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The influence of formaldehyde on the nasal mucosa

P. A. R. Clement, A. P. Stoop and L. Kaufman, Brussels, Belgium

SUMMARY

In 71 subjects (23 atopic patients, 22 hyperreactive patients and 26 normal test subjects) the authors twice performed a nasal provocation test with formaldehyde in three different concentrations. The test proved to be very much reproducible. There existed no clear-cut significant difference in the threshold for rhinorrhea, sneezing, tearing and pain in the three different groups. The difference in threshold for nasal blockade was very significantly different for the atopic and hyperreactive patients on one hand, and for the normal test subjects on the other hand. After the provocation a small increase in the mucociliary transport time was observed.

INTRODUCTION

According to Fasset (1963) aldehydes comprise one of the most important classes of industrial chemicals. According to the literature (Fasset, 1963; Kulle et al., 1975; Bardana, 1980; Björkman et al., 1982) the characteristic effects in humans of inhalation of formaldehyde gas are as follows: detection by odor well below 1 p.p.m. by nearly all persons; tingling sensation in the eyes, nose and posterior pharynx at 2-3 p.p.m.; at 4-5 p.p.m. the discomfort increases rapidly with some mild lacrimation, while concentrations of 10 p.p.m. are tolerated with difficulty for only a few minutes. More recently the interest in formaldehyde exposure has increased again since some investigators (Harris, 1953; Anderson et al., 1975; Elburg, 1978; Morin et al., 1978; Frigas et al., 1981; Cockcroft et al., 1982) reported indoor air pollution due to the increased use of chipboard and urea-formaldehyde foam as insulation material in the construction industry. Chipboard consists of wood shavings held together by a urea-formaldehyde glue which in the course of time releases formaldehyde gas. The field measurements in 23 dwellings performed by Andersen et al. (1975) showed on an average free formaldehyde levels of 0.52 p.p.m. which is more than the German threshold limit for occupational exposure. Bronchial constriction due to formaldehyde exposure has been very well documented in the literature (Popa et al., 1969; Hendrick et al., 1975; Hendrick et al., 1977; Kwong et al., 1983) and bronchial

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challenge tests with formalin have been performed by several authors (Popa et al., 1969; Hendrick et al., 1975 and 1977).
The influence of formaldehyde on nasal patency, however, has not been studied yet. Most investigators (Harris, 1953; Fasset, 1963; Kulle et al., 1975; Kwong et al., 1983; Wilhelmsson, 1985) report irritation of the nasal mucosa but objective findings in humans cannot be found in the literature. The aim of this study is to measure the influence of formaldehyde on nasal patency using passive anterior rhinomanometry (P.A.R.).

MATERIAL AND METHOD

A total of 71 subjects were distributed into three groups: the first group consisted of 23 atopic patients (typical history confirmed by skin test and RAST), the second group consisted of 22 patients with an aspecific hyperreactivity of the nasal mucosa (non-atopic patients with rhinitis complaints and a low nasal histamine threshold of less than 2 mg/ml: Clement et al., 1985) and the third group was composed of 26 normal test subjects. The third group had three nasal challenges (two with formaldehyde and one with placebo) while all the patients had a nasal provocation test twice with formaldehyde (in an aqueous solution) only. Three concentrations were used, i.e.: 0.003, 0.03 and 0.3 per cent and a pH ranging from 7.48 to 7.50. All subjects were first challenged with saline, and the nasal patency was tested using P.A.R. (Passive Anterior Rhinomanometry: Clement et al., 1981). Then the actual provocation test with formaldehyde was started using a Heyer nebulizer with 12 μ particles for three times 10 seconds in each nostril or a total formaldehyde exposure time of 60 seconds. The first provocation was performed with the lowest concentration of 0.003 per cent which is approximate 10 times lower than the concentration used by Popa et al. (1969). Immediately after provocation nasal patency was measured, and again after 5 minutes. If none of the nasal cavities showed a significant increase of the nasal resistance (i.e. twice the initial value) another nasal provocation was performed with the next formaldehyde concentration of 0.03 per cent. The method was repeated until a significant increase in nasal resistance was observed or until the highest concentration of 0.3 per cent was reached.
The following subjective parameters were also noted: rhinorrhea, sneezing, tearing and pain. To avoid direct stimulation of the ocular mucosa all provocations were performed with goggles.
Because formaldehyde can be very irritating, damage to the mucosa was excluded by measuring the mucociliary transport time using saccharin-toluidine blue (Brondeel et al., 1983). The mucociliary transport time was measured for the first time before the first provocation test (m_1b) and after the first provocation test (m_1a). The second provocation test was carried out one week later and this time the mucociliary transport was only measured after the provocation (m_2a).

In the third group (normal test subjects) a third provocation was performed one week after the second with placebo, and again the mucociliary transport time was measured after the test (m_3a).

RESULTS

A. *Rhinorrhea*

Sixty (84%) out of 71 subjects did not show any rhinorrhea during or after formaldehyde challenge. When rhinorrhea was experienced it occurred at a concentration of 0.003 or 0.03%. The second provocation one week later showed an identical result in 61 (85%) of the subjects. Table 1 shows the reproducibility for the different groups.

