

Original article

Unawareness and undertreatment of asthma: follow-up in a different geographic area in Denmark

Background: Early detection and treatment of asthma is important to minimize morbidity and healthcare costs. The objective of this study was to investigate asthma awareness and management in a western society.

Methods: In a random sample of 10 400 subjects aged 14–44 years, 686 (6.6%) reported symptoms of asthma in a standardized screening questionnaire. All 686 were evaluated by respiratory specialists and diagnosed by history, symptoms, lung function tests, bronchial challenges and allergy testing. Of these 686 participants, 69 (10%) had asthma alone, 205 (30%) had rhinitis alone and 217 (32%) had both asthma and rhinitis; 195 (28%) had nonasthmatic respiratory reports.

Results: Awareness of asthma was found among 163 (57%) of the 286 asthmatics, and 204 (95%) had doctor-diagnosed rhinitis as well. In a multivariate regression analysis, comorbidity with rhinitis ($\beta = 0.489$, $P < 0.001$), smoking ($\beta = -0.116$, $P < 0.01$), doctor-diagnosed bronchitis ($\beta = 0.086$, $P < 0.05$), and earlier emergency visits at hospital ($\beta = 0.147$, $P < 0.001$) was significantly associated with awareness. A difference in awareness was found between those who had asthma and rhinitis (62.2%) and those who had asthma alone (40.6%) ($P < 0.01$). Inhaled corticosteroids (ICS) were used by 27% of those with asthma, including 12% who used both ICS and long-acting beta-agonist.

Conclusions: More than half of the persons with asthma were aware of their disorder; and the awareness was more likely in those with comorbidity of rhinitis. In general, asthma management was inadequate.

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Key words: asthma; unawareness; underdiagnose; undertreatment.

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Accepted for publication 11 January 2009

Asthma is a chronic respiratory condition characterized by periods of relative stability and episodes of deterioration. Early diagnosis of asthma and good asthma-management minimizes development of chronic illness (1–3). However, delays arising from both the patient and the physician can lead to mismanagement of asthma (4–6). Further, Bousquet et al. (7) showed a substantial impact on morbidity in persons with both asthma and rhinitis because more attacks of asthma occurred resulting in a greater need for emergency room visits and systemic steroid.

Good asthma control is possible, allowing patients to experience few symptoms, unrestricted physical activity (8) and better quality of life (9); nevertheless, mismanagement occurs frequently (10). Seemingly, this is because patients are prescribed reliever therapy instead of inhaled corticosteroid (ICS) in both acute situations and day-to-day treatment (11, 12). However, it is possible that the recent introduction of fixed combination treatment including both ICS and long-acting beta-agonist (LABA) has increased the number of well-controlled patients (13). These new treatment possibilities could lead to a higher degree of asthma control over a period of time.

We repeated an examination of awareness of asthma in a cohort living in Denmark using the same technique as that used in the initial cohort survey approximately 5 years earlier. In the elapsed period between the studies, awareness of asthma diagnostics and asthma management were the focus of general practitioner (GP) education and further documentation (9, 14). Moreover, further education was given to our first cohort at a follow-up study in 2004 (15). It is unknown whether these initiatives influence general asthma management in developed countries, where the majority of asthmatics are cared for in primary care.

The aim of this study was to investigate the awareness of asthma, in order to draw comparisons between this and a former survey using the same techniques.

Material and methods

Screening population

From late 2005 to early 2007, a random population sample of 10 400 subjects aged 14–44 years and living in Denmark was drawn from the civil registration list. We selected this age group to

minimize entry of patients with respiratory symptoms pertaining to chronic obstructive pulmonary disease (COPD) rather than asthma, as COPD primarily increases from the age of 55 years. The population was drawn equally from urban and rural areas in northern Denmark. All subjects received a letter with a validated self-administered asthma and rhinitis screening questionnaire of '20 questions adopted from the ACAAI screening program' (16). All subjects were asked to complete the questionnaire over an Internet set-up. The response rate was 47%: 2647 respondents were symptom-free and 2250 respondents had respiratory and nasal symptoms. Those who had at least two positive responses to the questionnaire were invited to take part in this survey; those not fulfilling these inclusion criteria were ineligible for the study.

