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Pulmonary Function in Persons Who are Professionally Exposed to Formaldehyde Fumes

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A B S T R A C T

The present study examines long-term effects of occupational exposure to formaldehyde fumes on lung function. Forced spirometry and diffusing lung capacity were measured in 16 health-service professionals (8 medical doctors and 8 laboratory technicians) working at the pathoanatomic laboratory for at least 4 years with daily exposure 8±1 hours. Control group employed 16 males, which were matched by age and stature to members of the exposed group. Only non-smokers were included in the study. Spirometric parameters in study participants exposed to formaldehyde fumes compared to control group were not significantly different indicating absence of restrictive and/or obstructive deterioration of lung function in exposed group. The only parameter differing in two groups was blood volume of pulmonary capillaries (Vc') which was significantly larger in a group exposed to formaldehyde fumes. The possibility that the hyperemic lung reaction is the consequence of the exposure to formaldehyde fumes should be further explored.

Key words: *formaldehyde, pulmonary function, diffusing capacity, occupational health hazards*

Introduction

Formaldehyde is widely used as a preserving, disinfecting and embalming agent. In addition to its technical benefits, formaldehyde has eliminated many health hazards during histological procedures in anatomy and pathology laboratories. Paradoxically, formaldehyde itself is a noxious chemical, highly unpleasant to the user, and a well-recognized occupational health hazard[1–4]. Formaldehyde has been reported to produce allergic contact dermatitis[5], neurobehavioral changes[6] and carcinogenesis[7].

Symptoms of respiratory irritancy and effects on pulmonary function have been examined in studies of both indoor and ambient air exposure to formaldehyde[8–12]. Exposure to formaldehyde fumes is almost exclusively occupational, and has been investigated in workers in the production of resinembedded fibreglass[13–14], chemicals, furniture, and wood products[15–18] or through employment in the funeral services industry[19]. Short-term effects of formaldehyde exposure included symptoms of irritation of the eye and respiratory tract. Workers in these studies were exposed to mean formaldehyde concentrations of 0.16 ppm (0.10–0.12 mg/m^3) and greater. In a survey in which the dosage of exposure was considered[10,20] formaldehyde was a statistically significant predictor of symptoms of eye, nose and throat irritation, phlegm, cough and chest complaints. Short-term effects of occupational exposure to formaldehyde fumes on lung function were also investigated but with controversial conclusions. Some studies reported decreased lung function in workers exposed to formaldehyde[9–11] others concluded that the formaldehyde was not associated with decrements in lung function[8,12]. Asthmatic symptoms and lowered FEV_1, MEFs in studies by Fransman et al.[9] and by Bender[11] showed dose-response effects but in both studies authors concluded that lung function changes are re-

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versible. Since the long-term effects of professional exposure to formaldehyde fumes on lung function are not well established, the aim of the present study is to examine lung function parameters in persons working 4–20 yrs. in pathoanatomic laboratory.

Materials and Methods

The present study was designed to examine long-term effects of professional exposure to formaldehyde fumes on lung function. Exposed group encompasses 16 male health-service professionals (8 medical doctors and 8 laboratory technicians) working at the University of Split. All exposed examinees were working in the pathoanatomic laboratory for at least 4 years with daily exposure 8 ± 1 hours. Control group employed 16 males that were matched by age and stature to exposed group. To avoid possible additive or synergistic effects of smoking on lung function[21–23], only non-smokers were included in the study. All 32 examinees voluntarily participated in the present study.

The following pulmonary function measurements were considered: forced vital capacity (FVC), forced expiratory volume in 1st second (FEV_1), forced midexpiratory flow rates (PEF, MEF_{25}, MEF_{50}), diffusing lung capacity for carbon monoxide (DLCO), Kroch constant (DLCO/VA), blood volume of pulmonary capillaries (Vc') and membrane diffusion capacity (Dm).

Forced spirometry measurements were recorded by Masterlab from Jaeger instrument. The testing was performed in a sitting position without a noseclip. Each examinee was instructed to perform acceptable maneuvers. The FVC maneuver was repeated three times and the best values were taken from any of the acceptable tracings.

