Respiratory Symptoms and Occupational Asthma in Polyurethane Foam Production Workers

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Abstract

Toluene diisocyanate (TDI) and methylene diphenyl diisocyanate (MDI) and hexamethylene diisocyanate (HDI) are heavily used in the production of polyurethane foams. Occupational asthma (OA) is reported in approximately 5% of chronically exposed workers. This study aimed to evaluate the effects of isocyanate exposure on lung function in foam production workers in two different factories. Respiratory status was evaluated by a questionnaire modified from the occupational asthma report of ATS, physical examinaton and pulmonary function tests. Pulmonary function was evaluated using a mobile spirometer.

107 workers (1 female, 106 male) were included in the study. 77 of these were working in polyurethane foam production (49 in one, 28 in a second factory), 18 in a dye department and 12 (the control group) were working in the offices (mean age, 26, 30, 27.5 and 31, respectively). All 3 groups were comparable in age and smoking habits. There were also no significant differences in frequency of respiratory signs and symptoms. However, pulmonary function tests showed significantly lower forced expiratory volume (FEV) and forced vital capacity (FVC) values in the polyurethane group. Of the 32 workers who had respiratory findings suggestive of asthma and who underwent peak expiratory flow (PEF) meter follow-up, 17 were found to show positive variability. Non-specific bronchial provocation tests were performed on these 17 workers and 3 (all of them were polyurethane production workers) were diagnosed as occupational asthma (3.89%). The results of the study indicate a need for the screening and monitoring of all polyurethane foam workers for isocyanate-related respiratory disorders and OA.

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Introduction

Isocyanates are low molecular weight compounds used in the manufacture of polyurethane foams, varnishes, paints and plastic materials. Of these compounds, toluene diisocynate (TDI), methylene diphenyl diisocyanate (MDI) and hexamethylene diisocyanate (HDI) are the most commonly used (1). TDI and MDI are primarily used in production of flexible polyurethane foams and workplace exposures to this agent can cause asthma (2). Workplace-induced asthma is encountered in approximately 5-10% of TDI production workers (3,4). The only study from Turkey was on automobile and furniture painters from Eskişehir and the occupational asthma (OA) rate in this study was given as 9.6% (4).

Isocyanates were also reported to be potent irritants, producing

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acute lacrimation and respiratory irritation even at very low levels (5), and also capable of causing severe reactions (6) and protracted illness or loss of function (5,7-11). Hypersensitivity pneumonia has been the subject of a few reports (12-14) but this is very rare and depends on susceptibility factors as asthma does.

This study was undertaken to evaluate the effects of isocyanate exposure on lung functions and determine the prevalence of respiratory symptoms and OA among polyurethane foam workers.

Materials and Methods

Workers in two different factories in Manisa were included in the study. MDI and TDI were being used in both factories for the production of polyurethane foam. 107 workers (1 female and 106 male) were included in the study. 77 of these workers were in the polyurethane group, 18 in the dye group and 12 worked in the offices. This latter group served as controls. Polyurethane workers were exposed to TDI in the production of foam and isolation of refrigerators. Dye workers were using spray dye without isocyanate. The central climatisation system and air filtering were well equipped and isolated in the work places of all 3 groups. All workers were working for a mean period of 10 hours per day and 5 days per week. No masks or gloves were used during work.

The algorithm of the study was designed in accordance with the criteria of the United States National Institute for Occupational Safety and Health (NIOSH) for occupational asthma (4,15,16). The study was conducted in three phases.

Phase 1. This phase of the study consisted of an evaluation of the respiratory system by subjecting all participants to a structured interview (questionnaire) in addition to a physical examination and pulmonary function tests, all performed in the workplace. The questionnaire was a modified form of that given in the occupational asthma report of the American Thoracic Society (ATS) and included demographics and a history of work, of symptoms if any and smoking habits. (17,18). Following a complete examination of the respiratory system, all workers underwent pulmonary function tests using a mobile spirometer (MIR Spirobank- 0476). Peak expiratory flow (PEF), forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio and vital capacity (VC) were recorded. The procedure was performed according to ATS criteria, repeated 3 times for each worker and the best value was recorded and % predicted values were evaluated (17,18).

The presence of at least one of the characteristic symptoms of asthma which were cough, wheezing, dyspnea, chest tightness and their occurrence in the workplace and improvement during weekends, holidays and on the days away from work were considered as suggestive of occupational asthma. To be able to evaluate the atopic status, questions pertaining to symptoms and findings of allergic rhinitis, conjunctivitis and dermatitis were also asked

Phase 2. Workers suspected of having asthma or occupational asthma as a result of their answers to the questionnaire (the presence of at least one of the characteristic symptoms of asthma and occurrence of the symptoms in the workplace and improvement during weekends, holidays and on the days away from work), their physical findings and pulmonary function test results, were subjected to a PEF meter follow-up. Personal best peak flow meter NO 755 type was used. The test was given twice a day, in the beginning and the end of the work day. On each occasion the test was repeated 3 times and the maximum values obtained were recorded. The measurements were continued for 15 days including at least 2 holidays (days away from work) and PEF variability over 20% was accepted as asthma. Variability was calculated according to the formula given below:

$$\text{Daily PEF variability} \quad \frac{\text{PEF evening-PEF morning}}{{}^{1}/_{2}(\text{PEF evening+PEF morning})}$$

Phase 3. Workers with positive PEF variability results were subjected to a non-specific bronchial provocation test (NBPT) in the hospital by using nebulized metacholine. The test was given approximately 1 hour after a workshift. Basal pulmonary function values were recorded. Maximum metacholine concentration causing a 20% decrease in basal FEV_1 value was recorded as the provocative dose (PD20). A PD20 value below 8 mg/mL was accepted to indicate bronchial hyperresponsiveness.

