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Nocturnal Wheeze Measurement in Young Asthmatics

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ABSTRACT

Nocturnal exacerbation is one of the criteria for defining asthma severity. The aim of this study was to look at the relationship between subjective complaints of nocturnal asthma symptoms, objectively recorded wheezing, and spirometry values. Continuous overnight recording and analysis of respiratory sounds were performed in the homes of 12 young asthmatic patients (7 male), aged 7–18 years, who reported symptoms when seen in clinic. Patients kept an asthma symptom diary for 1 week. They had spirometry the evening before and the morning after the nighttime study. Wheezing was identified and quantified by an FFT-based computer algorithm. Seven patients reported nocturnal asthma symptoms the next morning. Three patients had sustained wheezing episodes lasting 21, 25, and 36 minutes, respectively. They all had a morning $FEV_1 \leq 51\%$ predicted, whereas none of the 10 without wheezing had a morning $FEV_1 \leq 51\%$ predicted. Two of them reported nocturnal asthma and one did not. There was a significant relationship between night-time wheezing and lower FEV_1 the next morning by both parametric (unpaired *t*-test, $p = 0.004$) and nonparametric (Mann-Whitney, $p = 0.009$) tests, and between night-time wheezing and larger diurnal variation in FEV_1 ($p = 0.038$, $p = 0.036$, respectively). There was no significant relationship between subjective complaints of nocturnal asthma and objective measurement of wheezing or the FEV_1 the evening before the nocturnal study. Night-time wheeze was associated with a morning $FEV_1 \leq 51\%$ predicted and more pronounced diurnal variation of FEV_1. Recalled nocturnal symptoms may not necessarily reflect wheezing and may reflect chest tightness or other sensations. Computerized acoustic monitoring provides objective evaluation of night-time wheezing.

INTRODUCTION

IT IS COMMON FOR MANY ASTHMATICS to feel worse at night. Nocturnal asthma (NA) symptoms were reported in 47–75% of asthma patients in a number of large surveys from different countries[1] and are accompanied by reduced lung function on waking, referred to as 'morning dipping.'[2] Some early studies ap-

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peared to indicate that the severity of morning dipping reflected the severity of asthma in general and that those with marked morning dipping were at greater risk of severe attacks or even death.[3,4]

Nocturnal exacerbation is one of the important criteria for defining asthma severity according to the National Institutes of Health's Global Initiative for Asthma (GINA) guidelines for managing asthma.[5] Attempts have been made to document nocturnal asthma noninvasively by recording breath sounds from sleeping patients. Baughman and Loudon[6] recorded breath sounds in 5 patients overnight on an intermittent basis and found most wheezes to be between 0400 and 0430. Lenclud et al.[7] monitored overnight tracheal sounds and airways resistance using esophageal balloon and facemask in 7 patients with nocturnal asthma and found a correlation between wheezing and airway resistance only in the more severe cases.

The present study was undertaken using newly developed, computer-based acoustic monitoring techniques suitable for continuous measurements of wheezing during the night at home.[8] The object of the study was to look at the relationship between the subjective complaints of nocturnal asthma symptoms and the objectively recorded wheezing and morning/evening FEV_1 (diurnal variation).

MATERIALS AND METHODS

Patients

Subjects were recruited from patients attending a Pediatric Pulmonary outpatient clinic over a 1-month period. Inclusion criteria were: (1) Diagnosis of asthma by GINA criteria[5]; (2) age 6–18 years; (3) ability to perform spirometry; (4) symptoms of asthma reported at visit; (5) consent given by subject or parent; and (6) no other chronic condition. The Institutional Ethics Committee approved the study, and informed consent was obtained from all participants. Overall asthma severity based on residual symptoms was classified using the updated (2002) GINA symptom-based classification,[5] which takes into account current treatment using the record of symptoms and drug consumption for the week prior to the nocturnal study.

Symptom recording

Patients were asked to monitor their asthma symptoms and keep a symptom diary for 7 days prior to the nocturnal study. They were asked to quantify daytime symptoms, nighttime symptoms, exercise limitation and use of short acting bronchodilators, where each category was graded as none ('0'), mild ('1') or significant ('2').

Spirometry

Spirometry was measured using a portable electronic spirometer (Microloop II Spirometer, Micromedical Ltd. Rochester, England) prior to taking any bronchodilator medication, during the evening before and on waking following the acoustic study. The diurnal variation of lung function was calculated as the evening to morning difference in FEV_1 as a percentage of the average of the morning and evening values (amplitude % mean of FEV_1).

