Asthma severity at night during recovery from an acute asthmatic attack

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Abstract

This study was undertaken to investigate the severity of night time asthma in children in hospital recovering from an acute attack of asthma. Twenty two children aged 5-14 years were studied. Coughing 'epochs' overnight varied from one to 156 (median 39.5) and mean overnight arterial oxygen saturation (Sao_2) from 82 to 98% (mean 91.3). Log_e values for cough showed a correlation with Sao_2 . An Sao_2 of <90% was invariably associated with coughing but Sao_2 above 95% did not preclude cough. Peak flow measured in the morning or evening correlated with Sao_2 but not with log_e cough, and clinical examination scores showed no correlation with overnight measurements. Night time Sao_2 correlated better with daytime tests of lung function than log_e cough. In general, night time indices of severity reflected daytime pulmonary function status but night cough was sometimes prominent in less severely affected cases. At the time of discharge, clinical indices of severity underestimated the degree of functional impairment at night.

Nocturnal symptoms, especially cough, are common and sometimes dominant features of asthma in children. Control of symptoms tends to deteriorate at night¹ and in adult asthmatics respiratory crises and death are more common at this time.^{2,3}

In children, nocturnal symptoms are often under reported,⁴ suggesting that night time morbidity may be underestimated. In a study of asthmatic children with prominent nocturnal symptoms, Thomson *et al*⁵ demonstrated that cough is most frequent during the two hours after retiring and again before getting up in the morning, and not between 3 and 5 am when peak flow is lowest.⁶ This has led to speculation about the relationship between night cough and wheeze in asthma⁷ and the interrelations of various measures of night time severity. The relationship between indices of night severity and daytime pulmonary function status, recently reported for adults,⁸ has similarly received little attention in children.

This study investigated the interrelation of night cough, overnight arterial oxygen saturation (Sao_2), evening and morning peak flow, and the relation of each to day time indices of lung function in a group of children about to be discharged from hospital after an acute attack of asthma.

Patients

Twenty two patients were recruited from the paediatric wards of the Leicester Royal Infirmary over an 18 month period. Those eligible for the study were schoolchildren (5-14 years) admitted for at least two nights with an acute asthmatic attack. As most asthma admissions in this hospital stay only one night, selection was biased towards those with more severe or prolonged attacks for whom hospital stay (including the days of admission and discharge) varied from three to five days (mean 3.5). The availability of staff and equipment were further constraints on patient selection. Thus if two or more children were suitable for study on the same night, one was chosen at random. The study was approved by the Leicester Health Authority ethical committee.

The children selected had a history of episodic wheezing and had demonstrated an increase in peak flow exceeding 15% after inhalation of a β_2 agonist. On admission to hospital they had extremely low or unrecordable peak flow readings but were competent at using a peak flow meter when well. Children entered the study on the day before planned discharge. Participation did not influence clinical management or decisions about the timing of discharge.

All had been treated with two hourly nebulised β_2 agonists and oral prednisolone (2 mg/kg/day) at the time of admission to the study. Two children also received intravenous aminophylline and hydrocortisone when the initial response to treatment was poor. When suitable patients had been identified, the nature of the study was explained to the parents and the child and informed consent was obtained. Details of the current admission and past history were obtained from interview with the parents and from previous medical records (table 1). Most attended the hospital as outpatients on a regular basis but five had not been admitted previously. At the other extreme, one 7 year old child had 25 documented asthma admissions, including four in the previous 12 months. All but one had received regular treatment at home and 15 were on prophylactic sodium cromoglycate or beclomethasone.