Data were recorded under SPSS pocket program (SPSS for MS Windows release 5.0, SPSS inc., Chicago) and the statistical analyses were done using the student t test, Mann-Whitney U, Kruskal-Wallis, chi-square, Fisher's exact chi square tests and Tukey's HSD test.

Results

Some demographics of the 107 workers included in the study are shown in Table I.

Age, prevalence and amount of smoking (in pack-years) were not different among the three groups ($p>0.05$). The other parameters of the study were also comparable

Table 1. Demographics of the groups				
Features	Polyurethane	Dye	Control	P value
Number of workers	77	18	12	
Mean age ±SD	28.35±5.32	28.38±4.70)	34.41±8.40	>0.05
Smokers	57 (74%)	13 (72%)	9 (75 %)	>0.05
Mean pack year±SD	7.28±5.46	7.50±5.83	10.1s±9.63	>0.05

between the groups and were found to be independent from age and smoking habits.

Frequency of respiratory and allergic symptoms pertaining to the eye, nose and skin in the 3 groups are shown in Table 2.

Table 2. Frequency of respiratory and allergic symptoms			
Symptoms	Polyurethane (%) N=77	Dye (%) N=18	Control (%) N=12
Cough	18 (23.4)	4 (22.2)	0 (0.0)
Sputum	22 (28.6)	5 (27.8)	3 (25.0)
Dyspnea	1 (1.3)	0 (0.0)	1 (8.3)
Ocular allergy	7 (9.1)	2 (11.1)	2 (16.7)
Nasal allergy	8 (10.4)	3 (16.7)	2 (16.7)
Dermal allergy	15 (19.5)	3 (16.7)	1 (8.3)

A history of cough was more common in the polyurethane group but did not reach statistical significance. No differences were found among the groups in prevalence of allergic symptoms.

Pulmonary function test values are shown in Table 3. FEV% and FVC% were significantly lower in the polyurethane group.

Table 3. Pulmonary function test values (mean ± SD)				
PFTs	Polyurethane N=77	Dye N=18	Control N=12	P Value
PEF % pred	85.24±21.88	90.11±23.84	98.25±28.17	0.17
FEV_1 %*	84.92±14.05	92.50±15.13	99.91±20.93	0.003
FVC %*	74.01±13.13	81.38±15.24	87.0±18.74	0.009
FEV_1/FVC	97.14±4.30	96.55±4.76	95.78±3.64	0.105
*: In Tukey's HSD test, the polyurethane group was different from the control group				

After completing Phase I, 32 workers (27 in polyurethane, 5 in dye group) with suggestive symptoms and pulmonary function values were evaluated by PEF monitorization. As a result of PEF meter follow-up, 17 of the workers (16 in polyurethane and 1 in dye group) were found to have PEF meter variability, which was consistent with OA, as shown in Table 4.

Table 4. PEF meter follow-up results				
PFTs	Polyurethane N=77	Dye N=18	Control N=12	P Value
PEF meter Follow-up	27 (35.0)	5 (27.7)	0 (0.0)	0.5
PEF variability positive	16 (20.0)	1 (20.0)	0 (0.0)	0.078

Seventeen workers who had PEF variability underwent NBPT. The provocation test was found to be positive in the 3 workers who previously had PEF variability consistent with occupational asthma. These three workers were all in polyurethane group. The PD20 values of these 3 positive cases were 4.0, 0.125 and 0.250 mg/ml. The prevalence of OA was 3.89%.

A comparison of some features of workers with OA with those free of any signs and symptoms of OA is given in Table 5.

Table 5. Some features of workers with OA and those without		
Features	Occupational asthma (+) (N=3)	Occupational asthma (–) (N=74)
Age (Mean±SD)	32.00±5.56	28.20±5.29
Smokers (%)	2 (66.7%)	55 (74.3%)
Duration of exposure (months) (Mean±SD)	132±129.93	34.04±39.51
Symptom on particular days of the week (%)	1 (33.0%)	0 (0.0%)
Nasal symptoms (%)	2 (66.0%)	6 (8.1%)

As the duration of polyurethane exposure increases, the prevalence of OA increases. The mean duration of work of 3 workers with OA was longer than the other workers, but statistical evaluation was not attempted due to the low number.

Discussion

Occupational asthma is defined as a disease characterised

by either or both variable airflow limitation and bronchial hyperesponsiveness (BHR) due to causes and conditions attributable to a particular working environment and not to stimuli encountered outside the workplace (15). About 250 agents capable of causing occupational asthma have been reported (19). The proportion of cases due to occupational exposure is unknown but estimates range from 15 to 20% in Japan and the USA (16).

