Nocturnal asthma: a study in general practice

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SUMMARY. Symptoms of nocturnal asthma were studied using questionnaires returned by 1199 general practitioners throughout the United Kingdom. Of 7729 asthmatic patients seen consecutively and prescribed a bronchodilator aerosol, 73% woke with asthma at least once a week and 39% woke nightly. The percentage of asthmatics waking at night at least once a week in this population, where 48% were prescribed corticosteroid aerosols, was very similar to the 74% found to have asthma attacks at night in an earlier study of new hospital referrals at a time when such medication was not available.

While sampling bias cannot be excluded, the clinical characteristics and profile of medications found in this study are similar to other reports and the evidence suggests that the general practitioners were managing these patients carefully. There was an overall association between the patients' perception of the severity of their asthma and frequency of waking at night (P<0.001). However, 26% of 2928 patients waking every night regarded their asthma as mild. These patients were taking significantly less medication than those also waking nightly but assessing their asthma as severe (P<0.001). The seriousness of nocturnal symptoms may be underestimated by asthmatics and they should be asked specifically about the frequency of nocturnal waking. Those with nocturnal asthma had a generally higher frequency of allergic and non-allergic provoking factors, but no single factor distinguished these patients from those without nocturnal symptoms.

There was a strong correlation between the frequency of nightly waking and the number of medications used (P<0.001). A higher frequency was also seen in patients treated with drugs often reserved in the UK for more severe asthma (for example, theophyllines and oral corticosteroids), suggesting that these drugs were not controlling asthma well in the doses prescribed. While suboptimal use of medication may in part explain these findings, this may not be the whole explanation. New medications and formulations still need to be developed.

Introduction

ASTHMATIC patients often wake during the night with wheezy breathlessness sometimes associated wih coughing. These symptoms are also common in the early morning and there is a close association between the two.[1]

Nocturnal asthma is important for several reasons. Frequent waking at night disturbs sleep and impairs the quality of mental performance the following day. Sleep loss results in daytime tiredness and diminishes the quality of life for children and adults alike. In addition, attacks of asthma at night are likely to be more frightening than attacks during the day. An editorial discussing grouped data from four studies reported that 93 (42%) of 219 deaths from asthma occurred between 24.00 and 08.00 hours.[2]

The frequency of nocturnal asthma and morning symptoms have been studied mainly among patients referred to hospital.[1,3,4] It is often assumed that such patients represent more severe cases and the present study was designed to obtain information about asthmatics throughout the country who were currently being treated by their general practitioner. The aim of the study was to determine the frequency and perceived severity of nocturnal symptoms in relation to medication and not to obtain prevalence data about asthma in the community.

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Method

Study population

Names and addresses of approximately 26 000 general practitioners throughout the United Kingdom were obtained from a standard mailing list (Walsh Selective Mailings Ltd). The doctors were sent an explanatory letter together with examples of two forms to be completed and were asked to take part in a questionnaire-based study of nocturnal asthma.

Twenty six per cent of the general practitioners contacted (6760) expressed a willingness to participate. Sets of eligibility forms and questionnaires were sent to the doctors who were asked to complete an eligibility form for every patient for whom they prescribed or re-prescribed a bronchodilator aerosol. Where the request for a prescription was by post or telephone, the patient was asked to attend the surgery to help the doctor complete the forms. For each consecutive eligible patient a more detailed questionnaire was then completed. Each general practitioner was asked to complete 10 questionnaires.

Eligibility criteria

For a patient to be eligible for entry to the study an affirmative answer to all of the following questions was required from the patient:

1. Have you had symptoms of 'wheezy' breathlessness or chest tightness at any time during the day or night over the past month?
2. Do you get substantial and immediate relief after using a bronchodilator aerosol or puffer?
3. Have these episodes recurred over a period of more than six months?

Patients with known heart disease or raised blood pressure were excluded.

In addition, the general practitioner was asked to provide further supporting information if available in each case, by completing a further question: Have you demonstrated variability of airflow obstruction in any of the following ways?

