Nasal histamine reactivity in woodwork teachers*

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SUMMARY *Woodworkers exposed to wood dust have an increased frequency of rhinitis. We have previously reported such rhinitis in woodwork teachers. To test whether their nasal complaints are related to nasal hyper-reactivity, we selected 14 woodwork teachers with work-related rhinitis and 14 healthy and non-allergic control persons for nasal histamine challenge using symptom scores (0-3 scale) and acoustic rhinometry for effect evaluation. Intranasal saline followed by doubled concentrations of histamine phosphate (from 0.062 to 16 mg/ml) was given at five-minute intervals. There was no significant difference between the groups regarding symptom scores or acoustic rhinometry during the challenge. The results indicate that nasal hyperreactivity is not a prominent factor in wood-dust-related rhinitis. Other mechanisms probably prompt the nasal complaints.*

Key words: wood dust, woodwork teachers, rhinitis, histamine challenge, acoustic rhinometry

INTRODUCTION

During the past ten years occupational rhinitis has aroused increasing scientific interest. Nasal tests are often more convenient for the individual than bronchial tests. A relationship between rhinitis and asthma exists and has been recently reviewed (Row-Jones, 1997; Vignola et al., 1998). It has been suggested that nasal problems may precede bronchial problems, for example in occupational asthma (Chan-Yeung and Desjardins, 1992; Oertmann and Bergmann, 1993; Chan-Yeung and Malo, 1995; Piirila et al., 1997). Better knowledge of occupational nasal problems and reactions might therefore help forecast and prevent upper and lower airway diseases.

Workers exposed to wood dust have an increased occurrence of rhinitis (Andersen et al., 1977; Wilhelmsson and Drettner, 1984). We have reported such rhinitis in Swedish woodwork teachers employed in the compulsory school system in Stockholm (Åhman et al., 1995a). Measured levels of total dust in their workshops ranged 0.12-1.18 mg /m^3. In this group, a subacutely impaired nasal function with reversible decrease in nasal peak flows and mucociliary clearance during a working week was found (Åhman et al., 1996a and 1996b). There was also a tendency to higher albumin concentration in their nasal lavage fluid (Åhman et al., 1995b). The studies indicate that several mechanisms (plasma leakage, recruitment of inflammatory cells, impaired mucociliary function and derangement of mucosal structure) may be involved in rhinitis related to wood dust exposure. Nasal hyperreactivity, which is another possible mechanism, has not been studied in such groups.

Recent control studies of nasal reactivity in occupational and environmental rhinitis report significant hyperreactivity using different methods for evaluation, i.e., rhinomanometry (Hytönen and Sala, 1996), the "opening" interrruption technique (Plavec et al., 1993) and rhinostereometry (Falk et al., 1994; Ohm et al., 1997). Acoustic rhinometry and nasal peak flow measurements have been used for evaluating antigen challenge in allergic rhinitis (Hilberg et al., 1995; Lane et al., 1996). There is a need to develop standardised methods for measuring nasal reactivity.

The present aims were to use acoustic rhinometry for determining nasal histamine reactivity and to evaluate whether this method could demonstrate greater nasal responsiveness in woodwork teachers with symptoms of occupational rhinitis than in healthy controls.

MATERIALS AND METHODS

Subjects

Between December 1997 and March 1998 a questionnaire was distributed to all woodwork teachers currently employed in the compulsory school system in Stockholm. The aim was to evaluate the health effects following interventive measures in the

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workshops. Of the 161 currently employed woodwork teachers, 138 (86%) answered. The results will be reported elsewhere. Of the 138 respondents, 14 woodwork teachers with symptoms of occupational rhinitis were selected consecutively as their questionnaire answers arrived, with their written consent to participate. A case was regarded as occupational rhinitis if it fulfilled the following criteria:

1. Nasal blockage or runny nose (obligatory symptom).
2. At least one additional nasal complaint (nasal irritation, sneezing, nosebleed or dry nose).
3. The symptoms should be work-related, i.e. increase during the working days and decrease off work.
4. No history of upper airway infection during the previous three weeks.