Methods

Lung function tests were carried out on the afternoon before overnight monitoring. Lung volume and airway resistance were measured by whole body plethysmography (Bodytest, Jaeger Ltd), maximum expiratory flow rates by an electronic spirometer (Gould) and peak flow with a Wright peak flow meter. All measure-

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Table 1 Details of study children

Age (years)	
Mean	9.0
SD	3.0
Range	5.2–14.4
Height (m)	
Mean	1.31
SD	0.17
Male:female ratio	15:7
Highest respiratory rate	
Mean	48
SD	12
Range	32–80
Intravenous medication	2
Length of stay in days	
Mean	3.5
Range	3–5
Previous admissions	
Mean	4.4
SD	6.3
Range	0–25
Regular medication	
Nil	1
β ₂ agonist	21
Sodium cromoglycate	7
Inhaled steroid	8
Symptoms at home	
Intermittent	12
Continuous	10

ments were made before and 10–15 minutes after inhalation of salbutamol. The results (except residual volume (RV) as a ratio of total lung capacity (TLC) were converted to percentage of the predicted values for height using published data on normal children^{9–13} to facilitate comparison between children of different ages. Daytime (awake) SaO₂ was measured in the late afternoon over at least 10 minutes, with the child resting and supine using the system employed for the night study.

Clinical examinations were carried out by one clinician (EWH) before each overnight monitoring and again the next morning. Pulse rate, respiration rate, blood pressure, and pulsus paradoxus were recorded. A subjective score (0–2) was given for hyperinflation, tracheal tug, intercostal recession, audible wheeze, and auscultatory wheeze. Peak flow was also measured at these times.

Overnight monitoring was done in a quiet cubicle adjacent to the ward area. A Biox 3700 Pulse Oximeter attached to a Squirrel data logger (SQ32–3V/IL/3D, Grant Instruments Cambridge Ltd) monitored SaO₂ and pulse rate (averaged over three seconds) at one minute intervals. A finger probe was secured firmly using adhesive tape and remained in situ overnight. The stored overnight data were examined to exclude any artefact due to a poor probe position and body movement. As the pulse rate was also recorded, this consisted of excluding SaO₂ readings associated with a sudden inappropriate fall in pulse rate. These exclusions comprised only a small fraction of each overnight record, and although these points were excluded from analysis, the large number of data points through the night meant that they would have had little discernible effect on the mean SaO₂. The results were analysed to give mean SaO₂ and percentage time <90% SaO₂.

Night cough was recorded on a tape recorder

using a cough monitor with a voice activated switch set at a selected trigger level, as described previously.⁵ The two microphones were mounted on freestanding tripods placed on either side of the bed, pointing towards the subject and adjusted so that coughing from any part of the bed would activate the switch. A BBC computer and specially designed programme facilitated analysis by giving the number of 10 second ‘epochs’ during which coughing occurred. This method gave qualitatively similar results to counting individual coughs. The extraneous noises that occasionally occurred were excluded from the analysis by listening to each tape during the analysis procedure. These were easily detected and there was no evidence that they disturbed the children or provoked them to cough.

Results

The children were discharged home on the day after the overnight study, except for one who continued on nebulised salbutamol for a further 24 hours before discharge. Treatment with inhaled bronchodilator and oral prednisolone continued at discharge. Other medication was continued as before admission.

NIGHT TIME MEASUREMENTS

Table 2 summarises the results for the night time measures of asthma severity. The number of coughing epochs throughout the night varied from 1 to 156 with a median value of 39.5 and a mean of 49.3. The data were normalised by taking log_e values.

The mean overnight SaO₂ for the group as a whole was 91.3% and the mean percentage time less than 90% saturation was 35.9%. Seven children had SaO₂ <90% for more than 50% of the time and three for more than 90% of the time. The difference between maximum and minimum overnight SaO₂ recordings ranged from 5 to 21% with a mean of 14.5%. On examining the individual SaO₂ traces, baseline values were remarkably constant during the night, with no evidence of change with time and no evidence of prolonged periods of desaturation. Figure 1 shows a typical overnight oxygen saturation trace and figure 2 a comparison of two methods of presenting the data obtained.