(a) Seen the patient in and out of an attack?
(b) Obtained peak expiratory flow rate measurements showing at least 15% variation? If so, please enter a pair of readings.
(c) Obtained peak expiratory flow rate or spirographic record of forced expiratory volume in one second showing at least 15% variation following a bronchodilator aerosol? If so, please enter a pair of readings.

The return of completed eligibility forms for patients not fulfilling the obligatory criteria was also requested to provide some information about excluded patients.

Questionnaire

The questionnaire asked for the doctor's name and the patient's sex, date of birth and weight. Seventeen questions relating to asthma asked for background information on the patient and the treatment prescribed, including: age of onset of wheezy breathlessness, with or without cough; possible trigger factors observed by the patient (including allergens and non-allergic fac-

tors); overall severity of asthma as perceived by the patient and graded as mild, moderate or severe (the frequency of attacks over the past month and loss of time from work over the past year were also noted); smoking history (patients graded as non-smokers, ex-smokers or smokers); and current and previous treatments for asthma and their effectiveness as perceived by the patient. These data were related to the frequency and severity of nocturnal asthma and morning symptoms.

The patient was asked a specific question concerning nocturnal asthma: Do you wake at night with chest tightness, wheeziness or coughing? If nocturnal asthma was reported, the frequency of waking was graded as: every night; less than nightly but at least three nights a week; less than three times a week but at least one night a week; or less than once a week but at least once during past month.

A similar set of questions was used to obtain information about morning symptoms on waking. The length of time over which nocturnal or early morning symptoms had been present was determined.

Questionnaires were returned over a period of one year between 1986 and 1987. This paper reports results relating to nocturnal asthma and early morning symptoms.

Hospital based study

The clinical characteristics and frequency of nocturnal asthma of the patients in this study were compared with the results of a hospital based study carried out in 1971.[1,5]

Statistical analysis

The chi-square test was used to test the independence of the tabulations. For some tables, a linear relationship was hypothesized between two variables; this was tested by fitting a linear model to the data and assessing the residuals for lack of fit. Pearson's product moment correlation coefficient was also used to assess the relation between two variables.

Results

A total of 7956 eligibility forms and 7778 questionnaires were returned by 1199 general practitioners. The mean number of completed questionnaires per general practitioner was 6.5 out of a maximum of 10 and only 49 could not be analysed because they were incomplete. Individual questions were sometimes incomplete so that the numbers in the analyses vary.

Validation of asthma by peak flow records

Fifty five per cent of the 7956 eligibility forms included supportive information of at least one peak expiratory flow rate measurement. Measurements on at least two visits were available for analysis in 2580 patients fulfilling the eligibility criteria and a greater than 15% difference between the two readings was found in 94%. There was a strong inverse correlation between the baseline peak expiratory flow rate and percentage reversibility; 133 (86%) of the 155 patients who showed less than 15% reversibility had normal readings on both occasions.

Reversibility following a bronchodilator aerosol had been tested in 1027 patients fulfilling the eligibility criteria; 87% of these showed a greater than 15% improvement. The inverse correlation with baseline peak expiratory flow rate was again observed, with normal initial values accounting for the absence of reversibility in many cases.

Patient characteristics

Fifty three per cent of the patients were male. The mean age of the patients at the time of the study was 38 years (standard deviation 21 years) with an age range of 3–86 years. Seventy six per cent reported their predominant symptoms as wheeze and cough and 24% as wheeze only. The age of onset of asthma is shown in Table 1. Sixty seven per cent of patients developed their first respiratory symptoms when they were under 30 years of age. The distribution was similar to that of the hospital based population. Smoking history could be assessed from 6793 of the questionnaires: only 19% of patients admitted to smoking, 30% were ex-smokers and 52% non-smokers. Seventy eight per cent of patients stated that their asthma was exacerbated by at least one common allergen and the dominant trigger factor was identified as one or more common allergen in 45% of the population.

