

Rhinitis: a complication to asthma

J. W. Hansen, S. F. Thomsen, H. Nolte & V. Backer

Department of respiratory medicine, Bispebjerg Hospital, Copenhagen University Hospital, Copenhagen, Denmark

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Correspondence

Jakob Werner Hansen, Respiratory Research Unit, Bispebjerg Hospital, University of Copenhagen, Denmark.
Tel: +45 353 13569
Fax: +45 353 12179
E-mail: jakobwerner@stud.ku.dk

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Abstract

Background: Asthma and rhinitis often co-occur, and this potentially increases the disease severity and impacts negatively on the quality of life. We studied disease severity, airway responsiveness, atopy, quality of life and treatment in subjects with both asthma and rhinitis compared to patients with asthma or rhinitis alone.

Methods: We examined 878 patients: 182 with asthma, 362 with rhinitis and 334 with both asthma and rhinitis. All had a clinical interview concerning severity of symptoms, treatment, and quality of life, a skin prick test, a lung function test and a bronchial provocation with methacholine.

Results: Patients with both asthma and rhinitis had less severe asthma based on the frequency of respiratory symptoms compared to patients with asthma alone (55% vs 66% $P = 0.01$). On the contrary, they were more airway responsive ($P < 0.05$) and had more perennial allergy ($P < 0.001$). Asthmatics had poor perception of the general health, independent of rhinitis ($P < 0.001$). No differences were found in asthma-specific quality of life, whereas rhinitis-specific quality of life was worse in those with both asthma and rhinitis compared to those with rhinitis alone ($P < 0.01$). Subjects with both diseases were undertreated in 85% of the cases.

Conclusion: We encourage that these observations be used in the evaluation and treatment of patients with asthma and rhinitis and that they contribute to the understanding of asthma and rhinitis as a uniform airways disease.

Asthma and rhinitis are chronic respiratory conditions characterized by periods of relative stability followed by episodes of deterioration [GINA (1), ARIA (2)]. The two diseases often co-occur and share inflammatory mechanisms, epidemiological patterns and symptoms. Furthermore, rhinitis seems to interfere with the achievement of optimal asthma control. Bousquet et al. (3) demonstrated that those suffering from both asthma and rhinitis more frequently had exacerbations, needed more systemic steroid and had more visits at emergency rooms. This suggests that patients with inflammation both in the nose and the lower airways are more likely to suffer from more severe disease, probably with low quality of life, and lower level of lung function as well as a more severe degree of airway hyperresponsiveness.

The fraction of the airway surface accounted for by the nose is absolutely minor compared with the bronchial surface (4). However, provocation of the nasal mucosa may cause release of inflammatory mediators in the lower airways leading to more severe asthma and increased airway hyperresponsiveness (5). Moreover, blocking the nose could lead to a direct provocation of the lower airway surface, as breathing

bring unfiltered air containing allergens, particles, smoke, turbulent and dry air through the mouth (6–8).

Adherence to asthma medication is generally low (9), but having symptoms from both the nose and lungs may increase the motivation to comply with treatment regimens. As a consequence, those with double disease might therefore have a significantly better treatment and better asthma control.

The aim of this study was to examine patients with both asthma and rhinitis compared to patients with asthma or rhinitis alone in respect to differences in disease severity, airway hyperresponsiveness, atopy, quality of life and treatment.

Methods

Study population

The study population comprised 10 877 subjects. The subjects were randomly selected from the Danish civil registration list, were aged 14–44 years and were living in urban Copenhagen, Denmark (10, 11). We selected this age group to minimize entry of patients with chronic obstructive

pulmonary disease (COPD). All subjects received a short questionnaire adopted from ACAAI, and a total of 5849 (54%) questionnaires were returned (12). Subjects who reported at least one symptom suggesting asthma and/or allergy, or were treated for these conditions, were invited to take part in a clinical examination. A total of 1186 subjects agreed to participate. Of these, 878 (74%) were classified as having certain asthma and/or rhinitis, and therefore were included for further analysis. Of the 878 patients, a total of 182 (20.7%) were found to have asthma, 334 (38.0%) had both asthma and rhinitis, and 362 (41.2%) had rhinitis. The examination included an interview, and lung function, airway responsiveness and skin test reactivity were measured. The Scientific Ethics Committee approved the protocol, and informed consent was obtained from all participating subjects and/or their parents.