The mean percentage of predicted peak flow for evening and morning for the cases where paired results were recorded was 69% and 67% respectively (SE of the mean difference = 5.0). Six children out of 16 and five out of 19 studied in the evening and morning respectively had a peak flow <80% of the predicted value. The mean peak flow variability (expressed as the

Table 2 Night time measures of asthma severity

Parameter	Mean	Range
Coughing epochs	49.3	1–156
Overnight mean SaO ₂ (%)	91.3	82–98
Evening PF as % of predicted value	72.3	31–129
Morning PF as % of predicted value	66.7	27–110
PF variability %	–7.1	–71 to +38
Evening clinical score	3.2	0–7
Morning clinical score	2.4	0–5

Peak flow (PF) variability is calculated as (PF_{pm}–PF_{am})/PF_{pm}×100.

Figure 1 Typical overnight SaO_2 trace. Mean saturation for this case was 90%. At points marked A, nebulised salbutamol was given. At B, the drop in saturation was associated with a sudden drop in pulse rate, indicating poor connection of the finger probe. At C, a further nebuliser was given and the child woke up. Recordings at all these points were excluded from analysis.

Figure 2 Duration of low SaO_2 compared with mean overnight SaO_2 .

Table 3 Pearson correlation coefficients for night time variables

	Log_e cough	Mean night SaO_2
Mean night SaO_2	0.564*	—
Evening PF	-0.324	0.578*
Morning PF	-0.257	0.481*
PF variability	-0.341	0.108
Evening clinical score	-0.111	-0.117
Morning clinical score	-0.107	-0.235

* $p < 0.05$.
PF, peak flow.

Table 4 Results of lung function tests

Parameter	Before bronchodilator			After bronchodilator		
	No	Mean	Range	No	Mean	Range
Vital capacity ⁹	17	74	31–124	17	78	42–124
RV ⁹	14	154	72–261	16	143	71–214
TLC ⁹	19	96	70–124	18	95	64–125
Thoracic gas volume ⁹	20	105	69–140	20	101	66–129
RV:TLC ratio	14	41	19–66	16	38	19–60
FEV ₁ ¹⁰	18	72	34–135	19	74	42–135
Forced vital capacity (FVC) ¹¹	15	85	47–133	15	91	53–137
FEV _{0.1} :FVC ¹⁰	18	75	57–96	19	74	57–94
MMEF ^{*10}	13	53	18–108	14	52	17–105
Maximum expiratory flow:						
50% FVC ¹²	15	55	23–118	15	57	25–118
25% FVC ¹²	13	43	10–101	14	39	7–102
60% TLC ¹¹	16	29	74–89	15	39	2–89
Peak flow ¹³	21	72	41–124	21	78	48–129
Airway resistance	21	231	105–504	21	176	63–274

Results are expressed as percentage of the predicted value for height based on published reference ranges, except RV:TLC where the ratio is given as a percentage.
*MMEF, maximum mid-expiratory flow.

percentage change in peak flow between evening and morning) was -7.1% ($\text{SD}=36$, pre-bronchodilator data).

The clinical assessment in the evening (maximum score=10) was mean 3.2, and the next morning was mean 2.3 (SE of the mean difference=0.32, $p < 0.05$).

CORRELATION OF NIGHT TIME VARIABLES

The data are shown in table 3. There was a significant negative correlation between overnight log_e cough and SaO_2 ($r = -0.564$, $p = 0.01$, see fig 3) but no correlation between log_e cough and any of the peak flow measures. There was a significant correlation between mean overnight SaO_2 and both evening and morning peak flow.

Neither evening nor morning clinical scores correlated with log_e cough, night SaO_2 or peak flow.

NIGHT TIME AND DAYTIME MEASUREMENTS

The mean daytime SaO_2 was 93.0% (range 89.0–96.5%).

Table 4 gives the results of lung function tests. They show varying degrees of hyperinflation and expiratory airflow limitation within the group.

There was a small but not significant difference between daytime and overnight SaO_2 .

Figure 3 Comparison of overnight cough and overnight SaO_2 .