Frequency of nocturnal asthma

The frequency of waking at night is shown in Table 2. Seventy three per cent of patients woke with asthma at least once a week,

Table 1. Characteristics of asthmatics in the present study compared with patients referred to hospital.

	Percentage of patients	
	Present study (*n* = 7729)	Hospital population[a] (*n* = 395)
Sex	(*n* = 7699)	(*n* = 395)
Males	*53*	*48*
Females	*47*	*52*
Age at onset (years)	(*n* = 6682)	(*n* = 395)
0–19	*57*	*63*
20–39	*19*	*21*
40–59	*17*	*11*
60+	*7*	*3*
Age at presentation (years)	(*n* = 6980)	(*n* = 395)
0–19	*25*	*35*
20–39	*30*	*35*
40–59	*24*	*21*
60+	*21*	*8*
Smoking status	(*n* = 6793)	(*n* = 395)
Current smoker	*19*	*13*
Non-smoker	*52*	*59*
Ex-smoker	*30*	*28*
Allergic provoking factors	(*n* = 7562)	(*n* = 395)
House dust	*56*	*42*
Pollen	*46*	*34*
Animals	*42*	*31*
Foods	*26*	*17*
Non-allergic provoking factors	(*n* = 7526)	(*n* = 395)
Exercise	*56*	*57*
Emotion	*45*	*47*
Infection	*57*	*50*

[a]References 1 and 5. *n* = total number of patients studied.

Table 2. Frequency of waking at night with asthma among 7661 patients.

	Number (%) of patients
Every night	3022 (*39*)
Less than nightly but at least three times a week	1876 (*24*)
Less than three times but at least once a week	781 (*10*)
Less than once a week but at least once during past month	1501 (*20*)
Not at all	481 (*6*)

63% at least three times a week and 39% woke every night. In the hospital study 74% of patients reported having asthma attacks at night.

Patients' assessment of severity of asthma

Overall, 46% of patients regarded their day and night time asthma as mild, 20% as moderate and 34% as severe. The association between perceived severity of asthma and the frequency of nocturnal waking was highly significant (χ^2 = 1423; df=4, $P<0.001$). However, of 2928 patients waking every night 774 (26%) assessed their asthma as mild. The frequency of attacks over the past month at any time of day or night was also related to the patients' assessment of severity of asthma (χ^2 = 554, df = 4, $P<0.001$). However, of 2895 patients who considered their asthma to be mild, 633 (22%) had asthma at some time during each day or night.

Nocturnal asthma and morning symptoms

The frequency of nocturnal asthma and of morning symptoms were closely related (χ^2 = 1714, $P<0.001$). Of 1254 patients waking every night, 1206 (96%) also had symptoms on waking in the morning at least three times a week. Conversely, of 1632 patients with only occasional nocturnal asthma, 647 (40%) had marked morning symptoms.

Comparison of those with and without nocturnal symptoms

Some of the trigger factors influencing the 7120 asthmatics with nocturnal asthma and the 481 without are illustrated in Figures 1 and 2. The frequency of all types of trigger factors, including individual common allergens, seasonal and non-allergic factors such as damp, cold, smoky atmospheres, exercise, emotion, infection and occupational exposures were all more frequent in those with nocturnal symptoms. However, there was no single trigger factor which was more common in those with nocturnal asthma than in those without.

Association between medication and nocturnal symptoms

The percentage of patients receiving each of the main types of asthma medication, irrespective of drug combinations is shown in Table 3. The frequency of nightly waking varied from 33% to 50% with a trend of increasing frequency of nocturnal asthma in patients receiving additional inhaled corticosteroids, theophyllines and oral steroids compared with those on inhaled bronchodilators alone.

