Published in : Allergy (2010), vol. 65, pp. 1290-1297.
Status : Postprint (Author's version)

The impact of concomitant rhinitis on asthma-related quality of life and asthma control

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Abstract

Background: Characterizing the interactions between the upper and lower airways is important for the management of asthma. This study aimed at assessing the specific impact of concomitant rhinitis on asthma-related quality of life (QOL) and asthma control.
Methods: A cross-sectional, observational survey was conducted among 1173 patients with asthma (aged 12-45) recruited by general practitioners and chest physicians. AR was defined by self-reported rhinitis symptoms and previously documented sensi-tization to inhalant allergens. The primary outcomes were (1) asthma control assessed by the Asthma Control Questionnaire (ACQ) and (2) asthma-specific QOL evaluated through the Mini Asthma Quality of Life Questionnaire (mAQLQ).
Results: AR was present in 73.9% of the population with asthma and nonallergic rhinitis (NAR) in 13.6%. AR and NAR were associated with an increased risk of uncontrolled asthma (i.e. ACQ score > 1.5) with adjusted odds ratios (OR) of 2.00 (95% confidence interval [CI]: 1.35-2.97) and 1.77 (95%CI: 1.09-2.89), respectively. Multivariate linear regression analysis showed that AR and NAR had a modest, although significant, negative impact on the global mAQLQ score (beta coefficient: -0.293, standard error [SE]: 0.063 and beta coefficient: -0.221, SE: 0.080, $P < 0.001$, respectively), even after adjustment for the level of asthma control and demographic characteristics.
Conclusion: This survey provides direct evidence that AR and NAR are associated with an incremental adverse impact on the disease-specific QOL of patients with asthma and the level of asthma control. Further investigations are required to determine whether appropriate treatment of rhinitis would efficiently reduce asthma morbidity.

Keywords : asthma ; quality of life ; rhinitis.

Abbreviations : ACQ, Asthma Control Questionnaire ; ACT, Asthma Control Test ; AR, Allergic rhinitis ; ARIA, Allergic Rhinitis and its Impact on Asthma ; mAQLQ, Mini Asthma Quality of Life Questionnaire ; NAR, Nonallergic rhinitis ; QOL, Quality of life.

Allergic rhinitis (AR) and asthma are highly prevalent conditions that generate a substantial health and economic burden (1-3). Despite the increased emphasis on the interactions between the upper and lower airways (3), there is limited evidence supporting an incremental impact of AR on asthma outcomes. Retrospective database studies indicated that the presence of AR is associated with a higher utilization of asthma-related healthcare resources, although controlled studies provided conflicting results regarding the benefits of treating AR on asthma-related morbidity (4-7). Bousquet and co-workers demonstrated that both AR and asthma interfere with health-related quality of life (QOL) assessed through a generic instrument, the Short Form-36 Health Survey (8, 9). They found that AR was associated with impairment in social functioning and mental well-being, while subjects with both asthma and AR experienced more physical limitations than patients with AR alone (9). However, the relative contributions of asthma and AR to decreased QOL could not be delineated because of the limited number of

subjects with asthma without AR. Surveys of large samples of adult patients with asthma seen by general practitioners documented that the presence of (allergic) rhinitis was associated with a lower level of asthma control but asthma-related QOL was not investigated (10, 11). Only one recent study of patients with severe asthma documented an inverse correlation between the severity of rhinitis and the level of asthma-related quality of life assessed through the Asthma Quality of Life Questionnaire (6).

The objective of this observational study was to assess the impact of concomitant rhinitis on asthma control and asthma-related QOL in a large population of patients with asthma.

METHODS

Study design

This cross-sectional survey was conducted among patients with asthma identified by general practitioners and chest physicians randomly selected throughout Belgium and Luxemburg. Patients aged between 12 and 45 who had been treated for asthma for at least 1 year were eligible for inclusion in the study. The patients were enrolled during two 4-month periods (i.e. from March to June 2007 and from September to December 2007) to take into account seasonal variations in allergens. Participating physicians were asked to include up to 10 consecutive patients with asthma for general practitioners and up to 16 patients for chest physicians.

