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Abstract

Objectives

Whereas accumulating evidence indicates close associations between rhinitis and asthma, little is known about the relationships between occupational rhinitis (OR) and occupational asthma (OA). This study analyses the prevalence of OR associated with OA, globally and according to the various causal agents, and investigates the temporal relationships between these two conditions.

Methods

Data on incident cases of OA (2008–2010) were collected through the French national occupational disease surveillance and prevention network, using a standardized form including information on occupation, causal agents, presence of OR, and respective dates of occurrence of rhinitis and asthma.

Results

Among the 596 reported OA cases with latency period, 555 could be attributed to identified agents: high molecular weight (HMW) agents (n=174); low molecular weight (LMW) agents (n=381). Overall, OR was associated with OA in 324 (58.4%) cases. The frequency of association was significantly higher for HMW agents than for LMW agents (72.2% vs 51.5%, p<0.001). OR occurred before OA significantly more frequently for HMW agents than for LMW agents (p<0.01).

Conclusions

These results show that OR is frequently associated with OA, especially when HMW agents are involved. They are consistent with the hypothesis that OR, in conjunction with OA, is more likely to be caused by sensitizers that cause disease via IgE-mediated mechanisms and suggest that symptoms of OR should be taken into account in the medical surveillance of workers exposed to HMW agents.

MESH Keywords Adult ; Air Pollutants, Occupational ; adverse effects ; chemistry ; Asthma, Occupational ; epidemiology ; etiology ; Female ; France ; epidemiology ; Humans ; Incidence ; Male ; Middle Aged ; Molecular Weight ; Occupational Diseases ; epidemiology ; etiology ; Occupations ; statistics & numerical data ; Odds Ratio ; Prevalence ; Rhinitis ; epidemiology ; etiology

Author Keywords occupational asthma ; occupational rhinitis ; high molecular weight ; low molecular weight

INTRODUCTION

Rhinitis is a common condition whose prevalence is increasing in industrialised countries. A close relation between asthma and allergic rhinitis has been reported by several epidemiological and clinical studies.[1, 2] Asthma and rhinitis often coexist, rhinitis usually preceding the development of asthma, suggesting that it might be a risk factor for asthma. This hypothesis is supported by a recent longitudinal population-based study that showed that allergic rhinitis is associated with increased onset of bronchial hyperresponsiveness, one of the hallmarks of asthma,[3] and that rhinitis, even in the absence of atopy, is a powerful predictor of adult-onset asthma.[4]

Occupational rhinitis (OR) is an inflammatory disease of the nose, characterised by intermittent or persistent symptoms, and/or variable nasal airflow limitation and/or hypersecretion arising from causes and conditions attributable to a particular work environment.[5] This condition, albeit common, has received little attention in comparison with occupational asthma (OA), probably because it is not considered to be a serious disease,[6, 7] despite its impact on health-related quality of life.[8] According to the results of cross-sectional studies conducted in various working populations,[6, 9] OR is usually 2–3 times more frequent that OA, but only a few papers have investigated the frequency of OR associated with OA.[10–15] These clinical studies suggest that the majority of patients diagnosed with OA also suffer from OR, but most of them are based on a limited number of subjects and on a limited number of aetiologies.

The aim of the present study was to assess the prevalence of rhinitis associated with OA, globally and according to the various causal agents, and to investigate the timing of onset of rhinitis in relation to that of OA, based on data from a French national surveillance programme.

METHODS

OA cases were collected through the French national occupational disease surveillance and prevention network (réseau national de vigilance et de prévention des pathologies professionnelles, rnv3p). This network includes the 30 occupational disease consultation centres in teaching hospitals, to which patients are referred for potentially work-related diseases, mainly by occupational physicians (about 60% of cases), but also by general practitioners or specialists.[16] It is supported by the French agency for food, environmental and occupational health and safety (Agence française de securite sanitaire de l'alimentation, de l'environnement et du travail, Anses), with the participation of the national health insurance system (Caisse nationale d'Assurance maladie, Cnam).