As a control group, 14 healthy and non-allergic hospital personnel were selected. The study was approved by the Ethics Committee of Huddinge University Hospital.

Methods

Immediately before the nasal histamine challenge, additional questions about nasal complaints, allergies and previous and current respiratory symptoms were answered. Naso-pharyngeal status was assessed using nasal endoscopy with a rigid 4 mm Hopkin's optic 30o (Karl Storz, Germany). A standard skin-prick test (Soluprick SQ, ALK, Hörsholm, Denmark) with ten common allergens plus saline and histamine control was applied on the forearm. A wheal exceeding 2 mm in diameter for at least one allergen was defined as a positive reaction classifying the individual as atopic.

A Rhin2000 rhinometer (SR Electronics ApS, Lynge, Denmark) was used. The acoustic system includes a continuously transmitted wideband sound from an electronic source in a probe. The upper end of the probe is adapted to the nostril with a nose adapter. The computer program displays the cross-sectional area of the nasal cavity on the horizontal axis and the distance from the nostril on a vertical axis and calculates the minimum cross-sectional area (MCA, cm^2) and the volume (Vol, cm^3) of the anterior (0-2.2 cm) and posterior (2.2-5.4 cm) nasal cavities (MCA-1 and MCA-2 and Vol-1 and Vol-2, respectively). Four curves of the selected cavity were measured, and the mean values were later used in the statistical analyses. Deviating curves were discarded.

After at least 15 minutes of rest, acoustic rhinometry of both nasal cavities was first performed. Based on this basal measurement and endoscopy, the larger nasal cavity was selected for histamine challenge. The right nasal cavity was selected as the test side in six woodwork teachers and in eight control subjects. Histamine was then applied in increasing concentrations every 10 minutes into the selected nostril using spray bottles delivering 50 µg histamine phosphate per ml. The following concentration steps were applied: 0 (=0.9% NaCl); 0.063; 0,125; 0,25; 0,5; 1,0; 2,0; 4,0; 8,0; and 16,0 mg/ml of histamine.

Five minutes after each histamine application, the subjects first rated their subjective complaints of nasal blockage, runny nose, nasal itching and sneezing using a 0-3 scale: 0=no symptoms; 1=weak symptoms; 2=moderate symptoms; and 3=severe symptoms. Immediately thereafter, acoustic rhinometry of the selected nasal cavity was performed. The challenge was interrupted after the highest histamine concentration (16,0 mg/ml) or earlier if severe complaints arose.

PC_{15}, PC_{20}, PC_{25}, PC_{30}, PC_{40}, and PC_{50} - defined as the histamine concentration reducing acoustic rhinometry by 15, 20, 25, 30, 40, and 50 % of the post-saline value, respectively - were calculated from the individual dose-effect curves of MCA-2 (within 2.2-5.4 cm from the nasal opening) and Vol-2 (distance 2.2-5.4 cm from the nasal opening; this distance is the more reactive part of the nasal cavity).

The Student's *t*-test (unpaired) was used to compare parametric data between the groups. Differences in the distribution of demographic data were evaluated by means of Fisher's exact test and rated symptom scores with the Kruskal Wallis test. Linear regression of the logarithmically transformed histamine concentration as independent variable, and of symptom scores and acoustic rhinometric data as dependent variables, was used to analyse the slope in the groups. The difference between these slopes for the woodwork teachers and for the control group was analysed by means of Student´s *t*-test (Armitage and Berry, 1994).

RESULTS

All woodwork teachers had symptoms of rhinitis (which agreed with the inclusion criteria) but they also stated more symptoms of conjunctivitis and pharyngitis, most of them work-related (Table 1).

Table 1. Demographic data and previous and present diseases and symptoms.

