

Original article

The diagnosis of asthma using a self-questionnaire in those suffering from allergic rhinitis: a pharmaco-epidemiological survey in everyday practice in France

Background: All recent guidelines recommend a search for asthma utilizing both specific interrogation and pulmonary function tests in patients suffering from allergic rhinitis. Although the mandatory place of spirometry has not been confirmed, a self-questionnaire containing nine specific questions on asthma symptoms in different daily life situations was found to be capable of discriminating asthmatics from nonasthmatics in a rhinitic population.

Objective: We addressed the questions of prevalence of asthma using a validated self-questionnaire and what might be the risk factors of being asthmatic according to that specific self-questionnaire.

Methods: Between April 2003 and September 2004, nearly 12 000 rhinitis patients were enrolled by more than 2300 physicians (78% general practitioners, 22% ear nose and throat specialists). Patients were consulting for an exacerbation of chronic rhinitis and did not have a previous diagnosis of asthma. Both doctors and patients filled out a specific questionnaire on rhinitis and asthma.

Results: Almost 30% of the patients had at least three positive answers to the self-questionnaire and could possibly be considered as asthmatics. We found five independent clinical risk factors for having ≥ 3 positive answers to the self-questionnaire. Severity of rhinitis (moderate-severe *vs* mild, OR = 1.84; 95% CI = 1.68–2.00), diagnosis of allergy (yes *vs* no) (OR = 1.86; 95% CI = 1.68–2.00), body mass index (≤ 18.5 *vs* > 30) (OR = 0.51; 95% CI = 0.39–0.66), type of rhinitis (persistent *vs* intermittent) (OR = 1.25; 95% CI = 1.15–1.37), and patient age (≤ 25 *vs* > 47) (OR = 0.73; 95% CI = 0.65–0.80).

Conclusion: Asthma symptoms are frequent in rhinitics without a prior history of asthma. Several variables were shown to be predictive of asthma in these patients.

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Studies have clearly established that allergic rhinitis is a risk factor for asthma (1–3). As many epidemiological studies have shown that asthma and rhinitis co-exist frequently, it is necessary to search for asthma in patients suffering from allergic rhinitis, especially as some symptoms of asthma and rhinitis overlap (3). According to all available guidelines, such a search should include both specific interrogation and pulmonary function measurements, though the contribution and obligatory or non-obligatory nature of the latter have never been specified (4, 5). Moreover, general practitioners (GPs) and ear nose and throat specialists (ENTs) who do not generally possess suitable equipment for measuring pulmonary function see the majority of patients affected. We are

therefore facing a gap between guidelines and their application in daily life.

We were not convinced by the literature indicating that pulmonary function tests in the diagnosis of asthma were mandatory and validated in allergic rhinitis patients. We therefore designed a pilot study and the results suggested that a self-questionnaire was capable of discriminating asthmatics from nonasthmatics in rhinitic patients with no prior diagnosis of asthma and that pulmonary function tests did not add much (6). Having set a validated and easy-to-use screening tool, we then designed two large surveys in GPs and ENTs in order to evaluate the prevalence of asthma using this self-questionnaire in a population of about 12 000 rhinitics,

known and treated for their rhinitis but again with no prior diagnosis of asthma.

Material and methods

Structure of questionnaires

The questionnaire filled out by patients involved a description of the following:

- 1 the patient's characteristics: age, sex, height, weight;
- 2 the clinical history of their rhinitis: date of first symptoms, frequency and intensity of symptoms (related to the ARIA classification) (3);
- 3 the presence of sinusitis, conjunctivitis; and
- 4 information concerning allergy: to what they are allergic, how was the diagnosis set.

The patients then filled out the Venables et al. (7) self-questionnaire described in detail elsewhere (6, 7). This questionnaire includes nine questions which assess the last 4 weeks for the presence or absence of asthma symptoms (cough, wheeze, chest tightness, difficulty with breathing) at different periods of time and in different situations all known to be relevant to asthma (e.g. running or climbing stairs at speed, sleeping, in the morning, whilst in a smoky room or dusty place). The questionnaire was translated into French.

Physicians participating in the survey also filled out a questionnaire on their professional practice, their prescribing of additional tests, referral to other doctors and their drug prescriptions concerning the patient they were including in the present study. This questionnaire, processed strictly anonymously, was essential in determining the characteristics of physicians who replied to this survey and in assessing the representative capacity of the sample of physicians questioned.

