reported that their child had had one or more attacks of wheezing and/or one or more attacks of dyspnoea and/or a prescription of inhaled corticosteroids for respiratory or lung problems by a medical doctor during the last 12 months. If parents reported no wheeze, no dyspnoea and no prescription of inhaled corticosteroids, the child was defined as having no asthma symptoms. The group of children with asthma

symptoms can be divided into children with frequent asthma symptoms and children with infrequent asthma symptoms, as follows. 2) Frequent asthma symptoms: parents reported that their child had had four or more attacks of wheezing and/or four or more attacks of dyspnoea during the last 12 months. 3) Infrequent asthma symptoms: parents reported asthma symptoms, but no frequent symptoms were reported. 4) Diagnosed asthma: parents reported that their child was ever-diagnosed with asthma by a doctor and reported that their child had had asthma during the last 12 months.

Sleep

Children reported on bedtimes and rise times on both school and nonschool days; sleep latency (how long it takes to fall asleep after lights off), frequency of nocturnal awakenings, sleep latency after nocturnal awakenings, feeling fit at rise time (measures of sleep quality), and daytime sleepiness/tiredness ("Do you feel tired or sleepy during the day?"). Based on the child's report of their bedtimes and rise times, their time spent in bed was calculated.

Confounding factors

The following variables were tested for possible confounding influences: sex of the child, age of the child (exact age at the time that the questionnaire was completed); educational level of parents (highest attained educational level for mother and father separately); and smoking inside the house. The last two variables were considered indicators of lifestyle that might affect asthma and sleep [23–26].

Statistical analysis

Analyses were conducted with SPSS version 17 (SPSS Inc., Chicago, IL, USA). To investigate the associations between asthma and sleep, regression analyses were conducted with the different sleep items as dependent variables and binary indicators of asthma symptoms, frequent asthma symptoms or diagnosed asthma (defined according to the descriptions above) as independent variables. For the dependent variable with two response categories (feeling fit at rise time), logistic regression analyses was used; for dependent variables with three to five response categories (sleep latency, frequency of nocturnal awakenings, sleep latency after nocturnal awakenings and daytime sleepiness/tiredness) ordinal regression analyses were conducted; and for the dependent variables with nine (bedtimes) or more (time spent in bed) response categories regular linear regression analyses were conducted.

The influence of possible confounding variables was investigated by adding these as a covariate to the regression models. If, after addition of the covariate, the regression coefficient of asthma changed by $\geq 10\%$ for several of the sleep outcomes, the covariate was considered to be a confounder.

To investigate whether the association between asthma and sleep differed for males and females, interaction effects between sex and asthma on the different sleep characteristics were examined. A significant interaction effect would indicate that the relationship between asthma and sleep was modified by sex (*i.e.* the relationship between asthma and sleep is different for males and females).

RESULTS

At 11 years of age, 116 (4.6%) children wheezed during the last year, 243 (9.6%) children had dyspnoea and 169 (6.7%) children had a prescription of inhaled corticosteroids. There were 317 (12.6%) children with asthma symptoms, of whom 97 (3.9%) had frequent symptoms and 220 (8.7%) had infrequent symptoms. 100 (4.0%) children had diagnosed asthma (table 1).

Differences in sleep between children with and without asthma

The mean time at which children went to bed and the mean time they spent in bed (difference between rise time and the time the lights were turned off) were not significantly different for children with asthma symptoms, children with frequent asthma symptoms (both compared with children without symptoms) or children with diagnosed asthma (compared with children who

do not meet the criteria for diagnosed asthma). When examining the results for daytime sleepiness/tiredness and sleep quality, a significant association was found only between children with frequent asthma symptoms and without symptoms on daytime sleepiness/tiredness. Children with frequent asthma symptoms significantly more often reported that they felt sleepy or tired during the day than children without asthma symptoms (table 2). There was a trend in the same direction for children with asthma symptoms (frequent and infrequent symptoms taken together) and children with diagnosed asthma. Children with asthma symptoms more often felt sleepy or tired during the day than children without asthma symptoms (of the children with asthma symptoms, 25.7% experienced daytime sleepiness/tiredness at least once a week *versus* 22.2% of children without symptoms). Children with diagnosed asthma indicated more often that they felt sleepy or tired during the day when compared with children who do not meet the criteria for diagnosed asthma (30.0% *versus* 22.4% of children in the respective groups experienced daytime sleepiness/tiredness at least once a week), yet these associations did not reach significance ($p=0.06$ and $p=0.11$; data not shown). Only results of the analysis comparing children with frequent asthma symptoms and children without symptoms are reported in the table.

Addition of sex, age of the child, educational levels of parents and smoking inside the house as covariates to the regression models changed the effect estimates for the associations with several of the sleep characteristics, but had little influence on the association between frequent asthma symptoms and daytime sleepiness/tiredness. In table 2, the results of both the crude and the adjusted analyses are shown. Next, we investigated interaction effects between asthma and sex to determine whether the associations between asthma and sleep differed for males and females. As no significant interaction effects were found, it appears that the relationship between asthma and sleep is not modified by sex.