All physicians working in the network centres were invited to report all new cases of asthma that they considered to be of occupational origin, with the exclusion of work-exacerbated asthma cases, using a standardised form, according to the methodology of the ONAP programme.[17, 18] The reporting form included information on the worker's age, gender, occupation at the time of diagnosis, type of industry, and suspected causal agent. It also provided information on methods of diagnosis: positive clinical history of work-related symptoms, spirometry with pharmacological tests, serial peak expiratory flow rates (PEFR), serial measurements of FEV_1 , serial measurements of nonspecific bronchial hyperresponsiveness (NSBHR), specific skin prick tests, specific IgE, specific nasal or bronchial inhalation challenge tests. Two categories were proposed to reporting physicians to characterise OA cases: asthma with latency period and asthma without latency period (RADS). In 2008, the reporting form was modified to include additional questions on the presence of OR and temporal relationships between OA and OR. The reporting form for each case was entered in a computer database. To avoid duplicates, the first three letters of the surname, the first name, and the date of birth were provided.

Analysis

The present study included all new reported cases of OA with latency period, in 2008, 2009, and 2010.

Cases of OA presumed to be of allergic origin, for which a causal agent was identified or suspected, were divided into two groups: cases related to high molecular weight agents (HMW), and cases related to low molecular weight agents (LMW), according to the classification proposed by Malo and Chan Yeung.[19] These two groups were compared according to gender, age, frequency of association with OR, temporal relationships between OA and OR, and methods of diagnosis, using chi^2 test or Student t test. In order to take gender and age into account, a logistic model comparing isolated OA and OA associated with OR was also constructed. A p value less than 0.05 was considered statistically significant.

Statistical analyses were performed using SAS version 9.1 software (SAS Institute Inc, Cary, NC, USA). The study was approved by the French Commission nationale de l'informatique et des libertes (CNIL), personal data protection commission.

RESULTS

In 2008–2010, a total of 620 cases of OA were reported, from 24 out the 30 occupational disease consultation centres, including 24 cases of RADS. Among the 596 cases of OA with a latency period, 323 (54.2%) were observed in females. The mean age of these cases was 39.8 (11.8) years, similar for men and women.

Main suspected causal agents are described in Table 1. Globally, the most frequently suspected causal agents were cleaning products including quaternary ammoniums (17.1%), flour (16.4%), persulphate salts (12.6%) and isocyanates (8.2%). Marked differences were observed between males and females in terms of the distribution of causal agents. Flour and isocyanates were the two most commonly suspected causal agents in males (30.8% and 13.9%, respectively), while cleaning products and persulphate salts were the most frequently suspected causal agents in women (28.5% and 22.3%, respectively). The greatest number of cases of OA was observed in bakers and pastry makers, hairdressers, cleaners, and health care workers [(15.6%, 13.9%, 13.4%, and 8.9%, respectively (Table 1)]. Bakers and pastry makers were the most common occupations among males (29.3%) and hairdressers, cleaners and health care workers were the most common occupations among females (24.8%, 21.4%, and 16.1%, respectively).

Among the 596 cases of OA with latency period, 41 could not be classified as HMW or LMW cases. The HMW group (n=174) comprised a large majority of men (66.7%), whereas the LMW group (n=381) presented a female predominance [63.5% (Table 2)]. Globally, OR was associated with OA in 58.4% of cases, but was significantly more prevalent in HMW cases than in LMW cases (73.6% vs 51.4%, $p < 0.001$). This result was also observed after adjustment for gender and age (adjusted odds ratio: 3.0, 95% confidence interval 2.0–4.6). Symptoms of rhinitis appeared before onset of OA significantly more frequently in the HMW group than in the LMW group (52.3% vs 38.8%, $p < 0.01$). For the main causal agents, flour, quaternary ammoniums, persulphate salts, and isocyanates, rhinitis symptoms preceded asthma symptoms in 59%, 32%, 46%, and 25% of cases, respectively. The various methods of diagnosis of OA reported are described in Table 3. In both groups, the diagnosis of asthma was confirmed in more than 90% of cases by pulmonary function tests including pharmacological tests, or, in the absence of pharmacological tests, by PEFR monitoring or FEV_1 monitoring. Immunological tests were performed more frequently in the HMW group.

Table 4 shows the distribution of the frequency of the rhinitis-asthma association according to the main suspected causal agents. Whereas the frequency of this association was close to 80% for flour, latex and laboratory animals, it was around 60% for persulphate salts and quaternary ammoniums, and only 33% for isocyanates.