Design

On the first visit to the clinic, all subjects completed several self-administered questionnaires before being clinically examined. Lung function was measured and blood was drawn for specific IgE test. This was followed by a bronchial provocation test and a reversibility test with inhaled beta₂-agonist. After completion of the questionnaires and tests, participants underwent a clinical examination, and their medical history was gathered by a respiratory physician through a questionnaire; 72% of the participants were guided through the questionnaire by the same senior respiratory specialist. Medical history data and the results of the clinical tests were thoroughly reviewed and registered by the first author (Vibeke Backer).

Study population

In total, 2250 persons (21%) reported lower or upper respiratory symptoms suggestive of asthma or rhinitis, of whom 686 participants accepted the study invitation and were examined.

Exclusion criteria

Patients were excluded if they had respiratory illness other than asthma (e.g. sarcoidosis). Furthermore, patients with asymptomatic airway hyperresponsiveness (AHR) (0.3%), asymptomatic atopy (1.5%), signs and symptoms of COPD (1.0%) and nonasthmatic respiratory symptoms among current smokers (10.8%) and nonsmokers (14.9%), were excluded.

Medical history

All participants completed several self-administered questionnaires before clinical and physical tests. Subjects were asked about respiratory and allergic symptoms [within the preceding 4 weeks and at any time (ever asthma)], use of medication, hospital referrals and GP or specialist visits. The interview questions about asthma were adopted from studies by the American Thoracic Society, Division of Lung Disease of the National Heart, Lung and Blood Institute (17). The severity of asthma (mild, mild persistent, moderate or severe) was classified according to the 2004 Global initiative for asthma (GINA) guidelines, based only on symptom frequency without up-grading with the intake of ICS (18), and asthma control was assessed according to the definition in the 2006 GINA guidelines (8). Details were collected on education, socioeconomic aspects, place of residence and lifetime consumption of tobacco in pack-years [tobacco consumption (g/day)/20 × duration of smoking (years)]. Height and weight were measured in all participants and body mass index was calculated [weight

(kg)/height (m)²]. Finally, Place of Residence was divided into city (> 100 000 inhabitants), town (< 15 000 inhabitants) or countryside (farmland).

Pulmonary function test and methacholine challenge test

Spirometry was performed on a 7-l dry wedge spirometer (Vitalograph®) in accordance with the European Respiratory Society (ERS), and the percentage of predicted normal values of forced expiratory volume in 1 s (FEV₁) (FEV₁ %pred) and forced vital capacity (FVC) (FVC %pred) and the FEV₁/FVC ratio were calculated (19). Airway responsiveness to inhaled methacholine was measured according to the method of Yan et al. (20) in all patients with FEV₁ > 70% predicted. The dose resulting in a 20% fall in FEV₁ (PD₂₀) was calculated, and the ratio dose-response (RDR) was calculated as the decline in FEV₁ from inhaled saline divided by the highest dose of methacholine administered (21). A constant of 5 was added to all RDR to eliminate negative and zero values. Logarithmic transformed values of RDR were used for analysis. Measurement of FEV₁ was repeated 15 min after administration of 2 mg terbutaline in those with FEV₁ < 70% or 15 min after the last inhalation of methacholine in those with either symptoms or a significant decrease in FEV₁ (i.e. 20%).

Specific IgE

Specific IgE to inhalant allergens was measured and radioallergo-sorbent test class 2 or more was considered a positive test, indicating atopy.

Diagnosis of asthma

The diagnosis of asthma was based on the presence of symptoms and signs of reversible airway responsiveness, such as AHR to inhaled methacholine < 8.0 µmol or at least 250 ml increase in FEV₁ after bronchodilator challenge. Furthermore, subjects were defined as having asthma if they had a history of symptoms and a daily use of systemic steroid, inhaled steroid, fixed combination of ICS and LABA or classical exercise-induced asthma symptoms and use of inhaled beta₂-agonist when needed. Additionally, subjects with seasonal symptoms of asthma, tested outside season, were included as having asthma if they reported recurrent seasonal symptoms and a relevant atopy or a history of rhinitis. Lastly, nonsmokers with respiratory symptoms and signs of mild AHR with a percentage fall in FEV₁ of 10% or more after inhalation of 8.0 µmol methacholine were classified as mild asthmatics.