		Woodwork teachers	Control group
Total number of subjects	(n)	14	14
Females	(n)	3	7
Smokers	(n)	2	3
Previous atopy (hayfever, asthma, eczema)	(n)	4*	0
Previous nasal disease or nasal operation	(n)	0	1
Current complaints:			
- conjunctivitis	(n)	6**	0
- impaired smell sense	(n)	2	0
- nasal blockage	(n)	13***	0
- runny nose	(n)	4*	0
- itching	(n)	1	0
- sneezing	(n)	6**	0
- dry nose	(n)	4*	0
- pharyngitis	(n)	6**	1
- asthma	(n)	1	0
Positive skin-prick test	(n)	6**	0
Age	(years, m ± sd)	46 ± 8§	37 ± 11
Height	(cm, m ± sd)	177 ± 10	178 ± 12

*$p<0.05$, **$p<0.01$ and ***$p<0.001$ versus control group (Fisher's exact test)
§$p<0.05$ versus control group (Student's *t*-test)

Twelve of the 14 woodwork teachers had most complaints in the day-time, especially towards the end of the working day. Eleven had nasal complaints during the whole year but all noted more nasal problems when they were exposed to wood dust and other irritants. The distribution of current smokers was roughly equal between the teachers and the controls. The teachers were somewhat older than the control subjects, and there were more women among the controls. Six woodwork teachers, but no control had positive skin-prick tests.

Immediately before the histamine challenge, rated nasal blockage was higher in the woodwork teachers than in the control group, but acoustic rhinometry did not differ significantly between the groups (Table 2).

Table 2. Rated symptom scores and acoustic rhinometry just before nasal histamine challenge.

		Woodwork teachers	Control group
Rated symptoms (n)	Score	(n=14)	(n=14)
- nasal blockage	0	5*	11
	1	6	3
	2	3	0
	3	0	0
- runny nose	0	13	12
	1	0	2
	2	1	0
	3	0	0
- nasal itching	0	13	14
	1	1	0
	2	0	0
	3	0	0
- sneezing	0	0	0
	1	0	0
	2	0	0
	3	0	0

*$p<0.05$ versus control group (Kruskal-Wallis test)

Compared with pre-saline acoustic rhinometry, post-saline measurements did not differ significantly, but there was a tendency to an increase in nasal volumes in woodwork teachers and a decrease in the control group (Table 3). However, the individual response to saline varied considerably.

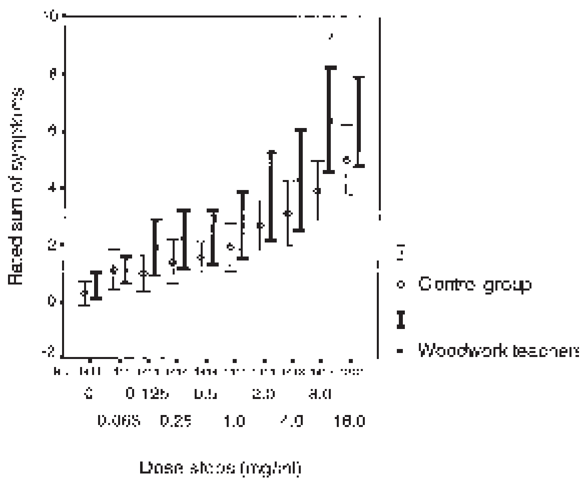


Figure 1. Rated sum of nasal symptoms at the different histamine dose steps.

Regarding rated symptoms, there was no over all significant difference between the woodwork teachers and the control group at the different dose steps. Only at histamine concentration 8 mg/ml did the woodwork teachers rate more symptoms than the control group (Figure 1). The slope of the dose-effect curve using the sum of rated symptom scores was slightly, but non-significantly, steeper for the woodwork teachers than for the control group. There was no significant difference between the groups regarding nasal cavity rhinometry at the different dose steps (Figure 2 and 3), the slope of the regression curves or the PC_{15} , PC_{20}, PC_{25} , PC_{30}, PC_{40} , and PC_{50} values (Table 4). However, there was an overall tendency to lower $PC_{15\text{-}50}$ in the teachers than in the controls.