Acoustic respiratory monitoring

A technician performed the nocturnal acoustic monitoring study at home within 1 week of the clinic visit. Recording and analysis of respiratory sounds were conducted with a computerized acoustic system previously described in detail.[8] Respiratory acoustic signals were recorded from five phonopneumography piezoelectric contact sensors applied over the trachea, both axillae, and both posterior bases, and connected to a computerized automatic wheeze detection device (PulmoTrack®1010, Karmel Medical Acoustic Technologies, Yokneam Illit, Israel). Recording was started when the patient went to bed, usually between about 2200 and 2400 hours, and ran continuously throughout the night.

Wheezing was defined in accordance with the European Task Force report on computerized breath sounds[9] as musical monophonic or polyphonic sounds with duration of at least 100 msec, with asthmatic wheezes being in the frequency range 150–800 Hz, provided these were expiratory polyphonic or monophonic or inspiratory polyphonic in character. The phase of respiration was determined by impedance recorded from

the axillary sensors. Events having a cumulative duration of less than 3 seconds in any minute (wheeze rate $< 5\%$) were considered not clinically significant.[8] The total time with a wheeze rate of $>5\%$ was recorded for each patient.

To verify the accuracy of the analysis further, random samples were manually analyzed for each hour of recording in which no abnormal acoustic events were detected by the computer program. In no instance was an abnormal respiratory acoustic event found that had not been detected by the computer algorithm.

Statistical analyses

Comparisons between groups of patients with or without nocturnal symptoms and with or without objective evidence of wheezing were made by parametric and nonparametric tests for unpaired groups as appropriate.

RESULTS

Out of 20 eligible patients, 14 consented to participate, of whom two were rejected for technical reasons (failure to fulfill protocol requirements). Relevant details of the patients and the results of spirometry performed in the clinic are given in Table 1.

Of the 12 patients, 11 were classified according to GINA severity steps 3 or 4. Most were prescribed an inappropriately low level of treatment for their asthma severity according to the GINA recommendations (Table 1). This may explain the patients' reported symptoms while on treatment.

The results of the nocturnal studies are summarized in Table 2. On the morning following the nocturnal study, 7 of the patients reported subjective symptoms of asthma during the study night, of whom 5 had also reported symptoms on the previous night. Two patients had an FEV_1 $<65\%$ of predicted the night prior and 7 had FEV_1 $<65\%$ of predicted the morning following the nocturnal study. The diurnal variation in FEV_1 (amplitude % mean FEV_1) varied widely: $>25\%$ in 3 subjects, 10–20% in 1, 0–10% in 5 and negative (i.e., morning value greater than evening value) in 3 subjects.

Objective measurement of nocturnal wheezing showed that only 3 patients had sustained wheezing during the night, lasting 21, 25, and 36 minutes, respectively. One of these patients also had further sporadic short wheezes. There was no significant difference between those with and without a subjective complaint of nocturnal asthma with regard to wheeze score and lung function tests (amplitude % mean FEV_1, evening FEV_1, morning FEV_1). Their data are shown Table 2.

TABLE 1. PATIENT CHARACTERISTICS

Number	*Gender*	*Age (year)*	*Clinic FEV_1 (%)*	*GINA total score*[a]	*GINA treatment score*[b]
1	F	13	85	4	2
2	M	7	69	1	1
3	M	12	60	4	1
4	F	17	87	4	3
5	M	12	84	4	3
6	M	18	85	4	3
7	F	9	73	4	3
8	M	10	44	4	1
9	F	15	107	3	1
10	F	17	73	4	3
11	M	17	57	4	3
12	M	13	67	3	1

[a]Global Initiative for Asthma classification taking treatment into account.

[b]Treatment recommended according to Global Initiative for Asthma symptom-based classification of severity.