Awareness of asthma

All subjects were asked: 'Have you ever been told by a doctor that you suffer from asthma?' or 'As an adult, have you been treated with asthmatic medication by your own doctor'. If the answer was 'yes' to one of the questions, the subjects were classified as being aware of asthma. Subjects who were not aware of having asthma, but who were diagnosed with asthma in this survey were classified as unaware asthmatics.

Diagnosis and awareness of rhinitis

Subjects with rhinitis were defined by symptoms of rhinitis, such as runny nose; blocked nose; sneezing; itchy nose, mouth, ear or eyes; red and watering eyes; reduced sense of smell or symptoms caused

by allergen exposure. Allergic rhinitis was defined as rhinitis asthma and a positive allergy test (specific IgE).

Subjects were asked, 'Have you ever been told by a doctor that you suffer from rhinitis or allergy?' Patients unaware of having rhinitis and who were diagnosed with rhinitis in this survey were classified as undiagnosed rhinitis.

Analysis

All data were entered in the database by one person, and afterwards 10% of all patient data were proofread. Quality control was then conducted by an experienced researcher on all outliers within the entire number of variables.

The data were analysed with the statistical pack 15.0 spss for Windows (SPSS, Copenhagen, Denmark). Incidence rates were calculated for the entire group and differences were tested by chi-squared analysis. Further, differences in mean ($\pm$ SD) values between participants with and without respiratory symptoms were tested by parametric analysis (Student's *t*-test). All included variables were examined in a univariate analysis with awareness as the dependent variable. In the case of a significant relationship, they were entered in a linear regression analysis with backward elimination of all nonsignificant parameters, after which a final regression analysis was performed. Lastly, an odds ratio analysis was applied in the case of dichotomy variables. A *P*-value < 0.05 was considered significant. The studies were approved by the local ethics committee of Aalborg, Denmark. All participants received information in both oral and written forms and gave their consent in writing before enrolment.

Results

The basic data of the 686 participants, 57% of them being female subjects, are shown in Table 1. Of those participating because of reports of respiratory symptoms, 69 (10%) had asthma alone, 205 (30%) rhinitis alone and 217 (32%) had both asthma and rhinitis. Nonasthmatics were excluded from further analysis.

Of the subjects excluded, eight (7.8%) of the 102 were nonsmokers, five (6.8%) of the 74 were smokers and one (10%) of the atopic subjects had GP-diagnosed asthma. We were unable to document this.

Awareness of asthma before the survey in the group diagnosed with asthma in this survey was found among 163 (57%) of the 286 asthmatics (Table 2), with a significant difference in awareness between those who had comorbidity of asthma and rhinitis (62.2%) compared with those having asthma alone (40.6%) (*P* < 0.01). As many as 204 (95%) of those with doctor-diagnosed allergic rhinitis were classified as having rhinitis prior to the survey.

In a multivariate regression analysis, factors conventionally connected with respiratory illness, such as comorbidity with rhinitis (β = 0.489, *P* < 0.001), smoking (β = -0.116, *P* < 0.01), doctor-diagnosed bronchitis (β = 0.086, *P* < 0.05) and earlier emergency visits at hospital (β = 0.147, *P* < 0.001) were significantly associated with awareness. The odds ratio of the factors of importance was as follows: rhinitis OR of 2.4 (95% CI: 1.4–4.2), smoking OR of 0.47 (95% CI: 0.29–0.76), symptoms of acute bronchitis (cough, phlegm, with possible fever) OR of 3.08 (95% CI: 0.64–14.7) and emergency visit OR of 7.9 (95% CI: 1.99–31.08).