Physicians and patients completed a questionnaire aimed at collecting information on demographic features (i.e. age, gender, and smoking habits) and outcomes related to asthma and rhinitis. A formal diagnosis of allergy was not an *a priori* inclusion criterion, although the questionnaire enquired whether sensitization to inhalant allergens (i.e. house dust mites, pets, molds, and tree, grass, or weed pollen) had been ascertained using either skin prick tests or measurement of specific IgE antibodies. The patient questionnaire was strictly anonymous and was completed during the clinical visit. The study protocol was approved by a central ethics committee (Universitair Ziekenhuis Antwerpen, Belgium), and the participants were requested to sign a statement of informed consent.

Asthma outcomes

The questionnaire collected information on the criteria used by the physicians for diagnosing asthma (i.e. clinical history alone, documentation of reversible airway obstruction on spirometry, or measurement of nonspecific airway hyperresponsiveness to pharmacological agents). The level of asthma control was assessed using the 6-item Asthma Control Questionnaire (ACQ) in which the final item on airway obstruction is omitted (12, 13). Responses to each item are rated on a 6-point scale, and the global score is the mean of the responses ranging from 0 (totally controlled) to 6 (severely uncontrolled). When the ACQ is used to identify patients whose asthma is inadequately controlled, the optimal cutoff score is 1.50 (positive predictive value = 0.88) (13).

Asthma-related QOL was assessed using the Mini Asthma Quality of Life Questionnaire (mAQLQ) (14). This 15-item self-administered questionnaire has been designed to evaluate asthma-specific QOL by addressing four domains: (1) symptoms (5 items); (2) limitations in daily activities (4 items); (3) emotional function (3 items); and (4) exposure to environmental stimuli (3 items). The degree of impairment during the preceding 2 weeks is scored on a 7-point scale ranging from 1 (severe impairment) to 7 (no impairment) for each item. The answers are summarized into four domain scores and a mean global score.

Rhinitis outcomes

The clinical diagnosis of current rhinitis was based on a patient's positive answer to the question *'In the last 12 months, have you had a runny or stuffy nose or episodes of sneezing when you did not have a cold or the flu?'* (15). AR was defined by the presence of rhinitis symptoms associated with a declared sensitization to at least one aeroallergen. Patients were categorized as having nonallergic rhinitis (NAR) when they reported rhinitis symptoms in the absence of documented sensitization to common allergens.

According to the Allergic Rhinitis and its Impact on Asthma (ARIA) recommendations (3), rhinitis was categorized into intermittent (symptoms < 4 days per week or for < 4 weeks) or persistent (symptoms > 4 days per week and for > 4 weeks) and further characterized according to severity as mild or moderate/severe (i.e. symptom rated as troublesome).

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Data analysis

Data are presented as mean ± SD for continuous variables and percentages for categorical variables. Comparisons between proportions and means were made using the chisquared test and Student's *t*-test, respectively. The factor that affected the primary outcomes (i.e. the dependent variables) of the study was explored through multivariate logistic regression analysis for the level of asthma control (i.e. ACQ score > 1.50 *vs* ≤1.50) and multivariate linear regression analysis for asthma-related QOL (mAQLQ score). The characteristics of rhinitis symptoms and sociodemographic features (i.e. age, gender, and smoking status) were incorporated into these regressions as the independent variables. The effect of rhinitis on the primary outcomes was tested using two separate models. The first model used the presence of AR, NAR, or 'no-rhinitis' as independent variables, while the second model incorporated both the duration of rhinitis (i.e. persistent *vs* intermittent) and the severity of the symptoms (i.e. mild *vs* moderate/severe).

The analysis was performed using the STATA 10.0 statistical software (StataCorp College Station, TX, USA). All tests were 2-tailed. A *P*-value <0.05 was considered significant.