Differences in sleep between children with frequent and infrequent asthma symptoms

Ordinal regression analysis showed a significant effect on daytime sleepiness/tiredness when comparing children with frequent and infrequent asthma symptoms (table 2). Children with frequent asthma symptoms significantly more often reported feeling sleepy or tired during the day than children with infrequent asthma symptoms. There were no significant associations between frequent asthma symptoms as compared with infrequent asthma symptoms and other sleep outcomes.

DISCUSSION

Children with frequent asthma symptoms experienced more daytime sleepiness/tiredness than children without asthma symptoms and children with infrequent asthma symptoms. This association was not confounded by sex, age, educational level of parents or smoking inside the house, and was not modified by sex. There were no associations between asthma and bedtime, time spent in bed or sleep quality.

Nocturnal awakening frequently occurs in asthma [1, 8–11, 16]; however, no effect of asthma on nocturnal awakenings was found in our study. We did find that 46.9% of the children with frequent asthma symptoms sometimes had nocturnal awakenings and 5.2% (almost) always experienced awakenings during

TABLE 1 Description of the study population[#]

Age years mean \pm sd	11.4 \pm 0.3
Males	1286 (50.9)
Asthma symptoms	317 (12.6)
Frequent asthma symptoms	97 (3.9)
Infrequent asthma symptoms	220 (8.7)
Diagnosed asthma (including asthma during the previous 12 months)	100 (4.0)
No asthma symptoms	2202 (87.4)
Specific aspects of asthma	
Wheezing during the last year	116 (4.6)
Dyspnoea during the last year	243 (9.6)
Corticosteroids	169 (6.7)
Ever-diagnosed with asthma	288 (11.4)
Sleep mean (sd min)	
Bedtime school day	20:43 h (27.4)
Bedtime not school day	21:41 h (39.7)
Time in bed school day	10:06 h (39.2)
Time in bed nonschool day	11:23 h (55.0)
Sleep latency	
Fall asleep immediately	619 (24.5)
Stay awake for a while	1509 (59.8)
Takes a long time to fall asleep	394 (15.6)
Nocturnal awakenings	
(Almost) never	1324 (52.5)
Sometimes	1090 (43.2)
(Almost) every night	110 (4.4)
Sleep latency after nocturnal awakenings	
Mostly fall asleep immediately	615 (51.3)
Mostly awake for a while	488 (40.7)
Mostly takes a long time to fall asleep	96 (8.0)
Feeling fit at rise time school day	
Yes	2061 (82.0)
No	452 (18.0)
Daytime sleepiness/tiredness	
(Almost) never	1069 (42.4)
<1 per week	880 (34.9)
\pm 1 per week	282 (11.2)
\pm 2 per week	165 (6.5)
\geq 3 per week	124 (4.9)

Data are presented as n (%), unless otherwise stated. [#]: n=2529.

TABLE 2 Effects of asthma on sleep characteristics[#]

	No asthma symptoms	Infrequent asthma symptoms	Frequent asthma symptoms	β (95% CI)	β (95% CI) [†]	p-value [‡]
Subjects n	2202	220	97			
Bedtime school days mean (sd min)	20:44 h (27.4)	20:42 h (27.3)	20:42 h (27.7)	-1.22 (-6.80–4.36)	-1.60 (-7.13–3.92)	0.57
Bedtime nonschool days mean (sd min)	21:42 h (39.8)	21:39 h (37.0)	21:40 h (44.0)	-1.34 (-9.53–6.84)	-0.81 (-8.88–7.26)	0.84
Time in bed school days mean (sd min)	10:06 h (38.9)	10:03 h (45.0)	10:08 h (33.1)	1.20 (-6.66–9.06)	2.27 (-5.54–10.07)	0.57
Time in bed nonschool days mean (sd min)	11:23 h (55.1)	11:17 h (54.9)	11:29 h (54.5)	6.16 (-5.04–17.36)	8.64 (-2.28–19.56)	0.12
Sleep latency						
Fall asleep immediately	540 (24.6)	58 (26.5)	20 (20.6)	0.26 (-0.15–0.66)	0.28 (-0.13–0.68)	0.18
Stay awake for a while	1318 (60.0)	127 (58.0)	58 (59.8)			
Takes a long time to fall asleep	338 (15.4)	34 (15.5)	19 (19.6)			
Nocturnal awakenings						
(Almost) never	1168 (53.1)	105 (47.9)	46 (47.9)	0.21 (-0.19–0.61)	0.25 (-0.15–0.65)	0.23
Sometimes	940 (42.7)	101 (46.1)	45 (46.9)			
(Almost) every night	91 (4.1)	13 (5.9)	5 (5.2)			
Sleep latency after nocturnal awakenings						
Mostly fall asleep immediately	536 (52.0)	56 (49.1)	21 (42.0)	0.35 (-0.20–0.89)	0.35 (-0.20–0.90)	0.21
Mostly awake for a while	416 (40.4)	45 (39.5)	25 (50.0)			
Mostly takes a long time to fall asleep	78 (7.6)	13 (11.4)	4 (8.0)			
Feeling fit at rise time school day						
Yes	1803 (82.3)	171 (78.1)	78 (83.0)	1.05 [§] (0.60–1.81)	1.00 [§] (0.58–1.73)	>0.99
No	387 (17.7)	48 (21.9)	16 (17.0)			
Daytime sleepiness/tiredness						
(Almost) never	943 (43.0)	92 (42.0)	28 (29.2)	0.58 (0.21–0.95)	0.63 (0.26–1.00)	<0.01
<1 per week	764 (34.8)	79 (36.1)	35 (36.5)			
±1 per week	244 (11.1)	20 (9.1)	17 (17.7)			
±2 per week	140 (6.4)	16 (7.3)	9 (9.4)			
≥3 per week	104 (4.7)	12 (5.5)	7 (7.3)			

