Sleep and Pulmonary Function in Children with Well-Controlled, Stable Asthma

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Summary: The aim of this study was to assess sleep and pulmonary function in asthmatic and control children. Forty children with well-controlled, stable asthma, and 34 controls (age range: 8.2 to 15.4 years) were monitored with wrist actigraphs and peak-flow meters for 3 consecutive days. In addition, asthma severity was assessed by subjective parental and self-rating scale and symptom checklist. Asthmatic children had poorer sleep quality in comparison to their controls, as manifested in lower percentages of quiet sleep ($p<.05$) and increased activity level during sleep ($p<.05$). As expected, asthmatic children had reduced morning peak expiratory flow measures ($p<.01$) and a higher evening-to-morning drop in peak expiratory flow ($p<.005$). Peak-flow measures were significantly correlated with subjective and objective sleep measures. In the asthmatic group, sleep measures were also correlated with subjective asthma severity indices and symptom checklists. We conclude that poorer sleep is associated with reduced pulmonary function. The reduced sleep quality, coupled with subjective reports of increased fatigue and reduced alertness found in asthmatic children, suggest that these children are at risk for developing neurobehavioral deficits associated with chronic sleep loss.

Key words: Sleep; children; asthma; peak flow; pulmonary; breathing; actigraphy

ASTHMA is one of the most prevalent childhood health problems. Recent surveys indicate prevalence rates ranging from 5% to 15% percent of children, with a tendency to increase over time.[1-5] Respiratory difficulties play a major role in the etiology of sleep disturbances. Sleep disturbances have been associated with asthma in children and adult patients. Nocturnal asthma and asthma-related sleep disruptions have been reported in more than 80% of adult asthmatic patients[6-8] and in 61% of the asthmatic children.[9] A few studies have demonstrated a poorer sleep quality of asthmatic patients in comparison to normal controls.[10-12] Tirosh and colleagues[5] found no evidence for increased rates of sleep problems in a survey of young asthmatic and healthy children, but they reported that asthmatic children

reach consolidated sleep at a later age than their controls.

Studies of the relationship between sleep and asthma have mostly been based on subjective reports (of the subjects or their parents), with their obvious limitations, or by single-night polysomnographic studies of a small number of subjects.[13] Recently, actigraphy has been established as a new objective monitoring method in sleep research and sleep medicine.[14] Actigraphy is based on miniaturized solid-state activity monitors, which are worn wristwatch-style and collect motility data for extended periods in naturalistic settings. The validity of actigraphy in distinguishing between sleep and wake states, and in its derived sleep-wake measures, have been repeatedly demonstrated in children.[14-17] Furthermore, a number of studies have shown that respiratory disturbances, such as those manifested in sleep apnea patients or in normal subjects in response to nocturnal nasal occlusion, result in specific activity patterns that can be identified by means of actigraphy.[15,18,19] However, Middelkoop and colleagues failed in a similar attempt to distinguish subjects diagnosed with sleep apnea

from controls.[20]

The first aim of the present study was to compare sleep and pulmonary function in children with well-controlled, stable asthma and in normal controls by using objective, nonintrusive monitoring methods. The second purpose was to assess the relationships between pulmonary function (and other indices of asthma severity) and sleep in normal and asthmatic children.

SUBJECTS AND METHODS

Subjects

Forty asthmatic children were recruited from the asthma-management clinic at First General Hospital. They included 12 girls and 28 boys ranging in age from 8.2 to 15.4 years (mean age=12.1). The control group was recruited from the healthy friends of the asthmatic children, and consisted of 20 girls and 14 boys ranging in age from 8.9 to 14.7 (mean age=12.4). The asthmatic children were all clinically identified as suffering from mild to moderate asthma,[21] and were clinically stabilized by budesonide. Their use included beta agonists "as needed" but not more than twice a week. It was recommended that the children refrain from using beta agonists, and their administration was controlled by the parents. One child was excluded because of beta agonist use during the monitoring period. Subjects were in a sustained stable condition with no asthmatic attacks during a period of at least 6 weeks prior to the study. All parents signed informed consent to allow their child's participation in the study.

Procedures

Each child was monitored for a period of 3 days, during which the child's sleep and pulmonary function were objectively and subjectively assessed.