Table 1 *Demographic and clinical features of the patients*

	All patients (n = 1173) n (%)	Allergic rhinitis (n = 867) n (%)	Nonallergic rhinitis (n = 160) n (%)	No rhinitis (n = 146) n (%)	*P*-value*
Gender (female)	573 (49.3)	427 (49.7)	79 (49.7)	67 (46.5)	0.781
Age[†]	29.9 ± 9.9	29.3 ± 9.8	31.7 ± 9.2	31.9 ± 10.1	<0.001
Enrollment by general practitioner	665 (59.3)	486 (59.4)	109 (68.6)	70 (48.6)	0.002
Smoking habits					
Nonsmokers	796 (68.6)	609 (71.1)	84 (52.8)	103 (71.5)	<0.001
Current smokers	224 (19.3)	155 (18.1)	47 (29.6)	22 (15.3)	
Ex-smokers	140 (12.1)	93 (10.9)	28 (17.6)	19 (13.2)	
Objective diagnosis of asthma[‡]	912 (77.8)	689 (79.5)	103 (64.4)	120 (89.2)	<0.001
Asthma treatment					
Short-acting bronchodilator	799 (68.1)	594 (68.5)	111 (69.4)	94 (64.4)	0.572
Inhaled corticosteroid	950 (81.0)	709 (81.8)	114 (71.3)	127 (87.0)	0.001
Daily dose of corticosteroid[§]					
Low dose	224 (27.6)	165 (26.8)	32 (33.3)	27 (27.0)	NS
Medium dose	324 (39.9)	247 (40.1)	33 (34.4)	44 (44.0)	
High dose	264 (32.5)	204 (33.1)	31 (32.3)	29 (29.0)	
Long-acting beta2-agonist	317 (27.0)	233 (26.9)	37 (23.1)	47 (32.2)	0.200
Leukotriene antagonist	459 (39.1)	352 (40.6)	58 (36.3)	49 (33.6)	0.197
Oral corticosteroid	49 (4.2)	42 (4.8)	2 (1.3)	5 (3.4)	0.100
Current conjunctivitis	839 (72.1)	723 (83.6)	105 (65.6)	11 (7.9)	<0.001

The results are presented as percentage of available data unless otherwise specified. NS, not statistically significant.
*Comparing patients with allergic rhinitis, nonallergic rhinitis, and no rhinitis.
[†]Mean ± SD.
[‡]Objective diagnosis of asthma = documentation of variable airway obstruction through spirometry or assessment of nonspecific bronchia hyperresponsiveness to pharmacological agents.
[§]Daily dose of inhaled corticosteroid expressed as beclomethasone dipropionate equivalent; low dose = less than 500 µg per day; medium dose = more than 500 µg but less than 1000 µg per day; and high dose = 1000 µg or more per day.

RESULTS

Demographic and clinical characteristics of the patients

A total of 1173 eligible patients with asthma were recruited by 100 GPs and 46 chest physicians. Of the 1628 initially recruited patients, 455 (27.9%) were excluded from analysis because they did not fulfill the inclusion criteria, i.e. age < 12 or > 45 years (n = 410), lack of information on asthma diagnosis (n = 33) or rhinitis diagnosis (n = 12).

The demographic and clinical features of the patients are summarized in Table 1. The mean (±SD) age was 29.9 ± 9.9; 49.3% were women, and 19.3% were current smokers. The diagnosis of asthma was based on lung

function tests in 912 of 1173 (77.8%) subjects. A high proportion of patients with asthma (81.0%) were treated with an inhaled corticosteroid alone or associated with either a long-acting beta$_2$-agonist (n = 403, 34.4%), a leukotriene receptor antagonist (n = 69, 5.9%), or both drugs (n = 330, 28.1%). Seven hundred and ninety-nine patients (68.1%) used an inhaled short-acting bronchodilator, which was the only anti-asthma medication for 7.6% of the population.