Figure 3 shows a significant association between the number of medications taken by the patients and the percentage of patients waking nightly (χ^2 = 69, df = 4, $P<0.001$). Of the 2928 assessable patients waking every night there was a strong linear correlation between the number of drugs taken and the patient's own assessment of whether their asthma was mild, moderate or severe (r = 0.251, $P<0.001$). Analysis of different drug combinations showed that nine combinations accounted for 76% of the 88 different combinations recorded. Each of the other combinations was taken by less than 2% of the population. The percentage of patients waking nightly on different drug combinations varied from 27% to 54% (Figure 4). The groups of medication shown on Figure 4 account for 78.1% of the combinations prescribed for the whole population. Patients receiving drug combinations commonly used in the UK in more severe asthma (for example, theophyllines and oral corticosteroids) had a higher frequency of nightly waking than those groups of patients on medication more commonly used in mild asthma.

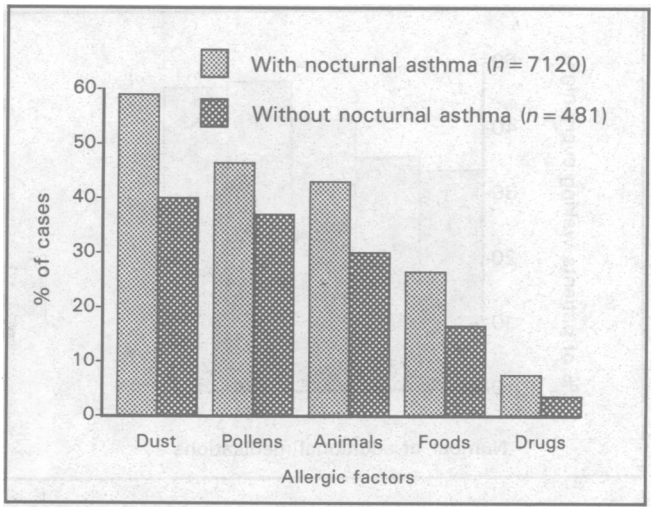

Figure 2. *Allergic trigger factors for those with nocturnal asthma and those without. Nocturnal asthma group versus no nocturnal asthma group, P<0.001 for all factors except drugs where P<0.01. n = total number of patients.*

Table 3. Frequency of waking at night related to treatment (7655 patients assessed).

Treatment	Number (%) of patients receiving treatment[a]	Percentage of patients waking: Every night	<nightly ⩾3 times a week	<3 times a week ⩾once a month	Not at all
Inhaled bronchodilator only	1757 (23)	35	25	33	8
Cromoglycate	1642 (21)	33	25	36	7
Inhaled corticosteroids	3479 (45)	42	24	27	7
Theophyllines	1531 (20)	47	25	23	5
Oral corticosteroids	1014 (13)	50	23	22	5

[a]Number of patients receiving each type of medication in addition to inhaled bronchodilator, irrespective of additional drugs used in combination.

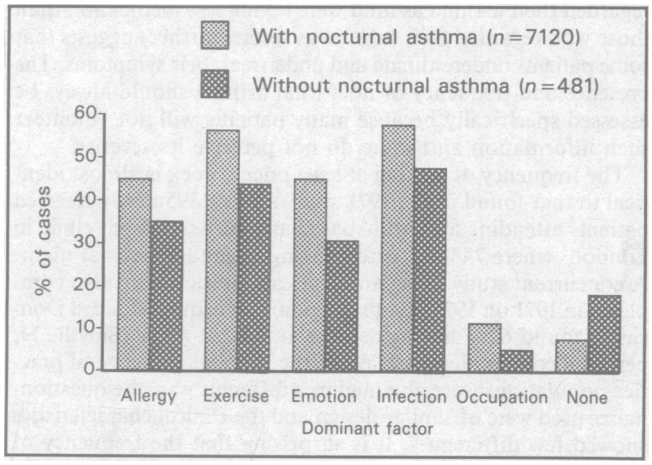

Figure 1. *Dominant trigger factors for those with nocturnal asthma and those without. Nocturnal asthma group versus no nocturnal asthma group, P<0.001 for all factors. n = total number of patients.*