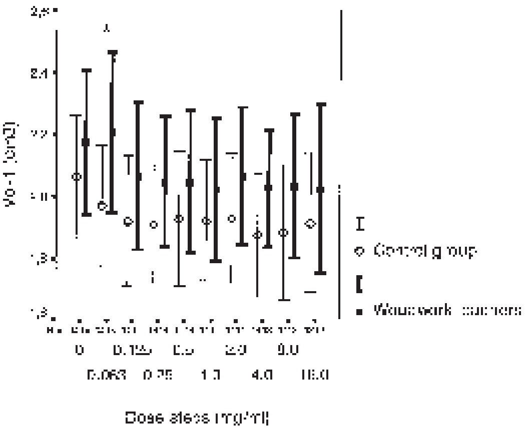
With all subjects pooled, $PC_{15\text{-}50}$ were in general lower in subjects with positive skin-prick test than in those with a negative test, but the difference did not reach statistical significance. Nor was there any significant difference between subjects with complaints versus those with no complaints of nasal allergy or nasal blockage.

Table 3. Acoustic rhinometry before and after saline.

			Woodwork teachers (n=14)	Control group (n=14)
MCA-1	(cm^2, mean ± sd)	pre-saline:	0.64 ± 0.19	0.64 ± 0.15
		post-saline:	0.69 ± 0.23	0.64 ± 0.15
MCA-2	(cm^2, mean ± sd)	pre-saline:	0.60 ± 0.25	0.66 ± 0.22
		post-saline:	0.61 ± 0.29	0.61 ± 0.25
Vol-1	(cm^3, mean ± sd)	pre-saline:	2.12 ± 0.49	2.07 ± 0.38
		post-saline:	2.17 ± 0.40	2.06 ± 0.35
Vol-2	(cm^3, mean ± sd)	pre-saline:	4.17 ± 1.94	4.65 ± 1.45
		post-saline:	4.27 ± 2.25	4.05 ± 1.66
Change (%) pre- to post-saline:				
MCA-1			+7.7 ± 15.7	+ 0.4 ± 12.3
MCA-2			+1.6 ± 15.9	−10.1 ± 21.5
Vol-1			+3.5 ± 8.1	− 0.1 ± 5.4
Vol-2			+1.2 ± 15.8	−13.0 ± 20.9

Table 4. Provocative concentration (PC) of histamine reducing acoustic rhinometry (Vol-2 and MCA-2 calculated for the distance 2.2-5.4 cm from the nasal opening) by 15, 20, 25, 30, 40, and 50 percent ($PC_{15\text{-}50}$) from the post-saline value.

	Woodwork teachers (n=14)		Control group (n=14)	
	Log PC (mean ± SD)	PC (geom. mean)	Log PC (mean ± SD)	PC (geom. mean)
Vol-2:				
PC_{15}	–1,40 ± 1,98	0,040	–0,97 ± 0,76	0,106
PC_{20}	–1,05 ± 1,81	0,088	–0,54 ± 0,91	0,285
PC_{25}	–0,71 ± 1,66	0,197	–0,12 ± 1,19	0,766
PC_{30}	–0,36 ± 1,52	0,437	0,31 ± 1,53	2,06
PC_{40}	0,34 ± 1,31	2,16	1,17 ± 2,30	14,8
PC_{50}	1,03 ± 1,22	10,7	2,03 ± 3,09	107
MCA-2 :				
PC_{15}	–1,12 ± 1,46	0,076	–0,90 ± 0,62	0,125
PC_{20}	–0,74 ± 1,31	0,182	–0,56 ± 0,64	0,278
PC_{25}	–0,37 ± 1,19	0,432	–0,21 ± 0,72	0,618
PC_{30}	0,01 ± 1,09	1,03	0,14 ± 0,84	1,38
PC_{40}	0,76 ± 1,00	5,78	0,83 ± 1,15	6,83
PC_{50}	1,51 ± 1,09	32,6	1,53 ± 1,50	33,9



*p<0.05 versus control group (Student's t-test)