Symptoms of current rhinitis (i.e. within the past 12 months) were reported by 1027 of the 1173 (87.6%) patients. Sensitization to at least one inhalant allergen had been documented by either skin prick tests or specific IgE measurements in 79.9% of the patients, including 867 patients (i.e. 73.9% of the whole population) who experienced rhinitis symptoms and who were accordingly considered as having AR. One hundred and sixty (13.6%) participants experienced current symptoms of rhinitis but were categorized as having NAR in the absence of declared sensitization to inhalant allergens, while 146 (12.4%) participants did not report rhinitis symptoms. AR was associated with sensitization to house dust mites in 79.2% of the patients, tree pollen in 40.8%, grass pollen in 41.9%, weed pollen in 44.4%, pets in 41.9%, and molds in 16.8%. The prevalence of AR was similar among patients recruited by general practitioners (486 of 665, 73.1%) and chest physicians (332 of 456, 72.8%), although IgE sensitization to at least one common allergen was slightly more frequently reported among patients enrolled by chest physicians (82.2%) than in those recruited by general practitioner (77.0%, P = 0.034). Patients diagnosed as having AR were slightly younger than those with NAR and those without rhinitis. More patients were current or ex-smokers in the NAR group (47.2%) than in the AR group (29.0%) and in those without rhinitis (28.5%). Patients with AR had more often a diagnosis of asthma documented by lung function tests (79.5%) than those with NAR (64.4%), but less often than those without rhinitis (89.2%). They were more often treated with an inhaled corticosteroid (81.8%) than patients with NAR (71.3%), although the distribution of daily dosage did not differ between the groups. Symptoms of conjunctivitis were more prevalent in patients with AR (83.6%) than in those with NAR (65.6%) and those without rhinitis (7.9%).

The characteristics of rhinitis symptoms are presented in Table 2. The nasal symptoms were characterized as persistent by 49.1% and moderate/severe by 75.4% of the participants with rhinitis symptoms. Rhinitis was qualified as mild intermittent in 20.5% of these patients, mild persistent in 4.0%, moderate/severe intermittent in 30.3%, and moderate/ severe persistent in 45.2%. Rhinitis was more often persistent and moderate/severe in patients with AR (50.9% and 77.3%, respectively) than in those with NAR. Noticeably, a high proportion of the patients (68.1%) with symptoms of rhinitis during the past 12 months experienced nasal symptoms at the time of the survey. Treatment of AR included an oral H1-antihistamine in 62.3% of the patients, nasal corticosteroids in 58.8%, or a combination of these two medications in 39.6%. Patients with NAR took less often these medications (39.4%, 41.2%, and 22.5, respectively; P < 0.001).

Table 2 *Characteristics of rhinitis symptoms*

	All patients with rhinitis symptoms (n = 1027) n (%)	Allergic rhinitis (n = 867) n (%)	Nonallergic rhinitis (n = 160) n (%)	P-value*
Duration of rhinitis				
Intermittent	490 (50.9)	409 (49.1)	81 (52.8)	<0.001
Persistent	472 (49.1)	424 (50.9)	48 (37.2)	
Severity of rhinitis				
Mild	237 (24.6)	190 (22.7)	47 (36.4)	<0.001
Moderate/severe	727 (75.4)	645 (77.3)	82 (63.6)	
ARIA classes of rhinitis				
Mild intermittent	197 (20.5)	154 (18.5)	43 (33.3)	<0.001
Mild persistent	38 (4.0)	34 (4.1)	4 (3.1)	
Severe intermittent	291 (30.3)	253 (30.5)	38 (29.5)	
Severe persistent	434 (45.2)	390 (46.9)	44 (34.1)	
Rhinitis treatment				
Oral H_1-antihistamine	603 (58.7)	540 (62.3)	63 (39.4)	<0.001
NCS	576 (56.1)	510 (58.8)	66 (41.2)	<0.001
Oral H_1-antihistamine *plus* NCS	379 (36.9)	343 (39.6)	36 (22.5)	<0.001
Nasal decongestant	177 (17.2)	157 (18.1)	20 (12.5)	<0.001
No medication	132 (12.7)	88 (10.1)	44 (27.5)	<0.001