Collection of questionnaires

The randomly selected physicians who agreed to participate in this survey were requested to fill out a questionnaire for the first six consecutive patients who came to their consultation for an exacerbation of chronic rhinitis during the period from April 2003 to September 2004. They gave them an anonymous self-questionnaire to be returned directly to the evaluation center. Patients with known asthma or patients having had asthma medication in the past, smoking more than five packs per year, or having nasal polyposis or any severe concomitant disease were not eligible for enrollment in the survey.

Rhinitis was defined in patients showing two of three symptoms: sneezing/nasal itching – nasal obstruction – rhinorrhea for more than 1 year.

This observational study does not require any ethical committee approval according to our national recommendations.

Statistical analysis

The files thus collected were forwarded to the Medical Biostatistics Department of the Institut Universitaire de Recherche Clinique of the University of Montpellier, where they were processed and analyzed using SAS software version 6.12. The descriptive study of the two databases (GPs, ENTs) used conventional parameters, means and standard deviations for quantitative variables, histograms and percentages for qualitative variables. An evaluation of the influence of the different areas of the self-questionnaire was performed by

means of a chi-square test and analysis of variance (ANOVA). The level of significance was set with an alpha risk = 0.05.

To appreciate and stratify any independent clinical risk factors linked to multiple (≥ 3 and ≥ 5) answers in the asthma self-questionnaire, a multivariate analysis was carried out using a logistic regression model with a stepwise selection (8). Although the patients recruited by the GPs and those recruited by the ENTs may be different in several ways, they were comparable in terms of the number of 'yes' answers on the self-questionnaires. Both the GP and ENT databases were combined. The variables included in the multiple regression model were group (patients recruited by GPs and patients recruited by ENTs), body mass index, severity of rhinitis, allergy diagnosis, type of rhinitis and age. This enabled us to adjust the odds ratio (OR) and to establish 95% CI. The adequacy of the model was checked by the percentage of concordance between predicted probabilities and observed responses and by the Hosmer–Lemeshow test.

Results

Patient description

In total, 11 994 patients, aged 37.1 ± 15.3 years, were seen for rhinitis under conditions which complied with the study protocol (Table 1). It also involved the participation of more than 2300 physicians (78% GPs, 22% ENTs). Six hundred fifty-two patients were excluded as they did not fulfill inclusion criteria. Amongst the included patients, 49.7% were female. They had been suffering from rhinitis for an average of 6.0 years (± 7.9). Patients seen by ENTs recalled sinusitis (27.6%) more often than those seen by GPs (12.8%, $P < 0.05$). Patients were mostly moderate-severe persistent rhinitics but all

Table 1. Patient characteristics

Items	GPs	ENTs	P
Included patients	9403	2591	
Excluded patients	351	301	
Mean age, years (SD)	36.7 (15.2)	38.6 (15.8)	0.0001
Male vs female ratio	1.02	0.99	0.54
Co-morbid associations (%)	33.6	36.7	0.0001
Sinusitis	12.8	27.6	0.0001
Conjunctivitis	25.9	16.0	0.0001
ARIA ³ type of rhinitis (%)			0.0001
Mild intermittent	35.8	22.3	
Moderate-severe intermittent	16.7	14.3	
Mild persistent	9.8	19.4	
Moderate-severe persistent	37.7	44.0	
Patients claiming to be allergic (%)	80.1	54.4	0.0001
To HDM	42.5	71.8	0.0001
To pollens	83.7	57.2	0.0001
To fungi	28.2	33.0	0.0003
Confirmed by any allergy test	60.2	81.4	0.0001
Confirmed by skin prick tests	76.2	73.7	0.08
Confirmed by Phadiatop TM (Pharmacia, Uppsala, Sweden)	41.3	43.2	0.21
Confirmed by specific IgE assays	35.7	28.8	0.0001

ARIA, Allergic Rhinitis and its Impact on Asthma classification of rhinitis (3); HDM, house dust mite; SD, standard deviation.

four ARIA groups of rhinitis were represented. When rhinitis was intermittent, there were less (33.0%) moderate to severe forms than when rhinitis was persistent (76.7%, $P < 0.001$). Although a proof for an allergen sensitization was not an inclusion criteria, 86.1% of the patients seen by GPs claimed to be allergic (mostly to house dust mites and pollens) compared with 54.4% of the patients seen by ENTs. Amongst them, 60.2% and 81.3%, respectively, had a confirmation of allergen sensitization in the past, either by allergen skin prick tests or by specific IgE measurements.