DISCUSSION

This study described 596 cases of OA with latency period, reported in 2008–2010 by experienced physicians working in occupational disease consultation centres belonging to the French national occupation disease surveillance and prevention network (rnv3p). Cleaning products, including quaternary ammoniums, were the most frequently suspected causal agents, and cleaners represented more than 13% of all subjects with OA. These findings corroborate data from workforce and population-based studies showing that, over the last 10 years, cleaners have emerged as one of the highest risk groups for OA in industrialised countries.[20–22] The main changes compared to previous data on OA, obtained from the French national surveillance programme ONAP 1996–1999,[18], apart from the increasing burden of cleaning products, are the decreased proportion of OA cases attributed to isocyanates and latex, and the increased proportion of OA cases attributed to persulphate salts, which was the major cause of OA in hairdressers.

These results confirm the frequent association of OA with OR, but the frequency of this association was found to differ considerably according to the various causal agents and their molecular weight. Globally, OR was associated with OA in about 6 out of 10 cases, which is lower than the proportion observed by Malo et al.[10], and Castano et al.,[11] in small series of OA confirmed by specific inhalation challenge tests: 37/40 (92%) and 13/17 (76%), respectively, but much higher than the frequency described by Seed et al. using data of the THOR network.[23] In a series of 172 subjects with OA ascertained by specific inhalation challenge, and 105 work-exacerbated asthma, Vandenplas et al.[15] observed that sneezing/itching and rhinorrhoea were more frequent in subjects with OA than in those with work-exacerbated asthma (78% and 70 %, versus 61% and 57%, respectively)

Very few data are available to assess variations in the frequency of association of OR with OA according to causal agents. In agreement with Castano et al.,[11] and Vandenplas et al.,[15] we found that OR was significantly more frequently associated with OA in the case of exposure to HMW agents, than in the case of exposure to LMW agents. We observed a high frequency of association (78.6%) for flour, which is by far the most frequent HMW causal agent. The frequency of association was lower for quaternary ammoniums (66.2%) and persulphate salts (60.5%), the two main LMW causal agents in our study. Figures for persulphate salts are similar to those reported by Moscato et al., [14] in a series of 21 cases of OA due to persulphate salts, confirmed by specific inhalation challenge tests (52%). The frequency of association was particularly low (33%) for isocyanates, confirming data from the THOR network. [22] According to the history obtained at the time of diagnosis of OA, symptoms of rhinitis more frequently appeared before symptoms of asthma in the case of HMW agents, than in the case of LMW agents, confirming previous data. [15]

Previous clinical studies have tried to stratify the relationships between OA and OR, according to the various causal agents, but were limited by the small size of the study populations. Epidemiological data from national reporting schemes provide another way to examine the association between OR and OA, and to establish the relative frequency with which various families of agents cause rhinitis or asthma.[23, 24] To the best of our knowledge, although OA surveillance programmes exist in several countries, only preliminary data from the THOR network have been previously published on OA-OR relationships.[22]

The major strength of our study is the large number of cases. Another strength, compared to most other surveillance programmes devoted to OA, is the advice from occupational disease specialists for the diagnosis of each case of OA. However, several limitations need to be discussed. The representativeness of our study sample is questionable due to the lack of precise information on the population from which the patients were derived, and due to the fact that reporting of cases is not compulsory. Nevertheless, there is no reason why this possible recruitment bias might affect the observed frequency of OR associated with OA, globally and according to the molecular weight of causal agents. The question of diagnostic accuracy is also a potential source of error and misclassification. In a very high proportion of cases, the diagnosis of OA was based on pulmonary function tests including pharmacological tests and reporting physicians were asked not to report cases of work-exacerbated asthma. However, diagnostic tools seldom included specific inhalation challenge tests, which are probably the most reliable test to distinguish OA from work-exacerbated asthma.[25] Consequently, it cannot be excluded that some cases classified as OA were in fact work-exacerbated asthma. Nevertheless, immunological tests have been shown to be good predictors of the positivity of specific inhalation challenges,[26] and are consequently useful to distinguish OA from work-exacerbated asthma. In our study, skin prick tests and specific IgE assays were performed and were positive in about two-thirds of cases attributed to HMW agents, which makes the diagnosis of OA highly plausible in the majority of the cases of this group.