The results are presented as percentage of available data.
ARIA, Allergic Rhinitis and its Impact on Asthma; NCS, nasal corticosteroid.
*Comparing patients with allergic rhinitis to those with nonallergic rhinitis

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Status : Postprint (Author's version)

Impact of AR on asthma control

In the whole population, the mean ACQ score was 1.54 ± 1.07, and asthma was considered as being well controlled (i.e. ACQ equal to or less than 0.75) in only 27.8% of the patients. The mean ACQ score (Table 3) was higher in patient with AR (1.58 ± 1.05) and NAR (1.66 ± 0.09) than in those without rhinitis (1.13 ± 1.09, $P < 0.001$). The presence of co-morbid AR resulted in a significantly higher risk of uncontrolled asthma (i.e. ACQ score > 1.5) with an OR (95% confidence interval [CI]) of 1.96 (1.32-2.94). This effect was also observed for NAR (OR: 2.01 [1.22-3.32]).

Both the severity and duration of rhinitis symptoms appeared to be important determinants of asthma control (Table 3). The odds of having uncontrolled asthma was higher (2.61 [1.90-3.59], $P < 0.001$) in patients with moderate/severe symptoms when compared to those who experienced mild symptoms. The risk of having uncontrolled asthma was significantly higher when the symptoms were persistent rather than intermittent (OR: 1.97 [1.52-2.55], $P < 0.001$).

The multivariate logistic regression analysis (Table 4) showed that the risk of uncontrolled asthma was increased by the presence of AR (adjusted OR: 2.00 [1.35-2.97]), NAR (OR: 1.77 [1.09-2.89]), and current smoking (OR: 2.49 [1.82-3.42]). When the duration and severity of rhinitis were introduced in the regression analysis, having persistent (OR: 1.54 [1.16-2.05], $P = 0.003$) and moderate/severe symptoms (OR: 2.33 [1.64-3.30], $P < 0.001$), as well as being a women (OR: 1.39 [1.06-1.82], $P = 0.016$) or a current smoker (OR: 2.19 [1.54-3.12], $P < 0.001$), was positively associated with uncontrolled asthma.

Table 3 *Impact of rhinitis on asthma contro*

	ACQ score*	*P*-value	Uncontrolled asthma (ACQ score >1.5)*n* (%)	Crude ORs (95% CI) for uncontrolled asthma	*P*-value
Presence of rhinitis					
No rhinitis (*n* = 146)	1.13 ± 1.09	<0.001	43 (29.5)	1	0.002
Allergic rhinitis (*n* = 867)	1.58 ± 1.05		390 (45.0)	1.96 (1.32-2.94)	
Nonallergic rhinitis (*n* = 160)	1.66 ± 1.09		73 (45.6)	2.01 (1.22-3.32)	
Severity of rhinitis					
Mild (*n* = 251)	1.24 ± 0.96	<0.001	71 (28.3)	1	<0.001
Moderate/severe (*n* = 730)	1.71 ± 1.06		369 (50.6)	2.61 (1.90-3.59)	
Duration of rhinitis					
Intermittent (*n* = 506)	1.42 ± 0.94	<0.001	186 (36.8)	1	<0.001
Persistent (*n* = 473)	1.77 ± 1.12		254 (53.7)	1.97 (1.52-2.55)	

ACQ, Asthma Control Questionnaire.
*Mean ± SD.