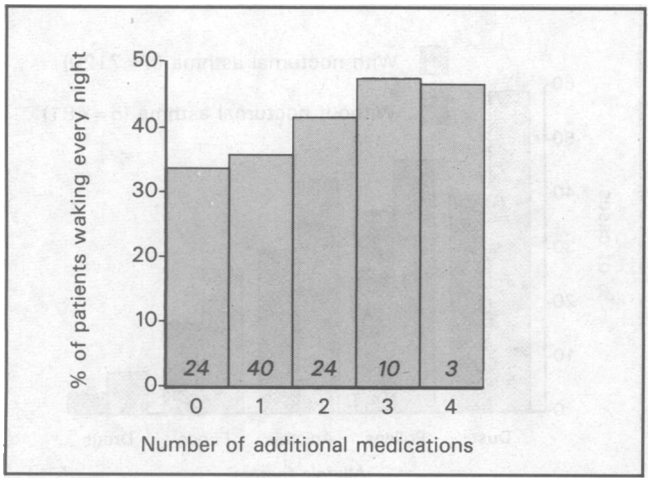

Figure 3. *Percentage of patients with nocturnal asthma waking every night in groups receiving medication in addition to inhaled bronchodilators. Percentage of whole population (n = 7042) shown at base of columns.*

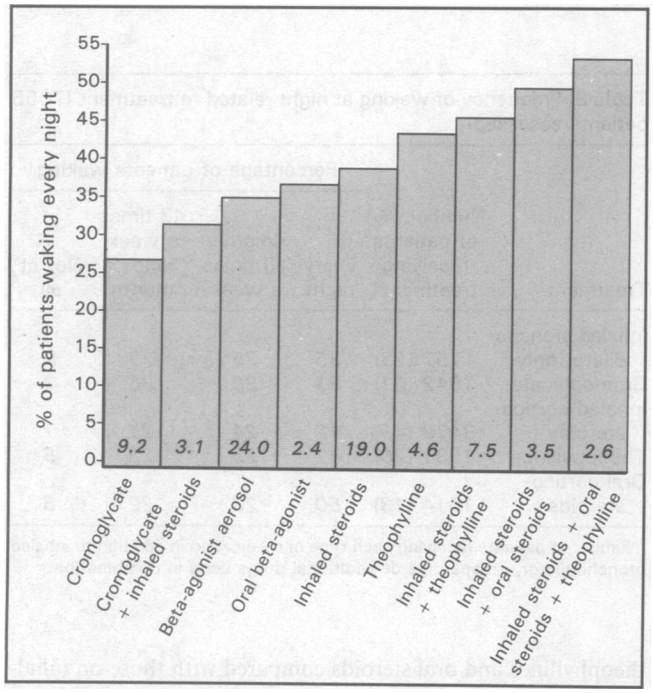

Figure 4. *Percentage of patients with nocturnal asthma waking every night in groups receiving the nine most common combinations of asthma medication in addition to bronchodilator aerosol. Percentage of whole population (n = 7042) shown at base of columns (third column refers to those receiving beta-agonist aerosol only).*

Discussion

Definitions of asthma and case identification always present difficulties and any large scale study based on questionnaires completed at a single interview must be as simple as possible. It was therefore decided to study only those patients for whom general practitioners were prescribing at least a bronchodilator aerosol. This is the most commonly prescribed medication used in the UK for the relief of asthma symptoms[6] and the intention was to select patients for whom at least some attempt was being made to control symptoms with medication. Using a set of eligibility criteria an attempt was made to define a group of patients in whom there was reasonable evidence of variable airflow limitation. Although two peak flow measurements were only available for about a third of the patients, the fact that 94% of these had a greater than 15% variation supports the other evidence reported in this paper that the survey population can reasonably be regarded as asthmatic.

Questionnaires were completed by only a small proportion (5%) of the general practitioners contacted initially. Therefore, the results do not necessarily reflect the frequency of nocturnal symptoms among all asthmatics in the UK. Neither could it be ascertained whether the cooperating physicians selected their more severe asthmatics patients, rather than following the request to complete and return forms on consecutive patients (including those not attending the surgery) for whom a bronchodilator aerosol was prescribed or re-prescribed.