The observed differences in the frequency of the OA-OR association and the temporal relationships between OA and OR according to molecular weight and the various causal agents can probably be explained by different pathophysiological mechanisms. Although it is generally accepted that HMW agents induce asthma via an IgE-dependent mechanism, the pathogenesis of OA caused by LMW agents remains uncertain and controversial. [26] For some LMW agents such as platinum salts and acid-anhydrides, the development of OA is accompanied by the production of specific IgE antibodies. Interestingly, in a series of 25 consecutive cases of trimellitic anhydride-induced OA, 22 (88%) reported rhinitis and in 17 of these 22 cases, rhinitis symptoms preceded asthma symptoms. [12] These figures are similar to those observed in OA induced by HMW agents. For most other LMW agents, the presence of specific IgE has either not been documented or documented only in a small subset of affected workers, without showing a consistent correlation with clinical symptoms. [27] Immunological cell-mediated mechanisms have been proposed, but non-immunological mechanisms, such as irritation or pharmacological mechanisms, may also be involved. The responsibility of repeated exposure to occupational LMW irritants in new-onset asthma, such as acids, bases, oxidants, electrophilic agents, isocyanates or aldehydes, has been suggested by numerous epidemiological studies and case reports. [28] Pharmacological mechanisms have been proposed for some LMW agents: release of histamine by persulphate salts, [29] quaternary ammoniums, [30] or opiates, [31] disruption of the cholinergic control of airway responsiveness by organophosphate insecticide, [32] calcium chelation by EDTA-containing detergents or disinfectants. [33]

Our results, in accordance with the THOR data,[23] are consistent with the hypothesis that OR in conjunction with OA, is more likely to be caused by sensitizers that induce disease via IgE-mediated mechanisms. The high frequency of the OA-OR association observed in our study when HMW agents were involved supports the concept of united airway disease, based on previous studies demonstrating a parallel significant reaction of the nose and lungs after challenges with occupational agents.[11, 34] Our findings also suggest that all causal agents of OA do not follow this model,[35] especially when LMW agents are involved.

Globally, the present study confirms a close link between OR and OA for cases related to IgE-mediated sensitisation. Our findings of a frequent association between OA and OR and the fact that symptoms of rhinitis preceded onset of asthma in a large number of cases, support the hypothesis that OR is associated with an increased risk of development of OA, clearly illustrated by a longitudinal study from the Finnish register of occupational diseases concerning 3,667 patients seeking compensation for OR, that showed a relative risk of asthma of 4.8 (95% CI: 4.3–5.4) among subjects with OR, compared to subjects with other occupational diseases.[36]

CONCLUSION

In a series of 596 consecutive cases of OA with a latency period, collected through a French surveillance programme involving teaching hospital occupational disease centres, we observed an association between OA and OR in more than one half of cases of OA, and the prevalence of rhinitis symptoms was higher for HMW agents than for LMW agents. Symptoms of OR were also more often reported to precede OA in the case of HMW agents, compared to LMW agents. These results justify screening for rhinitis symptoms in subjects at high risk of OA, especially in those exposed to HMW agents, in order to prevent the subsequent development of OA.[37]

What this paper adds

- Whereas accumulating evidence indicates close associations between rhinitis and asthma, little is known about the relationships between occupational rhinitis (OR) and occupational asthma (OA).

- In a large series of occupational asthma (n=596), we observed that OA and OR coexist significantly more frequently when HMW agents are involved.

- Rhinitis symptoms occurred before asthma symptoms significantly more frequently for HMW agents than for LMW agents, suggesting different pathophysiological mechanisms.

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Footnotes:

COMPETING INTEREST None declared

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Table 1

Main suspected causal agents and main occupations in subjects with occupational asthma