Sleep.—The children's sleep was monitored by miniature actigraphs (AMA-32, Ambulatory Monitoring Inc., Ardsley, NY) for 3 to 4 consecutive nights. The actigraph is a small wristwatch-like device that continuously monitors motion in 1-minute epochs (setting: zero-crossing, mode 18). Each child was asked to attach the actigraph to his or her non-dominant wrist during the entire bedtime period. The raw actigraphic data was translated into sleep measures using the Actigraphic Scoring Analysis program (ASA) for an IBM-compatible PC. These sleep-wake measures have been validated against standard polysomnography with sleep-wake scoring agreement rates higher than 90%.[15-17]

Actigraphic sleep measures included:
(1) Sleep-onset time: The time of the first minute identified as sleep by the sleep-wake algorithm;
(2) Sleep duration: Time between sleep-onset time and morning awakening;

Table 1.—Day-by-day reliability of peak expiratory measures, Day 1 / Day 2 Pearson correlations.

Measure	Asthma	Control	Total Sample
Evening PEF	.81 *	.94 *	.87 *
Morning PEF	.96 *	.96 *	.95 *
Evening to Morning PEF Drop	.20	.01	.17
PEF = Peak Expiratory Flow; * p<.0001			

(3) Sleep percent: percent of actual sleep time from sleep duration (excluding wakefulness after sleep onset);
(4) Longest sleep period: the longest period of continuous sleep without any wakefulness;
(5) Quiet sleep: percentage of sleep without any motion;
(6) Mean activity level during sleep.

In addition to the actigraphic assessment of sleep, each child completed a general 18-item, 7-point sleep questionnaire addressing sleep problems, morning and evening alertness, and fatigue. The parents completed a similar questionnaire describing their child's sleep patterns. The children also completed daily logs of their sleep patterns.

Pulmonary function.—Each evening prior to bedtime and each morning following awakening, the children tested themselves using a standard Wright peak-flow meter. The children were instructed to conduct each test three times, and to document the highest reading. Peak expiratory flow (PEF) measures are considered a reliable tool for estimating asthma severity. In addition, the asthmatic children and their parents completed a subjective assessment of the severity of the child's illness.

Asthma severity.—The children were instructed not to use beta agonists during the study. Three different subjective measures were used to assess asthma severity (in addition to the PEF measures). Two measures were based on a three-point self-rating scale, one completed by the parent and one by the child (mild, moderate and severe). The third measure was based on a clinical symptom checklist including symptoms like coughing, chest pains or pressures following intense activities, night waking, morning awakening, or in response to passive smoking or dust. This scale score ranged from 0 (no symptoms) to 9 (all symptoms).

Statistical analysis.—For assessing group differences, we used MANOVA with sex, group, and age as the independent variables. For the age variable, children were grouped into two age groups: "young" (<12-years) and "old" (>12 years). Dependent variables—PEF, actigraphic and subjective sleep measures—were averaged across the 3 days of monitoring.

Table 2.−Sleep and PEF measures (± standard deviations): Comparison between asthmatic and control children

	Asthmatic	Control	F
PEF Measures (% predicted)			
Morning PEF	86.2 ± 21	94.9 ± 16	6.04 **
Evening PEF	95.5 ± 17	98.2 ± 17	.43
PEF Drop	9.87 ± 13	3.09 ± 3.6	8.68 ***
Actigraphic Sleep Measures			
Sleep Onset (hrs)	23.2 ± 1.1	23.3 ± 0.9	.21
Sleep Duration (mins.)	491 ± 50	496 ± 43	.27
Sleep Percent (%)	92.1 ± 6.5	94.1 ± 3.3	1.33
Longest Sleep Period (mins.)	153 ± 63	172 ± 66	1.59
Quiet Sleep (%)	65.0 ± 12	70.4 ± 8.5	4.79 *
Mean Activity Level	10.4 ± 4.5	8.5 ± 2.2	5.16 *

* $p < .05$; ** $p < .01$; *** $p < .005$

Table 3.—Sleep and PEF measures: Pearson correlations for the total sample, asthmatic and control group (with Age partialled out)