Clinical interview and questionnaires

All participants were interviewed about respiratory and allergic symptoms (in the preceding 4 weeks and at any time in the past), knowledge about self-care, current medication and smoking habits. Lifetime tobacco exposure was calculated as pack years (tobacco consumption [g/day]/20 × duration of smoking [years]). Height and weight were measured, and body mass index (BMI) was calculated as [(weight [kg])/(height [m]²)]. A respiratory specialist diagnosed and graded the severity of asthma (intermittent, mild, moderate and severe persistent) according to the Global Initiative for Asthma (GINA) guidelines (1). In addition, the severity of rhinitis was categorized in accordance with the Allergic Rhinitis and Its Impact on Asthma (ARIA) guidelines (2). The Juniper AQLQ(S) questionnaire (13) and the RQLQ questionnaire (14) were used to assess the health-specific quality of life. These asthma- and rhinitis-specific questionnaires describe the patients' perception of the impact of their disease over the past 2 weeks on different domains of quality of life. Lastly, all participants filled in the SF-36 questionnaire concerning general health.

Spirometry and bronchial responsiveness tests

Spirometry was performed using a dry wedge spirometer, and the percentage of predicted normal values was calculated. Airway responsiveness to inhaled methacholine was measured in accordance with the method of Yan et al. (15). Each aerosol was inhaled starting with saline and followed by increasing doses of methacholine until a cumulative dose of 7.8 µmol had been reached. The test was terminated when the maximum concentration had been reached or when a 20% decline in forced expiratory volume in one-second (FEV₁) had occurred before the end of the dosing regimen. For all subjects experiencing at least a 20% decline in FEV₁, the concentration causing a 20% fall in FEV₁ (PD₂₀) was estimated, and the response-dose ratio (RDR) calculated as the decline in FEV₁ divided by the highest dose of methacholine given. Logarithmically transformed RDR values were used for the analysis. A positive test

result – airway hyperresponsiveness (AHR) was defined as a PD₂₀ below 3.9 µmol.

Skin prick tests

Skin prick tests (SPTs) were performed using standard dilutions of 10 common aeroallergens. The allergens used were birch, grass, mugwort, horse, dog, cat, house dust mite (HDM) (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*) and mould (*Alternaria iridis* and *Cladosporium herbarium*) with positive and negative references being histamine, 10 mg/ml, in 50% glycerol and glycerol, 50%, respectively. The concentrations of allergens were 10 HEP (Soluprick SQ system; ALK Abelló, Hørsholm, Denmark). Reactions were read after 15 min. A positive result (atopy) was defined as a positive reaction to at least one of the allergens, and a reaction was considered positive if the mean wheal diameter was at least 3 mm. The participants were requested to discontinue medications that contained antihistamines at least 3 days before skin testing. Subjects with asthma concomitantly with a positive skin prick test were regarded atopic (16).

Statistical analysis

The data were analysed with the statistical package SPSS 17.0 (SPSS Inc., Chicago, IL, USA) for Windows. Differences in proportions were tested with a Chi-square test, whereas differences in continuous variables were analysed with ANOVA, and in case of significance, the differences in characteristics according to the three groups were analysed by an unpaired *t*-test. In cases of skewed variables, non-parametric analysis was used.

Results

Basic parameters

The mean (SD) age was 29 (9) years with no differences between the three groups (Table 1). Men more often had rhinitis as single disease, whereas women had a higher frequency of asthma ($P < 0.05$). Subjects with both asthma and rhinitis had the highest BMI ($P < 0.05$), whereas those with asthma had the highest consumption of tobacco ($P < 0.001$).

Symptoms

There were no differences in severity of rhinitis symptoms according to ARIA guidelines between subjects with asthma and rhinitis compared with subjects with rhinitis alone. Also, there were no differences in specific rhinitis symptoms (Table 2). According to the GINA guidelines, the participating asthmatics in general had persistent symptoms (59%), and those with both asthma and rhinitis seemed to have less severe asthma compared to those with asthma alone (55.1% vs 66.3% $P < 0.05$). The majority of specific asthma symptoms were similar in the two asthma groups (Table 2).