TABLE 2. SYMPTOMS, PULMONARY FUNCTIONS, AND OBJECTIVE WHEEZE MONITORING RESULTS IN 13 PATIENTS

Number	*Evening FEV_1 (%)*	*Morning FEV_1 (%)*	*Amp-% Mean FEV_1*	*Nocturnal symptoms*	*Sustained wheeze score (%.min)*	*Sporadic wheeze count*
1	85	78	7.6	Yes	0	0
2	69	62	9.4	Yes	0	0
3	60	63	−5.6	Yes	0	0
4	87	85	2.3	Yes	0	0
5	84	51	50.0	No	190	0
6	85	65	33.6	No	0	0
7	73	93	−26.7	No	0	0
8	44	33	30.2	Yes	364	2
9	107	90	18.2	Yes	0	0
10	73	77	−5.3	No	0	0
11	57	51	9.5	Yes	226	0
12	67	61	6.6	No	0	0

Comparisons of wheeze score and lung functions between the groups with and without symptoms are shown in Table 3, and comparison of lung function between the groups with and without objective wheezing during the night are shown in Table 4 and Fig. 1. Because of the small number of subjects with objective wheezing,[3] statistical comparisons can only be approximate. Mean morning FEV_1 was significantly lower in the wheezing patients, (45% vs. 75% predicted; $p = 0.004$ by unpaired t test, $p = 0.009$ by Mann-Whitney test). Amplitude % mean FEV_1 was 29.5% vs. 4.5% ($p = 0.038$, $p = 0.036$ respectively), and wheeze had an FEV_1 below 51%. All 3 patients with nocturnal wheeze had a morning $FEV_1 \leq 51\%$ predicted, while none of the 10 without wheezing had a morning FEV_1 at or below 51% predicted.

One of the 3 patients in whom wheezing was recorded objectively reported no symptoms, while of 7 who reported symptoms; no objective wheezing was recorded in 5 of them. The diurnal variation in FEV_1 was markedly increased in 2 patients with objective evidence of nocturnal wheezing (one of whom did not report any subjective symptoms). It was also considerably elevated in 2 patients (18.2%, 33.6%) who had no objective evidence of wheezing (one of whom did not report subjective symptoms). There was no relationship between the GINA severity score and the objective finding of nocturnal wheezing.

DISCUSSION

This preliminary study demonstrates the utility of objective monitoring of nocturnal wheezing in asthmatic children. Patients with objective nocturnal wheezing were characterized by a low morning FEV_1

TABLE 3. WHEEZE SCORE AND LUNG FUNCTION IN PATIENTS WITHOUT (S−) AND WITH (S+) NOCTURNAL SYMPTOMS

	Wheeze score (%)		*Amp % mean FEV_1 (%)*		*Evening FEV_1 (% pred.)*		*Morning FEV_1 (% pred.)*	
	S−	*S+*	*S−*	*S+*	*S−*	*S+*	*S−*	*S+*
Number	5	7	5	7	5	7	5	7
Mean	31	84	11.1	10.5	76.4	72.7	69.4	67.3
Median	0	0	9.4	10.7	73	69	65	70
Minimum	0	0	−24.1	−4.9	67	44	51	33
Maximum	190	362	48.9	28.6	85	107	93	90

TABLE 4. LUNG FUNCTION IN PATIENTS WITHOUT (W−) AND WITH (W+) OBJECTIVE NOCTURNAL WHEEZE

	Amp % mean FEV_1 (%)		*Evening FEV_1 (% pred.)*		*Morning FEV_1 (% pred.)*	
	W−	*W+*	*W−*	*W+*	*W−*	*W+*
Number	9	3	9	3	9	3
Mean	4.5	29.5	78.5	62	75	45
Median	8.6	28.6	73	57	77	51
Minimum	−24.1	−11.11	60	44	61	33
Maximum	26.7	48.9	107	84	93	51

(≤51%) and a larger diurnal variation in FEV_1. There was no significant correlation between low FEV_1 on the evening before the nocturnal study and objective evidence of wheezing during the night. Also, there was no relationship between subjective complaints of nocturnal asthma and objective measurement of wheezing.

It is unlikely that the paucity of wheezing detected in our patients is due to technical factors. The computerized system has been found to be reliable in a number of previous studies,[6–8] complies with the specifications of the European Task Force,[9] and had only small (±10%) night-to-night variation.[8] Identifying basic breath sounds in all recordings examined, including the random sampling, further ensured the reliability of the system.