Diagnostic and therapeutic management of current rhinitis

A few additional tests were prescribed during the consultation, significantly more by ENTs (29.1%) than by GPs (10.3%, $P < 0.0001$) (Table 2). Referral to a specialist (chest or ENT physician for GPs and chest physician for ENTs) was more frequent for ENTs (29.3%) than for GPs (16%, $P < 0.0001$). Prescribed drugs were preferentially oral antihistamines (77.4% for GPs and 60.7% for ENTs) and nasal glucocorticosteroids (88.7% for GPs and 83.2% for ENTs). Amongst other drugs, oral corticosteroids were frequently prescribed (5.6% for GPs and 10% for ENTs), followed by nasal vasoconstrictors (1.7% for GPs and 5% for ENTs). A few anti-asthmatic drugs were also prescribed in a minority of patients.

Results of the asthma self-questionnaire

More than 55% of the rhinitis patients in both doctor groups had had at least one asthmatic symptom during the 4 weeks prior to the visit (Table 3). Almost 30% had at least three positive answers to the nine questions of the self-questionnaire and 11–15% had more than five

Table 3. Results of the asthma self-questionnaire

Items	GPs	ENTs	<i>P</i>
'Yes' answer to (%)			
At least one question	56.1	58.8	
At least three questions	31.8	29.3	0.015
At least five questions	15.1	11.0	0.0001
'Yes' answer to at least one question in the following domains (%)			
When running or climbing stairs	42.7	44.1	0.2
When sleeping	23.7	24.7	0.3
In the morning	24.5	24.4	0.9
Whilst in a smoky room or dusty place	34.4	29.7	0.0001
Chest tightness or difficulty of breathing	39.1	43.2	0.0002
Cough	33.0	35.1	0.04
Wheeze	40.0	36.2	0.0005

positive answers. Question 1, which inquires about cough while climbing stairs was the most frequently positive, followed by question 9 (wheeze whilst in a dusty place) and question 3 (chest tightness while climbing stairs). Globally, the most frequent asthma symptoms were chest tightness or difficulty in breathing, followed by wheeze and cough. The most frequent asthma-related situations were running or climbing stairs, followed by when sleeping and in the morning. Patients with >3 'yes' answers to the self-questionnaire were more often ($P < 0.0001$) prescribed additional tests (24.5%), more frequently ($P < 0.0001$) referred to a specialist (37.9%) and more often ($P < 0.0001$) prescribed an inhaled β_2 -agonist (17.7%) or an inhaled corticosteroid (18.6%) than patients with <3 'yes' replies (9.7%, 10.1%, 1.5%, and 4.1%, respectively).

A multivariate analysis was carried out using a logistic regression model to look for and classify independent clinical risk factors linked to multiple (≥ 3 and ≥ 5) answers to the asthma self-questionnaire. The analysis found five parameters linked to asthma (Table 4) – severity of rhinitis (moderate-severe *vs* mild), diagnosis of allergy (yes *vs* no), body mass index (split into the four WHO classes), type of rhinitis (persistent *vs* intermittent), and patient age (split in quartiles).

Discussion

In a recent pilot study (6) we validated a new, straightforward and costless approach to determine asthma in patients suffering from allergic rhinitis and unable to benefit from a diagnosis with pulmonary function tests. The self-questionnaire we used was developed by Venables et al. (7) and validated in 178 nonasthmatics and 33 asthmatics. At the threshold of three or more positive responses to the nine questions assessing the last 4 weeks for the presence or absence of asthma symptoms (cough, wheeze, chest tightness, difficulty with breathing) in different situations known to be relevant to asthma (e.g.

Table 2. Diagnostic and therapeutic management of current rhinitis

Items	GPs	ENTs	<i>P</i>
Prescription of additional tests (%)			
Any test	10.3	29.1	0.0001
Spirometry	46.1	12.8	0.0001
Chest X-ray	17.1	5.0	0.0001
Sinus X-ray	9.1	19.8	0.0001
Allergy skin tests	6.8	0.8	0.0001
Specific IgE assays	12.7	10.5	0.17
Phadiatop TM	10.1	27.2	0.0001
Referral to a (other) specialist (%)*	16.0	29.2	0.0001
Prescription of (%)			
Oral antihistamines	77.4	60.7	0.0001
Nasal corticosteroids	88.7	83.2	0.0001
Oral corticosteroids	5.6	10.0	0.0001
Nasal vasoconstrictors	1.7	5.0	0.0001
Inhaled corticosteroids	9.2	6.6	0.0001
Inhaled β_2 -agonists	8.0	1.3	0.0001