Table 1 Descriptive characteristics of subjects with rhinitis, asthma and asthma with rhinitis in a sample of 878 adolescents and adults

Variable	Rhinitis (n = 362)	Asthma (n = 182)	R + A (n = 334)	P-value
Demographics				
Sex				
Males	45.3	16.9	37.8	0.027
Females	38.2	23.6	38.2	
Age	29.1	28.7	29.4	0.764
BMI	24.4	24.2	25.2	0.033
Smoking				
Pack years	2.19	4.98	3.75	<0.001
Ever smoker	65.3	79.9	66.8	0.003
Current smoker	23.6	48.4	30.5	<0.001
Objective tests				
AHR	7.0	53.4	58.8	<0.001
LogRDR	-0.03	0.52	0.65	<0.001
FEV ₁ of predicted	97.8	89.2	90.7	<0.001
FVC of predicted	99.1	93.6	95.5	<0.001
FEV ₁ /FVC	84.9	81.9	81.5	<0.001
Positive SPT (%)	72.4	23.4	81.4	<0.001
Birch (%)*	44.5	22.5	44.8	0.024
Grass (%)*	62.3	27.5	62.2	<0.001
Mugwort (%)*	21.9	10.0	18.1	0.175
Horse (%)*	8.9	10.0	22.0	<0.001
Dog (%)*	34.4	12.5	53.7	<0.001
Cat (%)*	36.8	20.0	57.5	<0.001
<i>D. Farinae</i>	32.8	50.0	40.9	0.044
<i>D. Pteronyssinus</i>	26.7	30.0	33.6	0.243
HDM	35.6	57.5	44.0	0.015
Alternaria (%)*	5.3	2.5	8.9	0.145
Cladosporium (%)*	1.6	2.5	5.4	0.063
≥2 Sensitizations (%)	74.1	50.0	81.1	<0.001
Mean sensitizations	2.75	1.88	3.47	<0.001
Concurrent disorders				
Food allergy	12.3	6.7	18.0	0.001
Eczema	31.6	22.5	35.1	0.013
Recurring headaches	12.6	19.7	16.1	0.095
Recurring sinusitis	6.7	8.4	10.9	0.164

BMI, body mass index; AHR, airway hyperresponsiveness; Log-RDR, logarithm of response-dose ratio; FEV₁, forced expiratory volume in one-second; FVC, forced vital capacity.

*Birch, *Betula Verrucosa*; Grass, *Phleum Pratense*; Mugwort, *Artemisia vulgaris*; Altanaria, *Altanaria iridis*; Cladosporiu, *Cladosporium herbarium*.

However, coughing was slightly higher in the group who had asthma only (48.6% and 39.3%, respectively, $P < 0.05$).

Use of medicare

A total of 23.3% had visited their general practitioner (GP) during the last month with no significant difference between the three groups (rhinitis 8%, asthma 5% and double disease 10%). Of 18 patients (2.2%) whom had been hospitalized or visited an emergency room, 13 had asthma and rhinitis, 3 had

Table 2 Descriptive characteristics of subjects with rhinitis, asthma and asthma with rhinitis in a sample of 878 adolescents and adults

Variable	Rhinitis (n = 362)	Asthma (n = 182)	R + A (n = 334)	P-value
Rhinitis symptoms				
Mild intermittent	68.2	–	67.9	0.576
Severe intermittent	22.3	–	20.3	
Mild persistent	7.3	–	10.0	
Severe persistent	2.2	–	1.8	
Specific symptoms				
Rhinorrhea	43.5	–	44.5	0.784
Nasal congestion	37.2	–	41.3	0.271
Sneezing	48.3	–	48.2	0.972
Itchy eyes	37.8	–	38.3	0.890
Reduced sense of smell	16.2	–	19.6	0.250
Asthma symptoms				
Mild intermittent	–	33.7	44.9	0.067
Mild persistent	–	15.5	15.7	
Moderate persistent	–	27.1	20.2	
Severe persistent	–	23.8	19.3	
Total				
Persistent asthma	–	66.3	55.1	0.014
Specific symptoms				
Cough	–	48.6	39.3	0.041
Wheezing	–	30.4	28.6	0.666
Shortness of breath	–	31.6	26.7	0.237
Chest tightness	–	26.7	23.2	0.380
Quality of life				
Perception of poor health	5.8	18.7	16.2	<0.001
Feeling of sadness	19.4	24.8	25.2	0.167
Feeling of tiredness	55.5	68.7	67.3	0.002
Contract illness	16.2	22.9	27.6	0.008
Disease expectation	10.6	23.5	19.9	0.003

asthma and 2 had rhinitis ($P < 0.01$). Rhinitis patients had significantly fewer admissions ($P < 0.01$), whereas no significant differences were found between admission rates for those with asthma and rhinitis (4%) compared with those with asthma alone (2%). The mean number of days with asthma symptoms at admission was 2.06 days for those with asthma alone and 1.97 for those with asthma and rhinitis non-significant (NS).