Table 1. Reproducibility of the presence or absence of rhinorrhea.

	good reproducibility	no reproducibility	number of patients
atopic	21	2	23
hyperreactive	15	7	22
normal	25	1	26
total			71

B. *Sneezing*

Forty-eight (68%) of the subjects did not sneeze. Those who sneezed dit it at a concentration of 0.03%. In 56 subjects (79%) there existed a good reproducibility (Table 2).

Table 2. Reproducibility of the presence or absence of sneezing.

	good reproducibility	no reproducibility	number of patients
atopic	18	5	23
hyperreactive	18	4	22
normal	20	6	26
total			71

C. *Tearing*

All subjects (100%) experienced tearing of the eyes although goggles prevented direct contact of the formaldehyde with the eye mucosa. This result (Table 3) was reproducible in 62 subjects (87%).

Table 3. Reproducibility of tearing at the same concentration.

	good reproducibility	no reproducibility	number of patients
atopic	16	7	23
hyperreactive	20	2	22
normal	26	0	26
total			71

Tearing occurred during the second provocation at the same concentration in 16 of the atopic patients (70%), and in 20 and 26 respectively for the hyperreactive patients (90%) and normal patients (100%). In the latter two groups it always occurred at the highest concentration.

D. *Pain*

Pain was experienced by only 10 subjects (14%), of whom 6 had pain during the two consecutive provocations, and 4 only during one provocation. The reproducibility of the presence or absence of this symptom is shown in Table 4.

Table 4. Reproducibility of the presence or absence of pain.

	good reproducibility	no reproducibility	total number of subjects
atopic	23	0	23
hyperreactive	19	3	22
normal	25	1	26
total			71

There existed no significant difference (chi-square tests $p > 0.05$) in the three symptoms (rhinorrhea, sneezing and pain) among the different groups. Only for tearing, there existed a significant difference ($p \leqslant 0.05$) between the atopic and normal test subjects for both provocations, which means that there were some allergic patients (22% the first time and 35% the second time) who experienced tearing at a concentration level of 0.03% instead of 0.3%.

E. *Nasal blockade*

Chi-square tests showed a very significant difference of the concentration at which the nasal blockade occurred between the atopic and hyperreactive patients on one hand, and the normal test subjects on the other hand (Table 5).

F. *Mucociliary transport*

T-test showed that for the atopic and hyperreactive patients there existed no significant difference between the mucociliary transport time after the first (m_1a) and the second provocation (m_2a). This difference was slightly significant for the same parameters in the normal test subjects ($p = 0.06$). For all three groups together there existed a significant difference between the mucociliary transport time before (m_1b) and after (m_1a) the first provocation ($p = 0.05$). The mucociliary transport time went from an average value of 16.6 minutes before to an average value of 18.9 minutes after the first provocation.

Table 5. Formaldehyde threshold at which nasal blockade (twice the initial resistance value) occurred during provocation.

	concentration threshold	0.003%	0.03%	0.3%	no nasal blockade	significant difference
A. *Between atopic and hyperreactive*						not significant
B. *Between atopic and normal test subjects*						
first provocation	atopic	0	9	11	3	$0.001 < p \leqslant 0.01$
	normal	0	0	16	10	
second provocation	atopic	0	10	12	1	$p \leqslant 0.001$
	normal	0	0	15	11	
C. *Between hyperreactive and normal test subjects*						
first provocation	hyperactive	1	8	12	1	$p \leqslant 0.001$
	normal	0	0	16	10	
second provocation	hyperactive	0	0	16	1	$0.001 < p \leqslant 0.01$
	normal	0	0	15	11	

DISCUSSION

From our data it is obvious that formaldehyde can induce rhinorrhea (16%), sneezing (32%) and pain (14%) in patients and test subjects, but only in a minority of cases. Tearing on the other hand occurred in all patients and test subjects although the nasal provocation test was performed with goggles. This means that for these four symptoms the threshold for tearing is obviously lower than for the other symptoms. The fact that goggles did not prevent tearing means that it is probably induced by direct trigeminal stimulation, a fact that has been confirmed in tests with laboratory animals (Kulle et al., 1975). Consequently it seems that there exists no clear-cut threshold difference for trigeminal nerve stimulation among the three groups (only 24% and 34% of the atopic patients experienced tearing at a lower concentration of formaldehyde).

On the other hand there exists a very significant difference ($0.001 \leqslant p \leqslant 0.01$) in the nasal blockade threshold between the atopic and hyperreactive patients on one hand, and the normal subjects on the other hand. This could mean that this symptom is not triggered completely by the same mechanism as the other symptoms.

Concerning the mucociliary transport it is obvious that there is a significant ($p = 0.05$) difference in the mucociliary transport time before and after the nasal provocation with formaldehyde. This period of time, however, still falls within the values found by Brondeel et al. (1983) in normal test subjects (4–16 minutes) and atopic patients (7–25 minutes).

The question whether a formaldehyde provocation test can prove a hyperreactive state in an environment of particle board and urea-formaldehyde insulation foam, has not been solved by this experiment. It might be that with formaldehyde

resins other components rather than the free formaldehyde gas (Cockcroft et al., 1982) are responsible for the disease of the respiratory tract. This has been clearly demonstrated in formaldehyde dermatitis by Berrens et al. (1964). Therefore this matter calls for further research.

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P.A.R. Clement
E.N.T.-department
A.Z.-V.U.B.
Laarbeeklaan 101
B-1090 Brussels
Belgium