Impact of AR on asthma-related QOL

Patients with AR and NAR reported significantly lower overall and individual domain mAQLQ scores (i.e. worse QOL) when compared to those who did not report rhinitis symptoms (Table 5). The mean (95%CI) difference between patients with AR and those without rhinitis was 0.67 (0.42-0.92) for the overall score, 0.63 (0.36-0.90) for symptoms, 0.48 (0.27-0.69) for activities, 0.65 (0.34-0.96) for emotions, and 0.94 (0.72-1.16) for environmental stimuli. Comparing patients with NAR to those without rhinitis, the mean differences were 0.65 (0.32-0.97) for the overall score, 0.70 (0.36-1.05) for symptoms, 0.57 (0.29-0.84) for activities, 0.58 (0.18-0.97) for emotions, and 0.94 (0.72-1.16) for environmental stimuli. Overall and individual mAQLQ scores were significantly lower (i.e. QOL was worse) in patients with moderate/severe compared to mild rhinitis, as well as in those with persistent compared to intermittent rhinitis (Table 5).

In the multivariate linear regression analysis (Table 6), low mAQLQ scores were associated with higher ACQ scores (beta coefficient: -0.855, standard error [SE]: 0.019, $P < 0.001$), the presence of AR or NAR (beta coefficient: -0.293, SE: 0.063 and beta coefficient: -0.221, SE: 0.080, respectively, $P < 0.001$), and increasing age (beta coefficient: -0.005, SE: 0.002, $P = 0.010$). When incorporated in the model, the severity and the duration of rhinitis had both an adverse impact on QOL. Being a women resulted in a borderline negative effect in the tested models.

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Table 4 *Determinants of asthma contro*

Dependent variable	Independent variables	OR (95% CI)*	*P*-value
Model 1			
Uncontrolled	Presence of rhinitis:	1	0.002
asthma	No rhinitis	2.00 (1.35-2.97)	
(ACQ score > 1.5)	Allergic rhinitis:	1.77 (1.09-2.89)	
(*n* = 1150)	Nonallergic rhinitis		
	Age (years)	1.01 (1.00-1.02)	0.138
	Gender:	1	0.060
	Male	1.26 (0.99-1.60)	
	Female		
	Smoking habits:	1	<0.001
	Nonsmoker	1.02 (0.70-1.50)	
	Ex-smoker	2.49 (1.82-3.42)	
	Current smokers		
Model 2			
Uncontrolled	Duration of rhinitis:	1	0.003
asthma	Intermittent	1.54 (1.16-2.05)	
(ACQ score > 1.5)	Persistent		
(*n* = 942)	Severity of rhinitis:	1	<0.001
	Mild	2.33 (1.64-3.30)	
	Moderate/severe		
	Age (yrs)	1.01 (1.00-1.02)	0.151
	Gender:	1	0.016
	Male	1.39 (1.06-1.82)	
	Female		
	Smoking habits:	1	<0.001
	Nonsmoker	0.98 (0.64-1.50)	
	Ex-smoker	2.19 (1.54-3.12)	
	Current smokers		

*Multivariate logistic regression analysis.

Table 5 *Impact of rhinitis on asthma-related quality of life*

		mAQLQ domains				
	Global mAQLQ score	Symptoms	Activities	Emotions	Environment	*P*-value
Presence of rhinitis						
Allergic rhinitis (*n* = 822)	5.01 ± 1.16	4.90 ± 1.26	5.39 ± 1.19	5.05 ± 1.45	4.61 ± 1.38	*P* < 0.001*
Nonallergic rhinitis (*n* = 147)	5.03 ± 1.09	4.83 ± 1.22	5.30 ± 1.16	5.12 ± 1.41	4.72 ± 1.18	
No rhinitis (*n* = 138)	5.67 ± 1.06	5.54 ± 1.19	5.87 ± 1.04	5.70 ± 1.33†	5.55 ± 1.23	
Severity of rhinitis						
Mild (*n* = 251)	5.42 ± 1.02	5.26 ± 1.18	5.68 ± 1.01	5.51 ± 1.32	5.18 ± 1.22	*P* < 0.001‡
Moderate/severe (*n* = 730)	4.87 ± 1.14	4.77 ± 1.24	5.27 ± 1.21	4.90 ± 1.44	4.43 ± 1.33	
Duration of rhinitis						
Intermittent (*n* = 506)	5.23 ± 1.00	5.13 ± 1.09	5.56 ± 1.05	5.30 ± 1.30	4.85 ± 1.27	*P* < 0.001§
Persistent (*n* = 473)	4.77 ± 1.23	4.66 ± 1.34	5.18 ± 1.26	4.80 ± 1.51	4.37 ± 1.38	