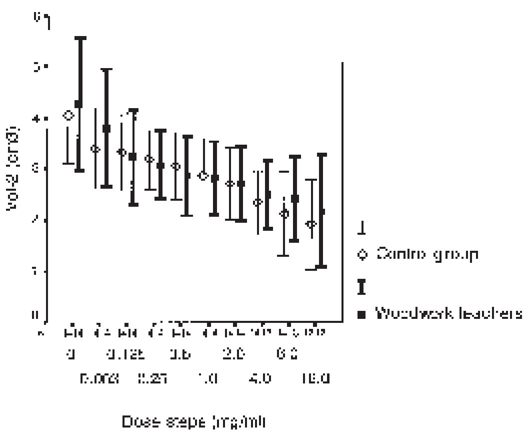


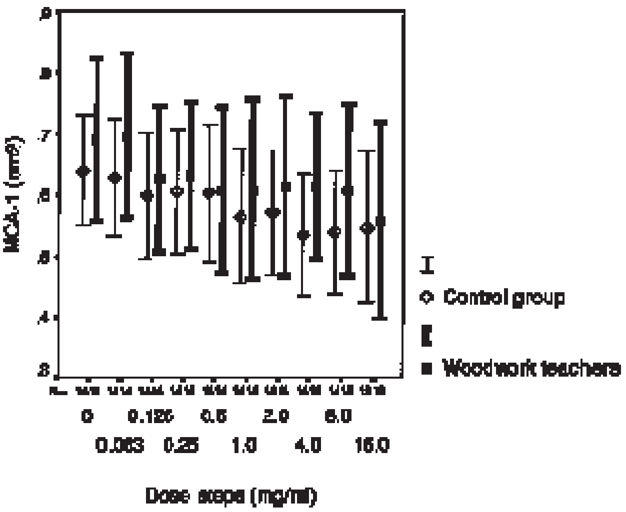
Figure 2. Vol-1 (upper figure) and Vol-2 (lower figure) at the different histamine dose steps.

The Pearson correlation coefficient for rated nasal blockage versus nasal dimensions was highest for Vol-2 ($r=-0.48$, $p<0.001$) and MCA-2 ($r=-0.34$, $p<0.001$) but lower for Vol-1 ($r=-0.15$, $p<0.05$) and MCA-1 ($r=-0.01$, $p>0.10$).

DISCUSSION

The woodwork teachers were selected from a questionnaire among subjects with work-related nasal complaints. Their complaints were confirmed in the present study from pre-challenge interview data including a higher rating score for nasal blockage compared to a healthy control group. The groups were therefore considered suitable for studying nasal histamine reactivity in wood-dust-related rhinitis.

Despite the picture of work-related rhinitis and nasal obstruction in the woodwork teachers group, there was no significant difference between the groups regarding pre-challenge acoustic rhinometry. This was somewhat unexpected. Previous studies have shown signs of swollen mucosa in wood workers' rhinitis (Wilhelmsson and Drettner, 1984). Hypothetically, nasal obstruction could be related to a swollen nasal mucosa which, in turn, should be accompanied by lower nasal volumes. Because the height was similar in the groups and atopic individuals were only seen among the teachers, these factors can hardly explain why pre-challenge acoustic rhinometry was similar in the groups despite the nasal obstructive symptoms in the teachers. A possibility is that mucosal swelling is not prominent enough in woodwork teachers' rhinitis to be detectable in small study groups. Another confounding factor might be that examinations were performed in hospital, for which reason acute exposure effects were not seen.