*Chest or ENT physician for GPs and chest physician for ENTs

Table 4. Predictors of asthma in patients without any prior history of asthma – results of the logistic regression

Variables	Unadjusted ORs	95% CI	Adjusted ORs	95% CI
At least 3 'yes' answers				
Severity of rhinitis (moderate-severe vs mild)	2.16	1.99–2.34	1.84	1.68–2.00
Diagnosis of allergy (yes vs no)	2.00	1.82–2.22	1.86	1.68–2.00
BMI				
≤ 18.5 vs >30	0.44	0.34–0.57	0.51	0.39–0.66
18.5 < ≤ 25 vs >30	0.50	0.41–0.60	0.54	0.44–0.66
25 < ≤ 30 vs >30	0.70	0.57–0.86	0.71	0.57–0.88
Type of rhinitis (persistent vs intermittent)	1.67	1.55–1.81	1.25	1.15–1.37
Patient age				
≤ 25 vs >47	0.68	0.61–0.70	0.73	0.65–0.80
25 < ≤ 35 vs >47	0.74	0.67–0.83	0.77	0.68–0.86
35 < ≤ 47 vs >47	0.77	0.69–0.87	0.77	0.69–0.87
At least 5 'yes' answers				
Severity of rhinitis (moderate-severe vs mild)	2.53	2.25–2.84	2.00	1.80–2.30
Diagnosis of allergy (yes vs no)	2.37	2.05–2.74	2.00	1.70–2.30
BMI				
≤ 18.5 vs >30	0.41	0.29–0.57	0.48	0.34–0.69
18.5 < ≤ 25 vs >30	0.52	0.41–0.66	0.58	0.45–0.74
25 < ≤ 30 vs >30	0.79	0.61–1.01	0.82	0.63–1.00
Type of rhinitis (persistent vs intermittent)	1.87	1.68–2.00	1.35	1.20–1.50
Patient age				
≤ 25 vs >47	0.64	0.55–0.74	0.72	0.61–0.84
25 < ≤ 35 vs >47	0.69	0.60–0.80	0.72	0.62–0.84
35 < ≤ 47 vs >47	0.77	0.66–0.88	0.77	0.67–0.90
Group (GPs vs ENTs)	1.44	1.26–1.65	1.30	1.10–1.50

running or climbing stairs at speed, sleeping, in the morning, whilst in a smoky room or dusty place), the authors could differentiate asthmatics from nonasthmatics with a sensitivity of 78% and a specificity of 95%. At the same threshold in patients with allergic rhinitis, we showed a sensitivity of 100% and a specificity of 59%. Pulmonary function tests did not improve these figures. At the threshold of five or more positive responses, we improved specificity (94.7%) without modifying sensitivity (100%) (6). Confident about the diagnostic power of the self-questionnaire, we then designed two large surveys in GPs and ENTs in which more than 12 000 rhinitis patients with no prior diagnosis of asthma were included. The prevalence of asthma, as defined by the presence of at least three positive answers to the self-questionnaire, was around 30% in this population, which is consistent with the 19–38% reported in the literature (1–3, 9–11). The risk factors for being asthmatic in our study were the severity of rhinitis, a diagnosis of allergy, a high body mass index, persistent rhinitis (vs intermittent), and older age. Similar risk factors for asthma were found in the literature for allergy, severity of rhinitis, chronology of rhinitis and the body mass index, highlighting the usefulness of the self-questionnaire to pick up undiagnosed asthma.