For a single breath (10 s breathhold) DLCO measurements an inspired concentration of 0.3% CO, 0% He, 21% O_2, and balance N_2 was used. Before the DLCO test was performed each subject was instructed in all required maneuvers, emphasizing the importance of giving a sign when at the level or residual volume (maximal expiration) inhaling the test gas mixture rapidly to vital capacity, continuing to hold the breath (assisted by the valve system) for 10 s, and exhaling volume of at least 2.0 L rapidly. The effective breathhold time included two-thirds of the inspiratory time and the portion of the expiratory time until one half of the alveolar sample was obtained. This procedure is automatically built into the instrument. Two satisfactory tests were carried out with an interval of at least 4 minutes between the two tests and their average was taken. The subjects rested for at least 30 minutes before the start of each test. One trained technician did 94% of the tests. All tests were performed between 9 a.m. and 1 p.m.

The reference values for DLCO, DLCO/VA where VA is the alveolar volume, Dm and Vc' were those of Cotes and Hall[24] and for forced spirometry parameters those of Cotes[25]. These reference values agreed well with values for healthy population tested in our laboratory[26].

Dm and Vc' estimates were done according to the Roughton and Foster's formula:

$$1 / TLCO = 1 / Dm + 1 / Vc'\Theta$$

Where TLCO is carbon monoxide transfer factor, Θ is the rate of CO binding to hemoglobin and is generally dependent on the examinee's mean oxygen tension in the pulmonary capillaries ($Pc'O_2$), Hb and COHb, as follows:

$$1 / \Theta \text{ (ml blood min mmHg ml}^{-1}\text{ CO)} = [0.006\ (Pc'O_2(\text{mmHg}) + 0.33)]\ 14.6 / Hb\ (\text{g/dl}^{-1})\ (1 - \%\ COHb / 100)$$

$Pc'O_2$ may be assessed as:

$$Pc'O_2\ (\text{mmHg}) = PAO_2\ (\text{mmHg}) - 10$$

or more accurately, from oxygen consumption and Dm. In order to calculate Dm and Vc' from equations (1) – (3), measurements were made at two levels of alveolar oxygen tension, room air and after breathing 100% oxygen for 10 min, providing two equations with two unknowns: Dm and Vc'. The explicit solutions are:

$$Vc'\ (\text{ml}) = (Hb / 14.6)\ \frac{0.006\ [PA\ O_2\ (\text{oxygen}) - PA\ O_2\ (\text{air})]}{1 / DLCO\ (\text{air}) - 1 / DLCO\ (\text{oxygen})}$$

$$Dm\ (\text{ml x CO/mmHg x min}) = \frac{1 / .(\text{oxygen}) - 1 / .(\text{room air})}{1 / .(\text{oxygen})\ 1 / DLCO\ (\text{air}) - 1 / .(\text{air})\ 1 / DLCO\ (\text{oxygen})}$$

The pulmonary function test results were interpreted using the criteria of Konig et al.[27]:

(a) normal finding: FVC ≥ 80% predicted; FEV_1/FVC ≥ 70%; MEF_{25}, MEF_{50}, and MEF_{75} ≥ 60% predicted and DLCO ≥ 80% predicted;

(b) restrictive impairment: FVC < 80% predicted and FEV_1/FEC ≥ 70%;

(c) obstructive impairment: FEV_1/FVC < 70%;

(d) isolated DLCO reduction: DLCO < 80% predicted, as a sole finding and

(e) DLCO > 120% predicted was described as isolated DLCO increase.

Comparison between study participants exposed to formaldehyde fumes and control group in diffusing lung capacity and in lung function parameters was carried out by means of Student's t-test for independent samples. The difference between groups at $p < 0.05$ was considered as statistically significant.

Results

Descriptive statistics of age, height, weight, body mass index (BMI = weight (kg) / height (m)^2), years of professional exposure to formaldehyde fumes and lung function parameters (percentage of expected values) in 16 exposed participants is presented in Table 1. Table 2 provides the results of the comparison of spirometric parameters in study participants exposed to formaldehyde

TABLE 1
AGE, HEIGHT, WEIGHT, BMI, YEARS OF EXPOSURE AND LUNG FUNCTION PARAMETERS (% EXPECTED) IN STUDY PARTICIPANTS EXPOSED TO FORMALDEHYDE FUMES (N=16)