Legend: Data are presented as mean ± SD; mAQLQ, Mini Asthma Quality of Life Questionnaire.
*Comparing 'no rhinitis' with allergic rhinitis and nonallergic rhinitis (with the exception of emotional functioning) after Bonferroni correction.
†*P* < 0.001 and *P* = 0.002 when compared with allergic rhinitis and nonallergic rhinitis, respectively.
‡Comparing moderate/severe to mild rhinitis.
§Comparing persistent to intermittent rhinitis.

Table 6 *Determinants of asthma-related quality of life*

Dependent variable	Independent variables	β (SE)*	*P*-value
Model 1			
Global	ACQ score	-0.855 (0.019)	<0.001
mAQLQ	Presence of rhinitis:	0	<0.001
score	No rhinitis	-0.293 (0.063)	
(*n* = 1085)	Allergic rhinitis:	-0.221 (0.080)	
	Nonallergic rhinitis		
	Age (years)	-0.005 (0.002)	0.010
	Gender:	0	0.058
	Male	-0.077 (0.041)	
	Female		
	Smoking habits:	0	0.271
	Nonsmoker	-0.090 (0.065)	
	Ex-smoker	-0.061 (0.054)	
	Current smokers		
Model 2			
Global	ACQ score	-0.843 (0.023)	<0.001
mAQLQ	Duration of rhinitis:	0	0.011
score	Intermittent	-0.125 (0.049)	
(*n* = 890)	Persistent		
	Severity of rhinitis:	0	0.039
	Mild	-0.118 (0.057)	
	Moderate/severe		
	Age (years)	-0.006 (0.002)	0.013
	Gender:	0	0.049
	Male	-0.090 (0.045)	
	Female		
	Smoking habits:	0	0.129
	Nonsmoker	-0.081 (0.060)	
	Ex-smoker	-0.128 (0.073)	
	Current smokers		

ACQ, Asthma Control Questionnaire; mAQLQ, Mini Asthma Quality of Life Questionnaire.
*Multivariate linear regression analysis.

DISCUSSION

This observational survey indicates that AR has an incremental adverse impact on asthma control and disease-specific QOL of patients with asthma. These findings confirm recent reports showing a negative effect of AR on the level of asthma control using the ACQ in population-based studies of adult patients with asthma seen by general practitioners (10, 11). In addition, we found a detrimental effect of concomitant AR on asthma-related QOL, even after adjusting for the level of asthma control and sociodemographic characteristics of the population (i.e. age, gender, and smoking habits). A previous population-based study using a generic QOL questionnaire documented that subjects with both asthma and AR experienced more physical limitations than those suffering from AR alone (9). In that study, the effect of AR on QOL in patients with asthma could not be specifically characterized because of the low number of subjects with asthma without AR in the surveyed population. More recently, a clinic-based study evaluated the impact of rhinitis on QOL using the 'Rhinasthma' questionnaire; an instrument that has been designed to assess the QOL related both to the upper and lower airways (16). The logistic regression analysis showed that rhinitis symptoms affected QOL related to the upper airways and the 'global summary score', while they had no effect on the level of QOL pertaining to the lower airways. The latter was predominantly influenced by the level of asthma control, as assessed by the Asthma Control Test.