Lung function and airway hyperresponsiveness

Patients with asthma had a lower lung function than patients with rhinitis (FEV₁ of predicted, 89% vs 98%, $P < 0.001$), as well as level of airway obstruction (FEV₁/FVC ratio, 82% vs 85%, $P < 0.001$). Patients with both asthma and rhinitis had similar lung function compared with patients with asthma alone (Table 1). A significant difference in airway responsiveness was found between those with asthma compared to those with rhinitis (LogRDR, 0.52 vs -0.03, $P < 0.001$). Furthermore, subjects with asthma and rhinitis had more severe AHR than subjects with asthma alone (Table 1).

Allergy

Participants with rhinitis and participants with both asthma and rhinitis more frequently had a positive skin prick test (81% vs 72%, $P < 0.01$) compared with patients with asthma alone (23%, $P < 0.001$). Those suffering both from asthma and rhinitis as well as rhinitis alone had equally often pollen allergy (61% vs 57%, $P = 0.3$), whereas those with both asthma and rhinitis more often suffered from nonseasonal allergies such as domestic pets and house dust mites than those with asthma alone (67% vs 19%, $P < 0.001$). Lastly, those with both asthma and rhinitis had the highest number of positive SPTs compared with asthma alone and rhinitis alone (mean number of sensitizations 3.5 vs 1.9 vs 2.8, $P < 0.001$), (Table 1).

Quality of life

General health quality of life (SF36)

Asthma patients showed more tiredness and had a higher disease expectation, compared to the rhinitis group (Table 2). On the contrary, there was no difference in the perception of health among patients with both asthma and rhinitis compared to patients with asthma alone (Table 2).

Asthma quality of life

We found no differences in mean activity score (5.93 vs 5.99), symptoms score (5.84 vs 5.80), emotional score (6.30 vs 6.24) and AQLQS score (6.06 vs 6.08) in patients with both asthma and rhinitis compared to patients with asthma alone, whereas there was a tendency towards a lower environmental score in the former group (5.96 vs 6.15, $P = 0.07$).

Rhinitis quality of life

Patients with both asthma and rhinitis had more severe sleep disturbances than those with rhinitis alone (mean sleep score of 0.75 vs 0.40, $P < 0.01$). Likewise, the general non-nasal health (1.01 vs 0.62, $P < 0.01$), the nasal symptom score (1.86 vs 1.53, $P < 0.05$), the emotional score 0.66 vs 0.51, $P = 0.08$) and the total RQLQ score (1.61 vs 1.39, $P = 0.08$) were higher in patients with both diseases, whereas the activity score, the practical score and the eye score were similar in the two groups.

Medication

Rhinitis participants with and without asthma showed similar frequency of rhinitis therapy (rhinitis medication, 40.1 and 44.3%, respectively, $P = 0.3$), and they were primarily treated with antihistamines (35.1 and 38.6%, respectively, $P = 0.3$). Having both diseases increased the chance of receiving any anti-asthmatic medication (asthma alone 33.0 vs asthma and rhinitis 41.6%, $P = 0.054$). Furthermore, patients suffering from both asthma and rhinitis were more likely to receive long-acting beta₂ agonist (LABA) (asthma 2.2 vs asthma and rhinitis 6.6%, $P = 0.039$) (Table 3). Among patients with both diseases, a total of 44% were undertreated in respect of both diseases and only 15% were

Table 3 Descriptive characteristics of subjects with rhinitis, asthma and asthma with rhinitis in a sample of 878 adolescents and adults

Variable	Rhinitis (n = 362)	Asthma (n = 182)	R + A (n = 334)	P-value
Rhinitis medication				
Antihistamines	35.1	–	38.6	0.333
Nasal steroids	9.9	–	13.2	0.182
Nasal cromoglycate	2.8	–	2.7	0.956
Any medication	40.1	–	44.3	0.256
Asthma medication				
B2 SABA	–	29.1	34.4	0.219
B2 LABA	–	2.2	6.3	0.039
ICS	–	16.5	21.6	0.167
Any medication	–	33.0	41.6	0.054
Hyposensitization	1.4	1.1	6.0	<0.001

sufficiently treated according to guidelines. Moreover, 26% were well treated for their rhinitis, but under treated for their asthma. Only 15% were well treated for asthma, but undertreated for rhinitis ($P \leq 0.001$).