However, it was possible to characterize in some detail the survey population which was found to be very similar to other reported asthma populations with respect to age of onset and trigger factors.[7-9] The relative frequency of different anti-asthma medications used by patients in this study was also similar to the national figures from the Department of Health and Social Security.[6] The percentages of aerosol bronchodilators and cromoglycate prescribed out of all drugs prescribed were very similar to the national figures; the percentage for inhaled corticosteroids was slightly higher and those for theophyllines and oral bronchodilator somewhat lower. However, no gross differences which might suggest a bias towards more severe asthmatics in this study were seen. The fact that 45% of patients in this survey regarded their asthma as mild also suggests that the skew if any, was not substantial. The large number of forms completed by each cooperating practitioner and the close association between severity of asthma and the numbers and types of medication prescribed suggest that the respondents were both interested and well informed about asthma.

The most important finding was that of 7661 asthmatic patients currently being treated by their general practitioners in different parts of the UK, 39% reported waking every night with asthma, 64% at least three times a week and 73% at least once a week. Overall, there was close correlation between the patients' perception of severity of asthma and the frequency of nocturnal symptoms. Nevertheless 26% of patients regarding their asthma as mild, admitted waking every night with asthmatic symptoms. Some nocturnal attacks may indeed be transient and mild, but this finding suggests that some patients are underestimating the seriousness of nocturnal asthma. The fact that among patients waking every night those who nevertheless regarded their asthma as mild were taking less medication than those who regarded their asthma as severe, further suggests that some patients underestimate and undertreat their symptoms. The presence and frequency of nocturnal asthma should always be assessed specifically because many patients will not volunteer such information and some do not perceive its severity.

The frequency of waking at least once a week is almost identical to that found in the 1971 study among 395 newly referred patients attending a hospital based asthma assessment clinic in London[1] where 74% reported having asthma attacks at night. A concurrent study using an identical questionnaire also completed in 1971 on 197 patients attending an asthma clinic in Doncaster found 62% having asthma attacks at night (Smyllie H, personal communication). While the hospital and general practice populations were obtained in a different way, the questionnaires used were of similar design and the clinical characteristics showed few differences. It is surprising that the frequency of nocturnal waking in the current survey was as high as in the hospital study conducted 15 years earlier; particularly as inhaled corticosteroids, prescribed for 48% of patients in the current study, were not available in 1971.

The information collected on medication was restricted to the number and types of drugs and did not include the amount of each drug prescribed, the amount that the patient took or the effectiveness of the patient's aerosol technique. Such details would have added considerably to the completion time for each questionnaire and the reliability of answers to such questions could not easily be assessed. Nevertheless the data indicated that the patients were receiving careful attention from their doctors and were being given more drugs in a reasonable way as their symptoms increased in severity. It is therefore unreasonable to assume that patients were failing to take their medication at a time when they perceived their asthma to be severe and had been given a greater number of drugs by their doctors. It appears that medication was being increased as the frequency of nocturnal waking rose, but in spite of this nocturnal symptoms were frequently not controlled. This observation does not mean that medication in individual patients is not influencing the frequency or severity of night time symptoms. Neither is it incompatible with the drug trials which have demonstrated some improvements in nocturnal symptoms in some patients.[10-12] The conclusion from this study, based on substantial numbers of patients treated routinely outside the rigorous conditions of drug evaluation studies, is that medication as currently used is not adequately controlling nocturnal symptoms in many patients. The data suggest that even with optimal prescribing and patient compliance the drugs that are currently available do not eliminate nocturnal asthma. More research on the causes and mechanisms of nocturnal asthma and new approaches to therapy are needed.

Clearly, in the meantime it is important to optimize control with available drugs. This will involve rigorous education of both patients and doctors on the use of drugs and better ways to monitor compliance. Anything that the pharmaceutical industry can do to improve the convenience of current medication will also help.

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