Asthma prevalance is reported to be below 5% in Turkey in the general population (20). The incidence among occupational exposures is not known, but the prevalence of occupational asthma among different occupational groups has been reported as 2.5- 13.6% (21,22).

Reports about isocyanate-induced asthma began to appear in the 1950s and since then asthma has proved to be the most conspicuous occupational heath liability of these chemicals, affecting 5-10% of chronically exposed workers (4). In present study, this ratio was found to be relatively low (3.89%). This may be due either to the small number of workers included in the study or the relatively satisfactory air-conditioning system of the factories.

TDI is the first commercially important member of the di- and poly-isocyanates and is heavily consumed. TDI and MDI are heavily used in the production of flexible polyurethane foams, the most popular material for construction of mattresses, furniture cushions and the seat cushions of automobiles and airplanes (5). Workplace exposures to this agent can cause asthma (2). In industrialized countries isocyanates are probably the most common cause of OA (1). In Turkey due to the lack of epidemiological data, we do not know the number of workers exposed to these agents and the only study conducted on automobile painters reported a ratio of 9.6% (4).

Mean age and smoking habits were similar in the 3 groups in our study. While the questionnaire results showed a higher prevalance of cough in the polyurethane group, this was not statistically significant, possibly due to the small numbers of the groups. This was also true for allergic symptoms. Jones (5) showed a significant association of prevalence of cough and phlegm and exposure after controlling for smoking age and sex. In our study gender, age and smoking status were also independent variables in the 3 groups and the prevalence of cough was highest in the polyurethane group.

Pulmonary function test results showed that FEV_1%, FVC% were significantly lower in the polyurethane group compared to both the dye and control groups. Jones (5) also showed that mean initial lung function and mean decline in FEV_1 were marginally worse in those with symptoms of chronic bronchitis.

Twenty six of the 32 workers with findings suggesting asthma as a result of the questionnaire and PFTs, were in the polyurethane group, 6 were in the dye group, but none were in the control group. 16 of the 17 workers who had PEF variability consistent with OA were in the polyurethane group and 1 was in the dye group. All 3 workers diagnosed as OA were in the polyurethane group.

For the diagnosis of OA, the questionnaire is the basic tool used in most epidemiological surveys and all individual assessments (4,23). However, questionnaires are sensitive but not specific tools. Documentation of objective changes in lung function and improvement away from work or deterioriation on returning to work is desirable for diagnosis (16). The PEF meter follow-up is valuable, especially when the values of non-working days get better, with a high sensitivity and specifity as 90 and 97% after correcting the results with NBPT (24,25,26). When changes in PEF are associated with parallel changes in NBPT, the diagnosis of OA is highly probable (23). Specific bronchial provocation test (SBPT) is the gold standard but is not available in each center and requires experienced personnel. PEF meter recordings together with typical symptomatic history and NBPT can lead to diagnosis (1,16). This was the method we used in our study. The absence of BHR as assessed shortly after a workshift virtually excludes asthma. The absence of BHR in 14 of the 17 workers made us exclude them. Various studies report that of patients who have respiratory symptoms and are exposed to isocyanate in the workplace, only half have positive isocyanate test (1,27). SBPT for TDI has difficulties in performing, limited diagnostic use and a large number of false negative results. In allergic asthma repeated inhalation of low doses of allergens that do not provoke by themselves any bronchoconstrictive response may induce an increase in non-specific BHR (28). Kubler wanted to hypothesize that non-spesific BHR might also increase after a negative occupational allergen challenge and might be useful in diagnosing OA and found that exposure to TDI induced a slight but significant increase in non-spesific BHR in the absence of any immediate or late response to isocyanate. He suggested to measure non-specific BHR even after a negative specific inhalation test to TDI as an additional diagnostic element for TDI-induced OA (28). We did not have chance to perform TDI challenge test but this finding above supported the importance of the observed increase in non-specific BPT after exposure of workers to their work environment as we had in our cases.

There are some studies showing a positive correlation

between the duration of work and occupational asthma (4) while there are some having no correlation (29). The effect of exposure is difficult to evaluate because of the healthy-worker effect, workers with occupational asthma tend to leave jobs with high exposure because of intolerable symptoms; those who remain are healthy "survivors" (16). The mean duration of work of these 3 workers in our study was longer than others. A dose–related excess decline in mean FEV_1 was found in non-smoking workers of this sector (5). Susceptibility is a reported adverse effect of chronic exposures on longitudinal decline of lung function. Early reports of excessive annual declines came mostly from studies of workers producing flexible polyurethane foams (5). The outcome of isocyanate asthma may be variable and OA may persist despite negligible TDI exposures. The best chance for altering the outcome of isocyanate-induced asthma is avoidance of further workplace exposure to this sensitizing agent (7).

The prevalance of OA asthma was not very high in our study but the workers with OA had longer duration of work and the workers in polyurethane group had lower pulmonary function value, so we conclude that polyurethane foam workers should be under long-term follow-up.

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