The clinical relevance of these findings, however, remains uncertain. Identifying an impact of concomitant AR on asthma control and asthma-related QOL may lead to assume that treatment of nasal disease would reduce the morbidity of asthma. A number of studies indicated that co-morbid AR is associated with a more frequent use of asthma-related medications and healthcare resources, and a higher cost-of-illness (4, 10). Epidemiological studies have suggested that treatment of AR is associated with a lower risk of emergency department visits and hospitalization for asthma (17-19), although these findings remain largely controversial (7). Juniper and cowork-

ers defined a 'minimal important difference' of 0.5 as the smallest difference in AQLQ score that would justify a change in the patient's treatment in the absence of troublesome side-effects or excessive cost (20) In this study, most of the mean differences in mAQLQ scores attributable to the presence of AR and NAR exceeded this 'minimal important difference'. However, the concept of 'minimal important difference' has been designed for interpreting changes in QOL over time in the same group of patients and may not be appropriate for comparing two populations at the same time point.

Although assessment of AR was the primary aim of this study, the results revealed that rhinitis by itself had a substantial impact on asthma outcomes independent of the allergic status. These findings are consistent with earlier clinical data, suggesting that nasal symptoms are associated with more severe asthma in nonatopic patients (21). In addition, it has been reported that rhinitis is a stronger risk factor for asthma in the nonatopic compared with the atopic population (22). These data outline the need to enhance our understanding of the association between the upper and lower airways in nonallergic patients (23).

The survey was conducted using validated questionnaires in a large population of patients with a physician-based diagnosis of asthma, among whom the diagnosis was ascertained by lung function tests in 77.8%. The subjects were enrolled over the pollen and mite seasons to overcome the possible seasonal differences in symptoms and reporting. Nevertheless, several potential limitations of this study should be considered. The sample of surveyed patients is unlikely to be representative of the general asthma population. Instead, the recruitment of patients with asthma through both general practitioners and chest physicians was intended to gather a sufficient number of patients with asthma with different levels of disease severity who did not experience rhinitis symptoms. The identification of AR was based on a symptom questionnaire and declared sensitization to allergens, which may have led to overestimation of the condition. The prevalence of AR among patients with asthma was similar to data found in the European Community Respiratory Health Survey (78%) (9). The pattern of severity and duration of rhinitis symptoms were also similar to the figures reported in a previous survey of the Belgian population (24) and surveys of patients recruited by general practitioners and chest physicians in other European countries (25, 26). An unknown proportion of rhinitis symptoms might have been misclassified as nonallergic, because the presence of IgE-mediated sensitization to common allergens was not assessed in all patients but was based on the physicians' report. Noticeably, a slightly higher proportion of patients enrolled by chest physicians (82.2%) had a documented sensitization to allergens when compared to those recruited by general practitioner (77.0%). Nevertheless, there is no indication that such a misclassification of AR as NAR could have affected the findings, because both conditions had an impact on asthma control and QOL. The study population included only patients aged above 12; assessing the impact of rhinitis in younger patients with asthma warrants further investigation using questionnaire instruments validated for children.

Despite its inherent limitations, this study provides direct evidence supporting an additive impact of AR and NAR on the physical and emotional well-being of patients with asthma and confirms the negative effect of allergic rhinitis, but also nonallergic rhinitis, on asthma control. These findings further highlight the impact of rhinitis on asthma and underscore the need for incorporating the management of upper airways in a global therapeutic approach of asthma, as recommended in the ARIA guidelines (3). Prospective investigations are, however, required to determine whether appropriate treatment of rhinitis would improve asthma outcomes.

Source of funding

This work was supported by Merck Sharp & Dohme Belgium.

Contributors

OV, MD, and CB generated and interpreted the statistical data and participated in the writing of the paper. EH coordinated the whole of the logistics. All members of the study board contributed to the design of this study and reviewed the manuscript.

Conflict of interest statement

The authors have formed an advisory board for this study and received honoraria for the meetings. EH is employed by MSD, Waterloo, Brussels. MSD supported the logistics of the survey.

Published in : Allergy (2010), vol. 65, pp. 1290-1297.
Status : Postprint (Author's version)

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