Data are presented as n (%), unless otherwise stated. For sleep latency, nocturnal awakenings, sleep latency after nocturnal awakenings and daytime sleepiness/tiredness the results of ordinal regression analyses are reported. [#]: regression coefficients are shown for children with frequent asthma symptoms compared with children without asthma symptoms; [†]: confounders included; [‡]: reported for the models with inclusion of the confounders; [§]: odds ratio.

the night. However, our results showed that nocturnal awakenings also occurred in children without asthma symptoms and the difference between these groups was not statistically significant. It might be that the question on nocturnal awakenings was not sensitive enough to find an effect, as children could only choose from three response categories ((almost) never, sometimes and (almost) every night).

As we did not find differences for any of the other sleep variables, we cannot give a straightforward interpretation for the finding of increased daytime sleepiness/tiredness in children with frequent asthma symptoms compared with children with infrequent or without asthma symptoms. However, it could be that children with frequent asthma

symptoms are more sleepy or tired during the day, partly because they have worse sleep quality (they have lower scores on most indicators of sleep quality, although not significantly worse), and partly because normal daytime activities are more tiring for them due to their asthma complaints. In addition, children with frequent asthma symptoms might become more sleepy or tired during the day than other children not only because of their asthma complaints, but also because of possible emotional/behavioural problems, which are more pronounced in children with asthma [7].

We found significant associations between asthma and sleep to be present only in children with frequent asthma symptoms. This result is in accordance with earlier studies that also found a

relationship between severity of asthma and the extent to which sleep was impaired [12, 16–19]. This indicates that an impact on sleep is evident only when asthma is not well controlled.

A possible explanation for the fact that we did not find associations between diagnosed asthma and any of the sleep characteristics could be that 77.0% of the children with diagnosed asthma had a prescription of inhaled corticosteroids, which has probably reduced nocturnal symptoms [27, 28]. Almost half (48%) of the children with diagnosed asthma had only infrequent symptoms. Although also 56.7% of all children with frequent asthma symptoms had a prescription of inhaled corticosteroids, still all children in this group had four or more attacks of dyspnoea and/or four or more attacks of wheezing in the last 12 months. Thus, this group does not include children who are symptom free because of their treatment. The fact that only about half of the children in the group with diagnosed asthma had frequent symptoms is likely to be the result of adequate treatment and may also explain why we observed no associations between diagnosed asthma and sleep.

In our study, parents reported about asthma symptoms and children reported about their sleep. We used questionnaires to measure sleep, which enabled us to assess a wide range of different aspects of sleep, including factors like “feeling fit at rise time” and “daytime sleepiness/tiredness”. However, we cannot exclude the possibility that self-reporting may have resulted in some misclassification of, for example, sleep duration. Use of objective measures (e.g. actigraphy) in addition to subjective measures might have been useful to support the findings. However, although actigraphy data are reported to be reliable and valid, they appear to have a low specificity in detecting wakefulness within sleep periods [29]. Although it is suggested that parents might underestimate the sleep problems of their children [30], there are studies, for example, that reported by DESAGER *et al.* [8], that have found relationships between asthma and sleep using parent reporting. Therefore, it would be advisable to include parental and child reporting about sleep in one study to enable comparison of results.

Our study offers a careful consideration on the association between asthma (using different phenotypes) and important sleep characteristics in a large sample of children. The results of our study provide support for the idea described in the introduction, that the severity or frequency of symptoms is an important factor influencing the relationship between asthma and sleep.

Conclusion

Our study found a difference in daytime sleepiness/tiredness between children with frequent asthma symptoms and children with infrequent symptoms or without symptoms. No differences on bedtime, time spent in bed or sleep quality were found. It can be concluded that children with asthma do not differ much from children without asthma with regard to sleep. However, we recommend that physicians pay attention to sleep in children with frequent asthma symptoms, considering the negative effects of daytime sleepiness/tiredness on behaviour, mood, cognitive functioning and school achievements of these children [3–6].

SUPPORT STATEMENT

Research relating to this manuscript was supported by The Netherlands Organization for Health Research and Development; The Netherlands Organization for Scientific Research; The Netherlands Asthma Fund, The Netherlands Ministry of Spatial Planning Housing, and the Environment; and The Netherlands Ministry of Health, Welfare and Sport.

STATEMENT OF INTEREST

Conflict of interest information can be found alongside the online version of this article at www.erj.ersjournals.com

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