Table 5 Pearson correlation coefficients of night time with daytime measures of asthma severity

	Log _e cough	Mean night SaO ₂
Mean daytime SaO ₂	-0.078	-0.585*
Peak flow during day	-0.361	0.520*
RV:TLC	-0.450*	-0.711*
Maximum expiratory flow:		0.720*
60% TLC	-0.378	0.328
50% VC	-0.225	0.330
25% VC	-0.498†	-0.236
Airway resistance	0.245	

VC, vital capacity.

* = $p < 0.05$.† = $p < 0.1$. Figure 4 Overnight SaO₂ compared with the degree of hyperinflation (RV:TLC).

(mean fall = 1.2%. SEM = 0.74, $p < 0.08$) with a significant correlation between the two variables ($r = 0.585$, $p < 0.01$, table 5). There was no correlation between log_e cough and daytime SaO₂.

The overnight SaO₂ correlated best with presalbutamol measures of RV:TLC (fig 4) and to a lesser extent with peak flow. There was no association of SaO₂ with maximum expiratory flow at 50% or at 25% of vital capacity.

Less marked correlations were found between log_e cough and the results of lung function tests. Log_e cough correlated with RV:TLC but not with the maximum expiratory flow at 60% of TLC or with peak flow. The evening and morning clinical scores also correlated with this hyperinflation ($p < 0.02$, $r = 0.605$; and $p < 0.005$, $r = 0.693$ respectively) but not with expiratory flow at 60%.

Discussion

In this group of asthmatic children, studied before discharge from hospital, there was a high prevalence of pulmonary function abnormalities both by day and night, with wide variation in severity. Although there was an inverse relation between log_e cough and SaO₂ measured overnight, several children coughed frequently despite relatively normal SaO₂ concentrations. Evening and morning peak flow correlated with SaO₂ but not with log_e cough, and peak flow variability did not correlate with either. Clinical scores showed no relationship with any measure of night time asthma. Among daytime measures the degree of hyperinflation correlated best with the night time variables, particularly SaO₂.

These results probably reflect the situation for most children at the time of discharge from hospital after a moderate to severe attack of asthma, as participation in the study had not influenced clinical decisions.

The median cough score (39.5, range 1–156) is much higher in this study than that reported for asthmatic children of similar age with persistent night cough studied at home, in whom median cough score was 6.6 episodes per night (range 0–272).⁵ It is also higher than the reported mean value of 14.6 episodes in adult patients with chronic bronchitis and persistent cough,¹⁴ although a different definition of a coughing episode was used. Higher median cough counts were obtained for adults admitted with acute respiratory problems¹⁵ but comparisons are difficult as these authors counted individual coughs.

This group also showed a high prevalence of hypoxaemia with eight out of 22 children having mean SaO₂ < 90%. Our method of collecting the SaO₂ data used lower sampling rates than other studies and did not allow us to look for dips in saturation associated with coughing bouts, but studies in adult patients suggest that dips in SaO₂ are strongly correlated with sleep state and not at all with episodes of coughing.¹⁴ Coughing often involves quite extensive body movements so dips during coughing may be difficult to interpret. SaO₂ normally decreases slightly at night and that fall is larger in asthmatic children.^{16, 17} The mean range of SaO₂ through the night for our patients was 14.5%, which compares with 5.1% and 6.8% for clinically stable asthmatics^{16, 17} and 8.9% for those on suboptimal treatment.¹⁷ All the individual measurements of SaO₂ were associated with a consistent recording of the pulse and therefore probably reflect a true increase in the variability of SaO₂ in this group. Although the mean saturation was below 90% in eight cases, all the children were considered fit for discharge the next day.

Evening and morning peak flow were both low with 38% and 26% of children respectively having a peak flow < 80% of that predicted. Mean values were lower in the morning than in the evening, but this effect was not significant. The evening and morning readings and the peak flow variability showed wide variation within the group.