	X	SD	Min	Max
Age (yrs)	38.06	8.16	25	52
Height (cm)	166.5	7.4	156	182
Weight (kg)	68.88	12.04	55	104
BMI (kg/m^2)	24.78	3.44	19.71	33.28
Exposure (yrs)	12.38	5.21	4	20
FVC (%)	111.43	14.35	90.1	139
FEV_1 (%)	111.95	13.09	91.7	137
FEV_1/VC (%)	107.81	5.69	93.9	117
PEF (%)	99.03	19.02	62.1	124
MEF_{50} (%)	104.27	22.95	71.9	139
MEF_{25} (%)	102.18	22.32	69.2	143
DLCO (%)	101.13	27.44	63	141
DLCO/VA (%)	95.94	11.13	70	112
Vc' (%)	103.38	18.18	76	132
Dm (%)	88.38	11.12	72	111

BMI – weight (kg) / height (m)^2, FVC – forced vital capacity, FEV_1 – forced expiratory volume in 1st second, PEF, MEF_{25}, MEF_{50} – forced midexpiratory flow rates, DLCO – diffusing lung capacity for carbon monoxide, DLCO/VA – Kroch constant, Vc' – blood volume of pulmonary capillaries, Dm – membrane diffusion capacity

TABLE 2
LUNG FUNCTION PARAMETERS IN STUDY PARTICIPANTS EXPOSED TO FORMALDEHYDE FUMES COMPARED TO CONTROL GROUP

	Exposed group (N=16)		Control group (N=16)		t-test
	X	SD	X	SD	p
FVC (%)	111	14	106	11	ns
FEV_1 (%)	112	13	102	9	ns
FEV_1/VC (%)	108	6	96	6	ns
PEF (%)	99	19	92	13	ns
MEF_{50} (%)	104	22	110	20	ns
MEF_{25} (%)	102	22	105	25	ns

FVC – forced vital capacity, FEV_1 – forced expiratory volume in 1st second, PEF, MEF_{25}, MEF_{50} – forced midexpiratory flow rates, ns – nonsignificant

fumes compared to control group. Exposed group did not show any difference in mean values of either examined forced spirometry parameters – FVC, FEV_1, PEF, MEF_{25}, MEF_{50} and MEF_{75}. However, 25% of exposed participants showed incipient changes in small respiratory airways.

The comparison of diffusing lung capacity for carbon monoxide (DLCO), Krogh constant (DLCO/VA), blood volume of pulmonary capillaries (Vc') and membrane diffusion capacity (Dm) in participants exposed to formaldehyde fumes compared to control group is shown in Table 3. The measured values of diffusing lung capacity for carbon monoxide (DLCO) and membrane diffusion capacity (Dm) in exposed group fell within expected referent values. While, blood volume of pulmonary capillaries (Vc') showed to be significantly higher in a group exposed to formaldehyde fumes in comparison with control group.

TABLE 3
DIFFUSING LUNG CAPACITY PARAMETERS IN STUDY PARTICIPANTS EXPOSED TO FORMALDEHYDE FUMES COMPARED TO CONTROL GROUP

	Exposed group (N=16)		Control group (N=16)		t-test
	X	SD	X	SD	p
DLCO (%)	101	27	105	6	ns
DLCO/VA (%)	95	11	90	5	ns
Vc' (%)	103	18	81	9	<0.001
Dm (%)	88	11	89	11	ns

DLCO – diffusing lung capacity for carbon monoxide, DLCO/VA – Krogh constant, Vc' – blood volume of pulmonary capillaries, Dm – membrane diffusion capacity, ns – nonsignificant

Discussion

Occupational hazards of formaldehyde were thoroughly investigated but the studies were primarily dealing with its possible carcinogenic effects[28–32]. Only small proportion of studies were oriented towards inflammatory reactions of respiratory system relating exposure to formaldehyde fumes inhalation to dynamic changes (short-term and long-term) in bronchial and pulmonary symptoms and function.

Various studies provided the evidences that formaldehyde is an irritant of the respiratory tract[13,17,19,33] that causes nonproductive cough, breathing problems, eye tears and nose dripping. There is a correlation between clinical symptoms and concentration of formaldehyde in the workplace[20]. Usual concentration provoking symptoms being from 10 to 20 ppm.

The possibility of the occurrence of asthmatic reactions, or even asthma itself was also suggested by some authors[34]. The inhalation of formaldehyde fumes causes bronchial hyperactivity[35] and – according to some authors – the reductions of air circulation speed as well[15]. However, the increases of respiratory values were reported in some other studies[16].

