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ORIGINAL PAPERS

FORMALDEHYDE – INDUCED BRONCHIAL ASTHMA – DOES IT REALLY EXIST?

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Abstract: These studies try to explain if there is a correlation between exposure to formaldehyde (FM) and bronchospastic reactions. 367 workers were examined in our study. They were aged 23 to 52. They had been exposed occupationally to FM at concentration not exceeding 0.5 mg/m^3. All subjects suffered from respiratory symptoms; 14 had chronic bronchitis, 2 bronchial asthma. A history was taken and spirometry performed (peak expiratory flow (PEF)) with use of a single blind crossover method, in a three-day clinical observation. All subjects were provoked with histamine (PC_{20}). Skin prick tests with common allergens, a patch test with FM and formaldehyde-specific IgE antibodies assay were performed. There were no significant differences in the respiratory parameters during the three-day clinical observation. Two subjects were supposed to have bronchial asthma induced by FM, but for lack of differences in respiratory parameters the occupational background of their asthma was excluded. None of the subjects complained of significant irritant symptoms. On the basis of our results one may doubt that FM is capable of acting as a respiratory sensitizer.

INTRODUCTION

Formaldehyde (FM) is a common environmental pollutant (1) present both in homes and workplaces. For many years FM has been considered as a potential cause of bronchial asthma, allergic rhinitis, contact dermatitis and acute respiratory mucosa reactions. The Occupational Safety and Health Administration (OSHA) estimates that about 1.3 million US workers are chronically exposed to FM (1). In Poland approximately 14,000 people are exposed to FM in workplaces in the textile industry.

Major outdoor contamination is due to combustion of wood, fuels and

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alcohol (1). Glues and dyes are the major sources of FM in homes. FM evokes a transient irritation of eyes and mucous membranes. Several authors reported bronchitis and parenchymal lung diseases due to excessive levels of FM.

Vaughn and Black (10) reported a possibility of FM-induced bronchial asthma in 1939. Some later data have also suggested an asthmogenic effect of FM because a bronchospastic reaction in a contaminated atmosphere was found. Allergic tests with FM were negative and other chemicals were not tested. Such controversial results point to the need for differentiation between an irritant and an allergic bronchospastic reaction to FM in chronically exposed subjects.

MATERIALS AND METHODS

The study was performed in two textile and one shoe manufacturing factories on 367 workers occupationally exposed to FM at a concentration not exceeding 0.5 mg/m^3 for at least one year (average $\pm$ 12 years). They were aged from 23 to 52 (average age 46).

The diagnosis of chronic respiratory disease was performed according to the criteria of the American Thoracic Society. Resting ventilatory function was measured by spirometry. Vital capacity (VC), forced expiratory volume (FEV_1) and peak expiratory flow (PEF) were estimated at the beginning of the work-shift and immediately afterwards.

The histamine provocation test was performed using the method described by Cockcroft (2) to calculate the histamine provocation concentration producing a 20 percent reduction in FEV_1 (PC_{20}). The histamine inhalation test was performed at the beginning of the work-shift at 6 a.m.

In subjects suffering from chronic cough, dyspnoea or sneezing, the test was repeated at the end of the work-shift. In those persons PEF was measured during the course of a three-day clinical observation in the following way:
Day 1 – PEF was performed at the beginning of the work-shift and every 60 minutes for at least 3 hours.
Days 2–3 – PEF was performed as on the first day but the subjects used a placebo or bronchodilatator (a single blind crossover method).

All workers were also tested with the skin prick method with the use of common allergens: house dust, Dermatophagoides, feathers, pollens (Beecham-Bencard Allergy Service). In all workers a total serum IgE level was performed. In patients with suspected respiratory allergic reactions the Phadiatop test (Pharmacia) was additionally performed. A formaldehyde-specific IgE antibodies assay (serologic assessment with ELISA) and a patch test for formaldehyde sensitization of the skin were performed in all patients with asthma or chronic rhinitis.