Discussion

We investigated the effects of having both asthma and rhinitis compared to having the two diseases individually in a large group of patients. Five main conclusions can be extracted from this work. (i) Subjects in primary care generally have persistent asthma, which is unchanged by the presence of rhinitis. (ii) Patients with both asthma and rhinitis are more often hospitalized and more frequently visit their GP. (iii) The health-specific quality of life is influenced negatively by the presence of asthma. Additionally, patients with both asthma and rhinitis have an impaired RQLQ and a tendency to an impaired AQLQ compared to patients with the two diseases alone. (iv) Subjects with both asthma and rhinitis have more airway responsiveness and are more likely to have atopy than those with asthma alone. Lastly, (v) Asthma and rhinitis is substantially undertreated, and the presence of both diseases in the same patient does not change this pattern.

Individuals with asthma alone, and asthma plus rhinitis have a lower general perception of quality of life measured by SF-36 compared to individuals with rhinitis alone. On the other hand, having double disease significantly impaired the rhinitis quality of life. Particularly, patients with asthma and rhinitis had more sleeping problems compared to patients with rhinitis alone, and also their non-nasal health was worse. Consequently, having asthma not only deteriorated quality of life, it also had an impact on the rhinitis symptoms, which became more troublesome, but not the other way around. This result differ from other studies (17) that have found that it was the presence of rhinitis that impaired the quality of life. The severity of asthma is well known to be correlated with quality of life (18), and the difference between these present findings and earlier surveys may be because of

a larger proportion of patients with severe asthma in our population. Furthermore, we did not examine patients with allergic and nonallergic rhinitis separately, which could also have influenced the results. Notably, earlier studies have found that subjects with non-allergic rhinitis have the lowest health perception with symptoms on every day basis, and no seasons without nasal congestion (10).

Studies have shown a higher frequency of GP visits among groups of patients with uncontrolled asthma and rhinitis (3). In the present group of subjects, 23% had visited their GP within the last month as a result of asthma and rhinitis complaints. Even though they had visited their GP recently, more than half of the patients complained of persistent symptoms, and one-third complained either of daily symptoms or of severe impairment of their daily life. These findings of under-treatment although visiting their GP illustrate either patients' delay or doctors' delay. Patients' delay is caused by neglect by having more than one disease or having respiratory disease at all, whereas doctors' delay in this case is difficult to show, and outside the area and focus of the present study. We found less persistent asthma among those with both asthma and rhinitis; however, these still account for more than half of those who are substantially handicapped by their respiratory situation. Rhinitis has a known impact on asthma and untreated rhinitis worsens asthma (3). There is a discrepancy between visiting ones GP and being given the optimal treatment. Those with double disease visited their GP more and had more asthma attacks needing emergency treatment than those with asthma alone, and these findings support findings from earlier studies in more severe cases. Therefore, attention to both diseases should be given, and as proposed by others studies, (19) asthma and rhinitis should be regarded as a uniform airways disease.

Subjects with both asthma and rhinitis were more often sensitized towards pets compared to the two other groups, and furthermore, those with asthma, regardless of the presence of rhinitis, also were more often sensitized to HDM.

Pets and HDM are perennial allergens that affect the status of rhinitis and asthma all year round. Furthermore, those with both asthma and rhinitis also had a higher frequency of pollen sensitization. Therefore, having both asthma and rhinitis may be a seasonal phenomenon with worsening in periods with allergen exposure. Particularly, this could be explained by prolonged periods of nasal stenosis and mouth respiration, which would be followed by a direct provocation of the respiratory tract. Lastly, patients with both asthma and rhinitis patients were also found to have multiple allergies more frequently than the other participants. This daily exposure to allergens, exacerbations in periods with pollen, and poly-sensitization, may have increased the degree of airway responsiveness in those with double disease, in turn increasing the risk of acute GP visits or hospitalization.

We found that only 15% of patients received the correct treatment for both of their diseases according to guidelines, leaving 85% who were only receiving treatment for one of their diseases or not received treatment at all. Notably, 44% of patients with both asthma and rhinitis were insufficiently treated for both of their diseases, but there was a tendency that having both diseases increased the chance of receiving any medication. Furthermore, subjects with both diseases were more often treated sufficiently for their rhinitis in contrast to their asthma.

Conclusion

We encourage that these observations be used in the evaluation and treatment of patients with asthma and rhinitis and that they contribute to the understanding of asthma and rhinitis as a uniform airways disease.

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