Sleep Measures	Group	PEF Measures		
		Morning PEF	Evening PEF	PEF Drop
Sleep Onset	Asthma	-.26	-.21	.13
	Control	.08	.05	-.07
	Total	-.12	-.09	.08
Sleep Duration	Asthma	.24	.22	-.09
	Control	-.04	-.09	-.24
	Total	.16	.10	-.14
Sleep Percent	Asthma	.29	.32	-.09
	Control	.22	.28	.32
	Total	.30 *	.30 *	-.11
Longest Sleep Period	Asthma	.15	.14	-.09
	Control	.24	.31	.30
	Total	.22	.23	-.07
Quiet Sleep	Asthma	.20	.18	-.11
	Control	.05	.08	.21
	Total	-.13	-.15	.01
Mean Activity Level	Asthma	-.36 *	-.33 *	.20
	Control	-.23	-.28	-.30
	Total	-.36 ***	-.31 **	.22

* $p < .05$; ** $p < .01$; *** $p < .005$

Results

Reliability of PEF measures.—Evening and morning PEF measures were found to be very stable and reliable on a day-by-day basis for the entire sample (see Table 1). However, evening-to-morning PEF drop (diurnal variation) had very low day-by-day reliability. Comparable reliabilities were found for both groups.

Group differences.—Group differences are summarized in Table 2. Regarding the PEF measures, asthmatic children had lower PEF means on their morning measurement in comparison to their controls. They also had a significantly larger drop of their PEF measures from the evening to the following morning.

Significant group differences were also found for the actigraphic sleep measures. Asthmatic children were significantly more active during sleep, and had lower quiet sleep percent.

Significant three-way age-by-group and sex-by-group interactions were found for the temporal sleep measures. Asthmatic boys fell asleep significantly earlier than asthmatic girls (23.06 vs 23.54, respectively), whereas the opposite was true for the control boys and girls (23.57 vs 23.11, respectively) ($p<.05$).

On the self-rating sleep scale, asthmatic children rated themselves as significantly more tired in the morning compared to the control children ($F=8.29$; $p<.01$). The asthmatic children had significantly more difficulty waking up in the morning ($F=6.74$; $p<.05$), and preference for late bedtime ($F=5.88$; $p<.01$).

Similar results were found on the child's sleep questionnaire completed by the parents. Asthmatic children were rated by their parents as more tired in the morning ($F=7.06$, $p<.01$) and less alert ($F=4.79$, $p<.05$) than control

Table 4.—Correlations between subjective sleep and alertness and PEF measures: Pearson correlations for the total sample, asthmatic and control group (with Age partialled out).

Sleep Measures	Reporter	Group	PEF Measures Morn. PEF	Even. PEF	PEF Drop
Frequent Night Wakings	Child	Asthma	-.52 #	-.46 *	.35 *
		Control	-.28	-.29	-.05
		Total	-.46 ##	-.39 ***	.32 **
	Parent	Asthma	-.39 *	-.17	.50 ***
		Control	-.16	-.14	.12
		Total	-.30 *	-.16	.37 ***
Tired in the Morning	Child	Asthma	-.12	-.19	-.04
		Control	-.20	-.21	-.05
		Total	-.19	-.19	.09
	Parent	Asthma	-.26	-.13	.29
		Control	-.36 *	-.33	.05
		Total	-.35 ***	-.24	.32 *
Alert in the Evening	Child	Asthma	-.01	.15	.27
		Control	.06	.10	.20
		Total	.03	.14	.18
	Parent	Asthma	-.49 ***	-.46 **	.29
		Control	.12	.17	.27
		Total	-.25 *	-.14	.29 *

* p < .05; ** p < .01; *** p < .005; # p < .001; ## p < .0001

Table 5.—Sleep and asthma severity indices: Pearson correlations for the asthmatic group.

Sleep Measures	Severity Indices Parent's Rating	Child's Rating	Symptom Checklist
Sleep Onset	.22	.22	.34 *
Sleep Duration	-.16	-.25	-.25
Sleep Percent	-.32 *	-.32 *	-.33
Longest Sleep Period	-.38 *	-.35 *	-.25
Quiet Sleep Percent	-.27	-.23	-.04
Mean Activity Level	.37 *	.31	.39 *

* *p* < .05; ** *p* < .01; *** *p* < .005

children. Asthmatic children were also rated by their parents as more restless during sleep than control children (F=4.35, p<.05).

Interestingly, distinct relationships were found between sleep and subjective sleepiness or alertness within the asthmatic and the control groups. In the asthmatic group, the only significant correlations (with age partialled out) were between later sleep-onset time and the child's increased difficulty in getting up in the morning (child ratings: r=.39; p<.05), and the child's increased alertness in the evening (parental ratings: r=.32; p<.05). In the control group, extended sleep duration was significantly correlated with the child's reduced alertness in the morning (child's ratings: r = -.37; p<.05; and parental ratings: r=-.40; p<.05) and the child's reduced alertness in the evening (parental ratings: r=-.63; p< 0001).