RESULTS

In all of 367 subjects, a chronic cough appeared to be the sole symptom of bronchitis. Ninety-two of them were heavy smokers, whereas 7 had earlier abandoned smoking. Fourteen other subjects suffered from dyspnoea with

clinical signs of chronic bronchitis. Acute episodes of dyspnoea, classified as bronchial asthma, were found in 2 subjects, an illness lasted 2 and 7 years, respectively.

Both subjects confirmed symptom exacerbation at their work-place. One person was a textile worker, whereas the second was a female office worker. The symptoms of her asthma had begun after exposure to an undetermined glue and occurred when she visited a work-place with significant exposure to FM. Sometimes sneezing also accompanied bronchospastic symptomps. An 8-hour long occupational exposure to FM (the concentration 0.5 mg/m^3) did not intensify either cough or dyspnoea. None of the bronchitic patients developed clinical symptoms of bronchial irritation. Mean values of ventilatory parameters in the group of 367 subjects were: VC = 3.47 $\pm$ 1.411, FEV_1 = 3.1 $\pm$ 0.19 l/s. In the group of bronchitic patients the mean value of VC was 3.03 $\pm$ 1.92 l and FEV_1 2.13 $\pm$ 1.82 l/s. In 14 bronchitic patients the changes of PEF during the three-day observation did not exceed 20% of the initial value; only 2 patients reacted with a decrease of PEF at the end of a non-placebo, non-bronchodilatator day, but no difference between placebo-and-bronchodilatator days were found. The mean value of PC_{20} in bronchitic patients was 5.61 mg/ml ($\pm$ 1.79).

The textile worker suffering from asthma, exhibited an exacerbation of subjective symptomps at the end of his workshift, but no significant differences in PEF exceeding 20% of initial values during the three-day observation were noted. In these 2 asthmatics PC_{20} was also determined after termination of the work-shift; in both cases a significant decrease from 3.41 to 1.97 mg/ml and from 2.70 to 2.01 mg/ml was noted after exposure to FM. In these subjects positive skin prick tests, Phadiatop test and elevated IgE level were found. No specific IgE antibodies were detected and skin patch tests to FM were negative.

Positive skin prick tests occurred in 18 out of the 367 workers. None of them suffered from chronic spastic bronchitis (but 2 were asthmatic). Seven other positive prick tests occurred in patients with pollen-induced symptomps. No specific IgE antibodies to FM were detected in bronchitic patients. Bronchial hyperreactivity to histamine (PC_{20} < 12 mg/ml) was found in 11 non-bronchitic patients.

DISCUSSION

FM is usually described as an immunogen (5). Hypersensitivity to FM in the form of contact dermatitis is well-documented. Ambient FM primarily affects the upper airways and eyes. The eyes of human subjects react with irritation to as little as 0.012 mg/m^3 FM (7). Some authors have also observed bronchospastic reaction in occupationally exposed subjects. However, the asthmogenic effect of FM seems to be controversial. Hendrick (3) described a dialysis nurse with a significant fall in FEV_1 after 2 to 4 hours exposure in a provocation test with FM. Schoenberg observed that workers developed chronic airway obstruction after long-term exposure to phenol-formaldehyde

resins (8). Other authors have not presented convincing data for differentiation between allergic and irratative bronchospastic reactions in occupationally exposed asthmatics. The objective results of our study did not confirm that FM could induce asthma. We did not observe any reaction to FM in the skin tests. No specific IgE antibodies to FM were detected. The objective ventilatory method did not reveal any bronchial reaction. A small decrease of PC_{20} in our subjects may be due rather to irritant than the allergic influence of FM. FM at a concentration below 0.5 mg/m^3 did not provoke significant irritant reactions, even in hyperreactive bronchitic patients. One can expect however such reactions at higher concentrations (6,7). Subjects with the bronchial hyperreactivity should not be employed in areas of exposure to FM. Our study suggests that FM is capable of acting as a respiratory irritant but there is no consistent evidence indicating that FM is capable of being a respiratory sensitizer. FM does not induce bronchial hyperreactivity but it can decrease PC_{20} in hyperreactive subjects. Such results allow us to doubt whether formaldehyde asthma really exists. Even if it does, it is a very rare disease (4, 9).

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