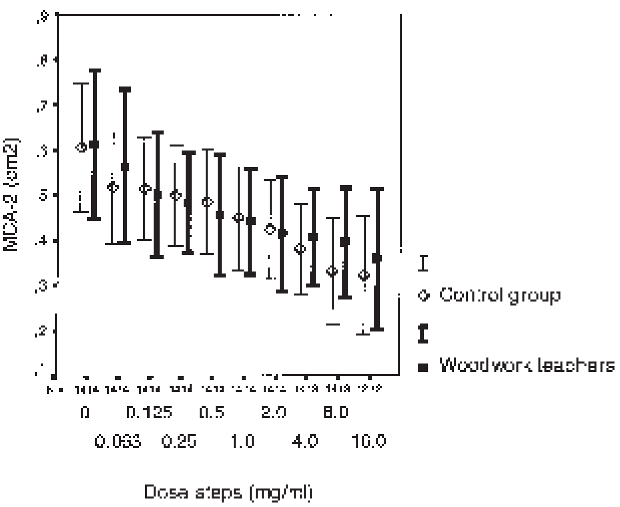


Figure 3: MCA-1 (upper figure) and MCA-2 (lower figure) at the different histamine dose steps.

The provocation was fulfilled to a high histamine dose giving all participants marked nasal complaints. During nasal histamine challenge, the woodwork teachers had more nasal complaints first at the highest histamine concentrations, and their dose-effect curve was not significantly steeper than the control group´s using rated symptoms or acoustic rhinometry as effect parameters. Therefore, nasal hyperreactivity is probably not a prominent feature of woodwork teachers' rhinitis, and larger study groups are probably required to detect significant differences between cases and controls.

The nose is a reactive organ as found after saline-provocation where great individual variations were seen (Table 3). Haavisto et al. (1998) drew the same conclusions after challenging subjects with non-allergic rhinitis and controls with saline. These authors found a non-specific reactivity of ±100-150% increase in nasal resistance after saline provocation. This must be taken into account when interpreting results of nasal provocation studies. The nose does not seem to be as stable as the bronchial tree, and bronchial histamine provocation is better standardised and more reproducible. For these reasons, nasal histamine or metacholine provocation tests have been difficult to standardise. This may partly explain why some authors have reported significant differences between the nasal responses to nasal histamine challenge in subjects with rhinitis and healthy controls (Clement et al., 1985; Okuda et al., 1983; van de Heyning et al., 1989; Hallén and Juto, 1993) while others have not (Doyle et al., 1990; van Wijk and Dieges, 1987; McLean et al., 1977). The fact that subjects with work-related rhinitis did not react more to histamine than non-rhinitic subjects did also raise the question of whether histamine is a suitable substance for testing nasal reactivity, an issue already raised by several authors (Doyle et al., 1990; van Wijk and Dieges, 1987; McLean et al., 1977).

Our study cannot be interpreted as being negative to acoustic rhinometry since the subjective evaluation of nasal symptoms during the provocation did not differ between the groups. Other studies show a poor correlation between the symptom and objective measures of nasal blockage (Åhman and Söderman, 1996a; Jones et al., 1989; Lane et al., 1996). In our study, the highest correlation was between rated blockage and Vol-2 reaching a maximum correlation coefficient of only –0.48. Our previous studies on woodwork teachers have shown that other factors than obstruction, especially impaired nasal muco-ciliary clearance, are of importance for the sensation of nasal blockage (Åhman et al., 1996b). Such mechanisms, and not mucosal hyperreactivity, might be predominant in wood dust related rhinitis.

In a previous study we found a tendency to higher albumin concentration in nasal lavage fluid from woodwork teachers, but no eosinophils were seen in the fluid. In patients with allergic rhinitis and vasomotoric rhinitis, nasal hyperreactivity is frequently seen. Nasal hyperreactivity has thus been shown to correlate with the eosinophil percentage in nasal lavage fluid (de Graaf-in't Veld et al., 1996). These facts also indicate that other mechanisms than nasal hyperreactivity act in wood dust related rhinitis.

Previous studies have shown that allergic subjects react to lower intra-nasal doses of histamine than non-allergic individuals do. In the present study we found the same for symptoms, i.e., allergic subjects got higher symptom indeces and lower PC_{15-50}. However, the difference was not significant, probably because there were so few allergic subjects (n=6).

In conclusion, our results do not indicate that nasal hyperreactivity is a prominent feature of wood-dust-related rhinitis.

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