The finding that a diagnosis of allergy is the most significant risk factor for asthma in our study is consistent with findings of a prospective population-based study that found an extremely strong association between rhinitis and asthma when these symptoms were related to allergy (12). In the European Community Respiratory Health Survey, data from 34 centers were analyzed in random samples of 20- to 44-year-old subjects. After adjustment for sex, age, smoking habit, family history of asthma, geographic area, and season at the time of examination, asthma was strongly associated with perennial rhinitis not only among atopic subjects (OR = 8.1; 95% CI = 5.4–12.1) but also among nonatopic subjects (OR = 11.6; 95% CI = 6.2–21.9) (13). In another study (14), the same authors demonstrated that the risk of asthma increased from 2.0% in subjects without rhinitis to 6.7% in subjects with rhinitis only when exposed to pollen, 11.9% in subjects with rhinitis when exposed to animals, and 18.8% in subjects with rhinitis either when exposed to pollen or to animals, highlighting the role of allergen sensitization. In the recent cross-sectional DREAMS survey (11), 591 patients consulting ENT or allergy specialists for allergic rhinitis were asked for 'diagnosed asthma'. Although this was an exclusion criteria in our study, the authors found the same rhinitis risk factors. Indeed, the prevalence of asthma was associated with the duration (intermittent vs persistent) and severity of rhinitis (mild vs moderate-severe). Again, in the European Community Respiratory Health Survey (15), men and women with a body mass index > 30 were at an increased risk of wheeze with shortness of breath, but not of nasal allergies. In the Swedish Military Service Conscription Register (16), high body mass index was associated with asthma without allergic rhinoconjunctivitis (OR 1.53; 95% CI 1.43–1.63), and with asthma with allergic rhinoconjunctivitis (OR 1.34; 95% CI 1.20–1.50), but not with allergic rhinoconjunctivitis (OR 1.00; 95% CI 0.97–1.03).

Patients recruited by GPs or ENTs may have different rhinitis characteristics. This was indeed the case with more mild intermittent rhinitis, more conjunctivitis, more patients claiming to be allergic in those seen by GPs (35.8%, 25.9%, 86.1% vs 22.3%, 16.0%, 54.4%, respectively, $P < 0.0001$) and more moderate-severe persistent rhinitis, more sinusitis in those seen by ENTs (44.0%, 27.6% vs 37.7%, 12.8% respectively, $P < 0.0001$). This may be a consequence of allergen sensitization with more pollen allergic patients in GP patients (83.7% of those claiming being allergic vs 57.2%, $P < 0.0001$) and more house dust mite allergic patients in ENT patients (71.9% of those claiming being allergic vs 42.3%, $P < 0.0001$). Although not all patients had a diagnosis of allergen sensitization, most of them (60.2% and 81.3% for GP and ENT patients, respectively) did, and during the consultation of inclusion, additional tests were prescribed in 10.3% and 29.1% of GP and ENT patients, respectively. As we introduced the diagnosis of allergy

in our multivariate analysis, this point was taken into account.

Although 30% of the patients were possible asthmatics, less than 10% received an anti-asthmatic treatment, suggesting that either untreated patients were not diagnosed as asthmatics or that they were considered as intermittent asthmatics. Prescribed drugs were preferentially oral antihistamines and nasal glucocorticosteroids as shown in similar studies in France in particular (17). Amongst other drugs, oral corticosteroids were prescribed in 5.6% (GP) to 10% (ENT) of the patients, certainly for the most severe ones. Vasoconstrictors were very seldomly prescribed, as they are not very popular in France.

The validation of a strategy to diagnose asthma based on a questionnaire and not based on pulmonary function tests in rhinitis patients is of importance for several reasons: (i) asthma guidelines (4, 5) only list the means of diagnosing asthma and do not categorize them; (ii) rhinitis patients frequently have asthma-related symptoms such as cough, chest tightness and nocturnal awakenings and all may not be asthmatics as in the present study. These patients are often seen by GPs and ENTs, who do not have (at least in France) the materials to measure airway obstruction. Therefore, the self-questionnaire developed by Venables et al. (7) and validated by Venables et al. (7) and our group (6) could be regarded not only as a useful screening tool or an aid in structuring the medical history but also as an accurate diagnosis instrument. Although spirometry does not serve for asthma diagnosis, it serves for classification of severity

to set the level of treatment and provides physicians with an objective instrument for tracking airflow caliber over time. Therefore, such a ready to use and powerful self-questionnaire may help in recognizing asthma in rhinitis patients, the most important risk factor for being or becoming asthmatic.

Contributors

Pascal Demoly and Jean-Pierre Daures designed this study and reviewed the data. Paola Dacosta coordinated the whole of the logistics. Marie-Cécile Bozonnet and Jean-Pierre Daures generated and interpreted the statistical data. All authors contributed to the writing of the paper.

Conflict of interest statement

The authors have no financial or personal relationships with other people or organizations that could pose a conflict of interest in connection with the present work. Sanofi-Aventis supported the whole of the logistics of the surveys.

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