Relationships between sleep and PEF measures.— To assess the relationships between sleep patterns and pulmonary function, we correlated the actigraphic sleep measures with the PEF measures for the total sample and separately for each group (see Table 3). Pearson correlations were calculated with age partialled out to control for potential developmental trends. Significant correlations were found between sleep measures of sleep percent and mean activity during sleep, and the evening and morning PEF measures. Poorer sleep quality was associated with lower PEF measures.

Examination of the subjective sleep questionnaire also revealed significant relationships between subjective sleep and alertness ratings and PEF measures (see Table 4).

Asthma severity.—Significant correlations were found among the three subjective asthma severity indices. Parental severity rating was significantly correlated with child severity rating (r=.61, p<.0001) and the symptom checklist score (r=.36, p<.05). Child severity rating was also significantly correlated with the symptom checklist score (r=.58, p<.0005).

From the three subjective asthma severity indices (parent, child and symptom checklist), only the measures based on the symptom checklist were significantly correlated with the PEF measures (with PEF drop: r=.43, p<.05; and with morning PEF: r=-37, p<.05). However, all three severity measures were significantly correlated with a number of actigraphic sleep-quality measures (see Table 5). Poorer sleep was associated with more-severe asthma.

DISCUSSION

The present study is the first home-based objective examination of the relationship between pulmonary function and sleep in asthmatic and normal children. The results suggest that pulmonary function and sleep are indeed closely related in asthmatic children, and that asthma and asthma severity indices are associated with poorer sleep quality.

The reliability of activity-based sleep-wake measures has previously been validated.[15-17] However, it should be noted that validation studies were not performed on children with breathing disorders, and the results should therefore be considered cautiously and validated in future studies using polysomnography or other reliable methods.

The reliability of the PEF measures was established for both groups, as evidenced in the significant high day-by-day correlations of the morning and evening PEF values. It is important to note that this reliability was similar in both groups, thus precluding the possibility of a measurement bias differentiating between the clinical and control groups.

The significant group differences in morning PEF and PEF diurnal variation values were expected as a clinical feature of the disorder even in its stable periods.[22-26]

The results also suggest that stable asthmatic children have distinct sleep patterns that differ from those of normal controls. Their lower sleep quality is manifested in the significantly increased activity levels during sleep and lower percentages of quiet sleep. These findings correspond to the earlier polysomnographic findings indicating that asthmatic children have reduced stage-4 sleep.[12] These findings also correspond to the reported circadian rhythmicity of the peak expiratory flow rates in children,[22-26] suggesting that sleep is gradually more disrupted as pulmonary function is increasingly compromised.

Although the correlations are mostly in the moderate-lower range, significant relationships do exist between peak-flow measures and sleep quality. These relationships strengthen the hypothesis that the group differences result directly from the disrupted lower morning PEF and PEF drop values, which were significantly correlated with poorer sleep in the asthmatic children. These relationships may account for the vulnerability of the sleep-wake system in asthmatic children, since their pulmonary systems are more susceptible to reduced functioning, as manifested also in the reduced PEF levels in our sample of stable asthmatic children.

The subjective reports of the children and their parents suggest that asthmatic children may be at risk for developing signs of excessive daytime sleepiness and fatigue. Likewise, the distinct pattern of correlations between sleep and sleepiness found within each group suggest that there are disorder-specific underlying mechanisms affecting the sleep-alertness system. It has been reported that neuropsychological functioning and school performance of asthmatic children might be compromised, and a debate in the literature has evolved around the possible causes for this cognitive deficit (eg, brain deficit, medication, or other physiological processes).[27-33] In addition, it has been argued that children suffering from other breathing disorders, such as sleep apnea syndrome, show deficits in their neurobehavioral functioning.[34] The issue of daytime alertness or sleepiness and its effects on neuropsychological functioning should be further explored to establish whether this sleepiness is clinically significant, and should be considered a risk factor for poorer cognitive functioning (eg, academic performance), psychosocial functioning (eg, psychopathological or temperamental manifestations), or other risks associated with disturbed sleep and increased sleepiness.

ACKNOWLEDGMENT

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