Clinical scoring systems^{18, 19} are partly subjective and difficult to validate, but do attempt to quantify the degree of clinical severity. The relatively low scores seen in this study reflect the fact that the children were considered ready for discharge—a condition of entry to the study. Clearly the scores obtained were poor indicators of functional severity in the children studied.

There was a correlation between overnight log_e cough and mean overnight SaO₂. Children with low SaO₂ had high cough counts but the converse was not necessarily true (fig 3). In a study of night cough in asthmatic children, Thomson *et al* found that most episodes occurred within two hours of going to bed or shortly before waking.⁵ Sleep status was not recorded in this study but electroencephalographic studies

in coughing adults have shown that 85% of night coughing occurs during wakefulness and that coughing rarely wakes patients from sleep.¹⁴ There was no evidence of hypoxaemia at the beginning or end of the night in this study, which makes a causal relationship between cough and hypoxaemia unlikely. The distribution of cough receptors in the airways and lungs has been the subject of a recent review.²⁰ It seems probable that during acute attacks of asthma the mechanisms responsible for airway narrowing and cough may to some extent overlap. There was, however, no association between log_e cough and peak flow. Cough occurs mainly at the beginning and end of sleep,⁵ whereas the nadir of peak flow is at around 4 am.^{6, 21} This may reflect differences between the pulmonary mechanisms in cough and airflow limitation. It has been shown that increased bronchial responsiveness is present in adult asthmatics whose predominant symptom is cough²² or marked variability in peak flow.⁸ Conversely, there is evidence that children with chronic cough have similar family histories and atopic characteristics to those of children with asthma,²³ and bronchial hyperresponsiveness which responds to theophylline.²⁴ These studies suggest that in such cases cough is best treated with bronchodilators.²²

There was a correlation between evening and morning peak flow and nocturnal SaO₂ though the behaviour of individuals was not predictable. Previous studies^{6, 17} in asthmatic children between acute attacks have shown no correlation between mean nocturnal SaO₂ or SaO₂ drop and degree of obstruction measured as forced expiratory volume in one second (FEV₁) but one study¹⁷ showed a correlation between maximum fall overnight of SaO₂ and maximum change in FEV₁. Hypoxaemia persisting after reversal of airflow obstruction merely reflects persisting ventilation/perfusion imbalance in the lungs.

The clinical assessment did not predict either night cough or SaO₂. Clinical indices of severity correlate poorly if at all with arterial oxygen tension in the acute attack.¹⁸ Our clinical assessments underestimated night time functional severity to a considerable extent.

In general, both overnight log_e cough and SaO₂ showed similar correlations with day time tests of lung function, but the relationship with night SaO₂ was always closer. In contrast to adult asthmatics with prominent cough²² there was little evidence in this study that those with more coughing had greater large airway involvement (as measured by peak flow or airway resistance). Increasing RV:TLC was the best single marker of poor night time function, correlating well with high cough rates and a low SaO₂. It is a measure of hyperinflation and, by implication, peripheral airways obstruction, which in turn influences ventilation/perfusion ratios. However, the association is not necessarily causal and in the case of cough is unlikely to be so. In children, the normal range for the hyperinflation ratio²⁵ is 22% + 8% and only two in this study group were within the normal range. This ratio also correlated with the clinical score, in contrast to the findings in an out-

patient study which showed no association between clinical examination and lung function abnormalities.²⁶ Although flow rates at low lung volumes (50% and 25% of vital capacity) showed no association with SaO₂, once this was corrected for the degree of hyperinflation (60% of TLC) a significant correlation emerged. Thus, reduced flow rates were also a good marker for low nocturnal SaO₂ but only if corrected for the degree of hyperinflation.

As cough, expiratory airflow limitation, and hypoxaemia are all features of severe asthma, some correlation between these variables is to be expected. Night cough is certainly a feature of severe dysfunction in asthma, but can be a persistent symptom in its absence. Its inter-relationship with wheeze needs further investigation.

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