Uncontrolled asthma according to the 2006 GINA definition (8) was found among 61% of the participants in this survey. For change in asthma awareness over a period of time, this data showed a different distribution compared with the earlier findings by the same study group regarding asthma awareness, asthma severity and asthma treatment (Table 3). In general, subjects were under-treated, as 49% had no prescribed asthma medication at the time of enrolment; ICS was used by 26% of those from the rural area and as many as 12% used fixed combination therapy.

Table 1. Basic parameters of the entire population in clinical examination study

	Asthma	Asthma and rhinitis	Rhinitis	Neither	All	<i>P</i> -value
Number	69	217	205	195	686	
Gender (male)	21 (40%)	107 (49%)	92 (45%)	78 (40%)	298 (43%)	<0.05
Age (years)	31.57 (9)	31.21 (9)	32.47 (9)	33.53 (9)	32.28 (9)	<0.05
BMI	26.64 (6)	25.69 (5)	25.02 (5)	25.13 (5)	25.43 (5)	NS
FEV ₁ (l)	3.52 (0.8)	3.62 (0.8)	3.78 (0.8)	3.70 (0.7)	3.68 (0.8)	<0.05
FVC (l)	4.38 (1.0)	4.55 (1.0)	4.59 (1.0)	4.50 (1.0)	4.53 (1.0)	NS
FEV ₁ /FVC ratio	81% (7)	80% (8)	83% (6)	82% (7)	82% (7)	<0.001
FEV ₁ %pred	94 (13)	93 (14)	99 (11)	99 (11)	96 (13)	<0.001
FVC %pred	96 (12)	95 (12)	98 (11)	98 (12)	97 (12)	NS
Median GINA score	2	2	0	0	1	<0.001
% atopy	7 (10)	155 (74)	109 (54)	10 (5)	281 (42)	<0.001
Log-RDR	0.49 (0.5)	0.55 (0.5)	-0.03 (0.3)	-0.07 (0.3)	0.19 (0.5)	<0.001
Smokers (%)	49	33	41	44	40	<0.001
Mean pack years	2.78 (6.0)	4.30 (7.0)	3.76 (6.9)	5.70 (8.7)	4.05 (7.27)	<0.01
Pack years	8.3 (7.9)	8.9 (7.8)	9.2 (8.3)	13.0 (8.8)	10.1 (8.5)	<0.01
Among smokers						

BMI, body mass index; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; GINA, Global initiative for asthma; RDR, ratio dose-response; NS, nonsignificant.

Table 2. Basic parameters of the asthma population entering this study

	Asthma	Asthma and rhinitis	All	P-value
Number	69	217	286	
FEV ₁	3.5 (0.8)	3.6 (0.8)	3.6 (0.8)	NS
FEV ₁ %pred	94 (13)	93 (14)	93 (13)	NS
FEV ₁ /FVC%	81 (7)	80 (8)	80 (8)	NS
Log-RDR	0.49 (0.5)	0.55 (0.5)	0.54 (0.5)	NS

FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; RDR, ratio dose-response; NS, nonsignificant.

Table 3. Asthma and variables of importance in this survey and the former survey performed year 2000 in the Capital city of Copenhagen

	The former survey (20)	This New cohort	P-value
No. asthmatics	493	286	
Awareness of asthma	43%	57%	<0.01
Severity*			
GINA 1	31%	29%	NS
GINA 2	20%	25%	NS
GINA 3	24%	29%	NS
GINA 4	25%	7%	<0.001
Treatment			
0	67%	49%	<0.01
SABA	13%	20%	NS
LABA	2%	1%	NS
ICS	18%	26%	NS
Systemic steroid	0%	3%	NS
Fixed combination	2%	12%	<0.01

Awareness of asthma is defined as 'doctor's diagnosis of asthma' and/or current anti-asthmatic treatment.

GINA, Global initiative for asthma; SABA, short-acting beta-agonist; LABA, long-acting beta-agonist; ICS, inhaled corticosteroid, including combination therapy; NS, non-significant.

*Severity defined on symptoms and level of FEV₁, independent of anti-asthmatic treatment.