Results of investigations of effects on pulmonary function in occupationally exposed populations are somewhat conflicting. Pre-shift reductions (considered indicative of chronic occupational exposure) of up to 12% in parameters of lung function (e.g., forced vital capacity, forced expiratory volume, forced expiratory flow rate) were reported in a number of smaller studies of chemical, furniture and plywood workers[15–18,36]. In general, these effects of lung function were small and transient over a work shift, with a cumulative effect over several years that was reversible after relatively short periods without exposure (e.g. 4 weeks); effects were more obvious in non-smokers than in smokers[37,38]. In the subset of these investigations in which exposure was monitored for individuals (i.e., excluding only that of Malaka and Kodama 1990[18]), workers were exposed to mean concentrations.

The present study examines lung function parameters in laboratory technicians and medical doctors professionally exposed to formaldehyde. The long-term effects of exposure were examined by comparing their spirometric indicators and diffusing capacity parameters with non-exposed subjects. The study showed that flow/volume curves were within reference values in all 16 examined subjects (Table 1).

The clinical symptoms of nonproductive cough and eye tears were present in 80% of exposed subjects, whereas 20% of the examinees have subjectively present breathing complaints.

When compared to unexposed controls the only lung function parameter significantly differing in exposed group was the blood volume of pulmonary capillaries, which was significantly higher in exposed group. The increase of the blood volume of pulmonary capillaries in persons exposed to formaldehyde is also radiologically confirmed[39,40]. One of the explanatory hypotheses includes the hyperemic lung reaction as the consequence of the exposure to environmental irritants including formaldehyde.

Although mean values of all other parameters were within normal ranges it should be mentioned that the lungs' diffusion capacities in 16 examinees professionally exposed to formaldehyde showed to be rather divergent. Increased diffusion capacity has been recorded in eight examinees (50%), a decrease of diffusion capacity has been recorded in three examinees, whereas only in five examinees the recorded values fall within normal range. The diffusion capacity of the lungs showed a tendency to be related with the years of exposure: exposure to formaldehyde fumes inhalation up to ten years causes an increase of the diffusion capacity of the lungs; exposure to formaldehyde fumes inhalation more than ten years causes a decrease of the diffusion capacity of the lungs. A larger sample is needed to provide sufficient evidences to confirm above findings.

Conclusions

The present study of lung function in 16 persons working in pathoanatomic laboratory being daily professionally exposed to formaldehyde fumes showed that:

– No respiratory function impairments, either of the obstructive or restrictive type, were detected;

– No relation between clinical symptoms and pulmonary function tests has been found;

– When compared to unexposed controls the only lung function parameter significantly differing in exposed group was the blood volume of pulmonary capillaries, which was considerably higher in exposed group. The possibility that the hyperemic lung reaction is the consequence of the exposure to formaldehyde fumes should be further explored.

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PLUĆNA FUNKCIJA U OSOBA PROFESIONALNO IZLOŽENIH PARAMA FORMALDEHIDA

S A Ž E T A K

Dinamička spirometrija i difuzijski kapacitet pluća određen je u 16 ispitanika koji rade u patoanatomskom laboratoriju. U istraživanje su uključeni samo nepušači. Minimalna dnevna izloženost formaldehidu je bila osam sati, a svi ispitanici rade najmanje četiri godine u laboratoriju. Kontrolnu skupinu sačinjavalo je 16 ispitanika slične dobi koji nisu bili izloženi udisanju formaldehida. Nisu pronađene značajne smetnje u ventilacijskim vrijednostima kao ni restrikcijski, a ni opstrukcijski poremećaji ventilacije. Povećan difuzijski kapacitet zabilježen je u 50%, a smanjen u 18,8% ispitanika skupine izložene formaldehidu. Ova studija je pokazala da je među provedenim testovima plućne funkcije samo razina volumena krvi plućnih kapilara statistički značajno različita između dviju skupina. Ispitanici profesionalno izloženi parama formaldehida pokazali su povećanje u odnosu na kontrolnu skupinu u razini volumena krvi plućnih kapilara. To je po mišljenju autora posljedica hiperemijske reakcije u plućima, što je radiološki i potvrđeno.