	Whole population	Men	Women
	n (%)	n (%)	n (%)
Agents			
Cleaning products (including quaternary ammoniums)	102 (17.1)	10 (3.7)	92 (28.5)
Flour	98 (16.4)	84 (30.8)	14 (4.3)
Persulphate salts	75 (12.6)	3 (1.1)	72 (22.3)
Isocyanates	49 (8.2)	38 (13.9)	11 (3.4)
Animals	22 (3.7)	10 (3.7)	12 (3.7)
Wood dusts	21 (3.5)	17 (81.0)	4 (19.0)
Aldehydes	19 (3.2)	7 (2.6)	12 (3.8)
Resins and glues (excluding isocyanates)	16 (2.7)	10 (3.7)	6 (1.9)
Latex	15 (2.5)	-	15 (4.6)
Amines	13 (2.2)	5 (1.8)	8 (2.5)
Other or undetermined	166 (27.9)	89 (32.6)	77 (23.8)
Total	596 (100.0)	273 (100.0)	323 (100.0)
Occupation			
Bakers and pastry makers	93 (15.6)	80 (29.3)	13 (4.0)
Hairdressers	83 (13.9)	3 (1.1)	80 (24.8)
Cleaners	80 (13.4)	11 (4.0)	69 (21.4)
Health care workers	53 (8.9)	1 (0.4)	52 (16.1)
Wood workers	32 (5.4)	23 (8.4)	9 (2.8)
Painters	19 (3.1)	19 (6.9)	-
Construction workers	18 (3.0)	18 (6.6)	-
Laboratory technicians	18 (3.0)	4 (1.5)	14 (4.3)
Metal workers	18 (3.0)	15 (5.5)	3 (0.9)
Other	182 (30.5)	99 (36.3)	83 (25.6)
Total	596 (100.0)	273 (100.0)	323 (100.0)

Table 2

Characteristics of the study population and frequency of association of rhinitis with asthma according to the molecular weight of suspected causal agents

	HMW	LMW	Total	p value
	n =174	n =381	n =555	HMW/LMW
Gender:				< 0.001
- male: n (%)	116 (66.7)	139 (36.5)	255 (45.9)	
- female: n (%)	58 (33.3)	242 (63.5)	300 (54.1)	
Mean age (SD) (years)	34.5 (10.6)	41.6 (11.7)	39.4 (11.8)	< 0.001
Mean duration of asthma symptoms before diagnosis of OA (SD) (years)	5.1 (7.7)	5.0 (7.4)	5.0 (7.5)	
OR associated with OA: n (%)	128 (73.6)	196 (51.4)	324 (58.4)	< 0.001
Timing of OR in relation to OA:				0.007
- before: n (%)	67 (52.3)	76 (38.8)	143 (44.1)	
- at the same time: n: (%)	41 (32.0)	90 (45.9)	131 (40.4)	
- after: n: (%)	9 (7.0)	17 (8.7)	25 (8.0)	
- missing data: n: (%)	11 (8.6)	13 (6.6)	24 (7.4)	

OR, occupational rhinitis
OA, occupational asthma
HMW, high molecular weight
LMW, low molecular weight

Table 3

Diagnostic tools according to the molecular weight of suspected causal agents

	HMW	LMW
	n = 174	n = 381
Spirometry with pharmacological tests	159 (91.4)	352 (92.4)
PEFR[1] monitoring	21 (12.1)	42 (11.0)
FEV_1 [2] monitoring	6 (3.4)	36 (9.4)
BHR[3] monitoring	11 (6.3)	34 (8.9)
Skin prick tests	121 (69.5)	28 (7.3)
Specific IgE	117 (67.2)	19 (5.0)
Nasal specific inhalation challenge	6 (3.4)	61 (16.0)
Bronchial specific inhalation challenge	3 (1.7)	18 (4.7)

Data are presented as n (%)
HMW, high molecular weight
LMW, low molecular weight
PEFR, peak expiratory flow rate
FEV_1, forced expiratory volume in 1 second
BHR, bronchial hyperresponsiveness

Table 4

Frequency of association OR-OA according to suspected causal agents

Suspected causal agent	OA	Associated rhinitis
	n	n (%)
HMW agents	174	128 (73.6)
Flour	98	77 (78.6)
Latex	15	12 (80.0)
Laboratory animals	14	11 (78.6)
Other animals	12	8 (66.7)
Mites	10	6 (60.0)
Other	25	14 (56.0)
LMW agents	381	196 (51.4)
Quaternary ammoniums (QA)	77	51 (66.2)
Persulphate salts	76	46 (60.5)
Isocyanates	49	16 (32.6)
Cleaning products (excluding QA)	24	13 (54.2)
Wood dusts	21	10 (47.6)
Aldehydes	19	14 (73.7)
Amines	13	7 (53.8)
Acrylic compounds	12	6 (66.7)
Metals	11	2 (18.2)
Welding fumes	10	1 (10.0)
Other	69	28 (40.5)

OR, occupational rhinitis
OA, occupational asthma
HMW, high molecular weight
LMW, low molecular weight