There have been several published studies in which asthmatic patients were observed and monitored continuously during the night. In four of these, pulmonary resistance was measured using an esophageal balloon and face mask in small numbers of patients specifically selected because of symptomatic nocturnal asthma.[7,10–12] All four studies demonstrated an increased resistance during the night, but no awaking occurred in these patients.[10,11] In the study by Bellia et al.,[10] a correlation was found between magnitude of increase in resistance and the morning dip in PEF. Lenclud et al.[7] studied 7 adult asthmatics and found a significant correlation between wheezeing and increased expiratory resistance. For 5 of their subjects who had significant wheezing, the sum of the product of percentage wheezing and time was 400–800%.min, which is somewhat greater than our values of 190–360 %.min. It is possible that their subjects were more severe asthmatics than ours or that they included as wheeze some continuous adventitious sounds such as inspiratory monophonic or very high frequency sounds, which we excluded. In another study, Kiyokawa et

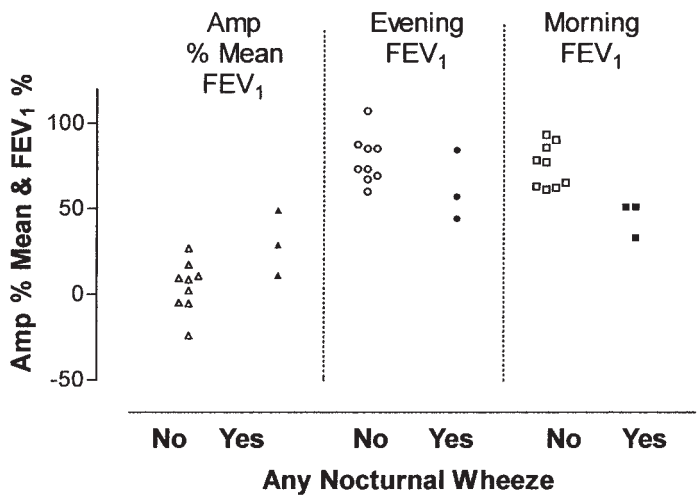

FIG. 1. Diurnal variation in FEV_1 and FEV_1 the evening before and the morning after the nocturnal study in relation to the objective documentation of nocturnal wheezing by the patients.

al.[13] recorded tracheal breath sounds overnight in 27 adult asthmatics and then manually evaluated each record for wheezing. Only 8 of 23 occasions where patients reported wheezing had objective confirmation. However, wheezing was also found in 2 of 15 occasions where no symptoms were reported. These results are in agreement with our present study in which we found that most of the patients who reporting nocturnal symptoms did not have objective evidence of wheezing. The small sample size in our study, however, precludes this from being a definite conclusion.

A number of studies compared the physical sign of wheezing[14] to lung function in awake patients. In a study by McFadden et al.,[15] patients with acute asthma had a mean FEV_1 of 31% predicted when wheezing, and 63% predicted when they became wheeze and symptom free. Commey et al.[16] found an FEV_1 of 72% predicted in 40 asthmatic children with no objective wheezing, whereas mean FEV_1 was 60% predicted in 22 who had wheezing. In a study of 93 asthmatic adults, Shim et al.[17] found a mean PEF of 60% predicted in those without wheezing, 49.4% predicted in those with expiratory wheezing, and 35.8% predicted in those with inspiratory and expiratory wheezing. Similarly, in an emergency room study of 71 asthmatic children, Kerem et al.[18] found a mean FEV_1 of 55% predicted in nonwheezing children and a mean FEV_1 of 37% predicted in wheezers. In these studies, it is unclear whether wheezing was assessed during quiet or deep breathing, and it is possible that lung function would need to be lower during quiet breathing, as during sleep studies, for wheeze to be detected. Taking all these studies into account, we estimate that wheezing is heard when FEV_1 is around 50% of predicted. Thus, it is interesting that all 3 of our patients who had nocturnal wheeze had morning FEV_1 values of 51% or less. PEF is more easily measured at home, but is less reliable than FEV_1 because it is very dependent on patient effort and cooperation. Various studies have demonstrated its poor concordance with other parameters of asthma severity.[19]

It is possible that wheezing reflects a unique aspect of the pathophysiology of asthma that is not solely related to airflow obstruction but may also depend upon airway wall characteristics.[14] It must be emphasized that we measured wheezing and not airway resistance or oxygen saturation, so that our findings relate to this physical sign associated with asthma but not to whatever patients feel subjectively and report as 'nocturnal asthma.' It is possible that nocturnal asthma reported by 5 of our patients who had no wheezing were generated by chest tightness or other sensations unrelated to overt wheezing, which cannot be verified from the present study.

In summary, computerized wheeze monitoring provides objective evaluation of nighttime wheezing. Nocturnal wheezing is associated with significantly lower early morning FEV_1 and more pronounced diurnal variation of FEV_1. Recalled nocturnal symptoms may not necessarily reflect wheezing, and may reflect chest tightness or other sensations.

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