Discussion

Awareness of asthma was found among only 57% of the participating asthmatics, and asthma treatment was managed unsatisfactorily. In this study, comorbidity of rhinitis, symptoms diagnosed as acute bronchitis and emergency visits because of respiratory symptoms were the most important factors increasing the awareness of asthma, whereas smoking reduced the awareness. These findings of this survey were more positive than similar findings generated 5 years earlier (22) where almost 70% of participants were unaware of having asthma.

A limitation of this and former study could be a low participation rate, as asthma was documented in only 286 (2.8%) of the entire population. The frequency of adult asthma in Denmark is 5%, indicating that this population concerning asthma is likely to underestimate the problem. This under-diagnosis, rather than over-diagnosis of asthma (23–25) could have been reduced if all participants had been seen more than once (both inside and outside season), had performed mannitol provocation test

(26), sputum eosinophils (27) and peak-flow day-to-day variability (28) and eNO (29) had been measured. Although some misclassification was possible, the same mistakes were made by the same research group in the former study 5 years earlier. The increase in asthma awareness therefore seems true.

Unawareness of asthma is a universal problem (4, 30, 31) leading to reduced quality of life (9, 14, 32). We had examined a similar population 4 years before this study – the difference being that the earlier study was in a more densely populated urban area (750.000 inhabitants vs 300.000) and found very unsatisfactory diagnostic findings and very inconsistent asthma management (22). Although findings were more severe in the first study, unawareness of asthma remains a societal problem, one that is probably accompanied by low physical activity and weight gain eventually leading to diabetes. There is, therefore, good reason to increase the efforts directed towards diagnosing asthma in adolescents and young adults. Many different factors are of significant importance for both undiagnosed cases and mismanagement of asthma, some of which are related to an urban lifestyle rather than a more rural lifestyle (14). In larger cities, there is less understanding and treatment of many chronic diseases because of abuse of drugs, tobacco or alcohol and limited physical activity (33). These findings add weight to the evidence of smoking blurring the awareness of asthma. Among young adults, smoking might be regarded as the cause of respiratory symptoms. However, patients diagnosed with acute bronchitis were more often diagnosed with comorbid asthma. An important finding in this survey was that among patients with rhinitis, GPs had more often diagnosed asthma than in those without rhinitis. This might be the key to increasing general awareness of asthma as 60% of those with rhinitis have comorbidity with asthma. Furthermore, those with both illnesses have more severe and variable asthma, needing more attention and treatment; consequently, symptoms of exacerbation might lead them to visit their GP more frequently (7).

Well-controlled asthma was found in one-third of the asthmatics; indicating that there is still room for improvement in asthma management. In the period between the first and the second studies, fixed combination with ICS and LABA was introduced. This accounts for some of the differences between the first (2%) and the second survey (12%) and might explain the increased degree of well-controlled and partly controlled asthma, with fewer respiratory symptoms in general being seen in this survey compared with the survey from 2000 (1, 3), although these minor differences are not sufficient to explain all the differences between the two treatment regimes.

In conclusion, the awareness of asthma was relatively satisfactory; undertreatment remained a problem, although less uncontrolled asthma was seen. These findings could be partly explained by the more common

use of combined treatment with ICS and LABA in 2005 than in 2000. The presence of rhinitis could be the key to increasing awareness of asthma in the future.

Conflicts of interest

Dr Vibeke Backer wrote both this article and the 2005 protocol. She examined the majority of patients (70%) and undertook all the data management and the analysis. Dr Vibeke Backer has no conflict of interest in this article. Dr Henrik Harving received an unrestricted

grant from AstraZeneca, which was used for remuneration of the laboratory technicians and project nurses. The grant also covered the costs of Vibeke Backer's weekly flight tickets between Copenhagen and Ålborg. Dr Henrik Harving has no conflict of interest. Dr Hendrik Nolte was employed as chief physician at Bispebjerg hospital during this study. Since then he has changed employment and is now working at Shering Plough in New York. Dr Hendrik Nolte has no conflict of interest in this article. Dr Lars Pedersen drew the patients from the CPR register in order to secure equal distribution of patients in the sample. Nanna Dam, BSc Pharm., is employed by AstraZeneca and holds stock in AstraZeneca and GlaxoSmithsKline.

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