Original Article

Cohort Study on Respiratory and Neurological Disorders among Workers in a Bone Glue Factory in Egypt

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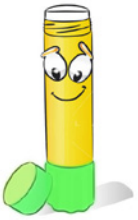

Abstract:

Background: Glues are strong, liquid adhesive derived from animal tissues. It has been shown that glue sniffing is associated with demyelinating polyneuropathy. The low molecular weight agents which cause occupational lung disease have generally included the isocyanates exposure to which could result in asthma among workers. Toluene is also used widely in glue and adhesive industry and households where toluene exposure and abuse can occur.

Objectives: To study some respiratory and neurological disorders that may arise in workers in a bone glue factory in Queisna industrial zone, Menoufyia governorate, Egypt.

Methods: In a historical cohort study, the exposed participants (n=50) were recruited from workers in a bone glue factory in Queisna industrial zone, Menoufyia governorate. The unexposed group was selected from workers' relatives who had never worked in glue industry. All participants completed a pre-designed questionnaire on personal and occupational histories. Pulmonary function tests as well as electromyography (EMG) were performed for all participants. Urinary hippuric acid was also measure in all participants.

Results: The prevalence of cough, asthmatic attacks and paresthesia were significantly higher among exposed than unexposed participants. Abnormal spirometric measurements (particularly towards obstruction), abnormal EMG and positive urinary hippuric acid were significantly more prevalent among exposed than unexposed group.

Conclusion: Spirometry and EMG should be included in the periodic medical examination for exposed workers for early detection of respiratory and neurological disorders. Urinary hippuric acid could be a useful indicator of the nerve conduction abnormalities and should be measured periodically for these workers.

Keywords: Adhesive; Nervous system diseases; Electromyography; Hippuric acid

Introduction

Glues are strong, liquid adhesive derived from animal tissues. Animal glue primarily consists of gelatin and low molecular weight residues of collagen, keratin, and elastin.[1]

The low molecular weight agents which cause occupational lung disease have generally included the isocyanates (present in glue industry) exposure to which could result in asthma in 2% to 10% of workers.[2,3]

An under-recognized aspect of glue sniffing is the potential damage to nerves due to inhalation of vaporized glue. Glue

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sniffing has also been associated with demyelinating polyneuropathy. Because of the potential for severe permanent disability or even death, n-hexane polyneuropathy from glue sniffing remains one of the serious public health threats.[4]

Toluene is used widely, not only in glue and adhesive industry, but also in households where toluene exposure and abuse can occur. Urinary hippuric acid and o-cresol excretion rates are used as markers for toluene exposure.[5]

For making bone glue, bones are degreased with solvents. Then, hydrochloric acid in an 8% solution is applied to the bones. The acid removes calcium phosphate and other minerals and leaves collagen in the same shape as the piece of bone. The acid is then removed from the collagen; the product is dried to produce commercial-grade ossein or bone protein (also termed acidulated bone) that is the basis for bone glues.[6] Cooking the product for a certain period at a correct temperature breaks down the collagen and converts it into glue. The resulting liquid, the so-called "glue liquor," is extracted and reheated again to thicken the glue.[7] Chemicals like alum or acid followed by egg albumin may be added to remove impurities. These chemicals cause the impurities to precipitate or fall out of the glue.[7] Different additives are mixed with the glue liquor to make brown, clear, or white glue. Sulfurous acid, phosphoric acid, and alum are among these additives. The glue can be chilled into either sheets or blocks which are then suspended on nets to dry and become more concentrated. The product is finally pumped into bottles or jars for sale.[6]

We conducted this study to evaluate some respiratory and neurological disorders that may arise in workers in a bone glue factory in Queisna city, Menoufyia governorate.

Materials and Methods

This historical cohort study was conducted from the beginning of May 2011 to the end of July 2011 in a bone glue factory in the industrial zone in Queisna city, Menoufiya governorate, Egypt. Workers in this factory work in three 8-hour shifts a day for seven days a week. The total work force of the factory was 54 subjects distributed per shift in 1) collecting bones unit, and 2) units for degreasing, boiling of bones and using of solvents.

Out of 54 occupationally exposed workers, 50 participated in this study after excluding non-responders (n=4, 7%) and applying the exclusion criteria. An age- and sex-matched unexposed group of 50 individuals who had never worked in glue factories, were recruited from workers' relatives. They were also matched for residence, education level and socioeconomic status.

Workers with past history of neurological or psychiatric disorders or under treatment of bronchodilators or antipsychotic drugs before being employed in the factory were excluded from the study.

An interview was done at the work place in a quiet room during the morning shift one hour after breakfast. It was done for six workers a day with every setting took almost 30 minutes. The purpose of the study was first explained to the managers and employees of the study site. All participants were volunteers. Written informed consents were signed by all participants before being enrolled into the study and each was asked to do his best. The Menoufiya Faculty of Medicine Committee for Medical Research Ethics reviewed and formally approved the study before its beginning.

Personal Interview

Each participant was asked to complete a pre-designed questionnaire included

Table 1: Comparison between exposed and unexposed regarding respiratory manifestations.

Respiratory manifestations	Participants		RR (95% CI)
	Exposed n (%)	Unexposed n (%)	
Rhinitis	5 (10)	1 (2)	5 (0.6–41.38)
Cough	20 (40)	5 (10)	4 (1.63–9.82)
Wheeze	4 (8)	1 (2)	4 0.46–34.55)
Expectoration	9 (18)	3 (6)	3 (0.86–10.43)
Dyspnea	2 (4)	1 (2)	2 (0.19–21.36)
Chest pain	4 (8)	3 (6)	1.33 (0.30–5.65)
Asthmatic attacks	11 (22)	2 (4)	5.5 (1.28–23.56)

questions about age, gender, residence, marital status, educational level, special habits and socioeconomic status.

The participants were also asked for detailed occupational history—their present occupational history (duration of employment, nature of job, the way of dealing with raw materials and final products, the average hours of work per day, number of days worked per week); past occupational history (place, nature and duration of previous occupations); any additional jobs; medical history of chest and neurological symptoms; family history—consanguinity, its degree and any diseases running in families as neurological diseases, hypertension and diabetes mellitus (DM); and past history of diseases like DM, hypertension, neurological, hepatic and renal diseases or use of antipsychotic drugs.

Clinical Examination

General clinical examination including measurement of blood pressure, weight, height and pulse rate followed by thorough chest and neurological examinations were done for each participant.

Spirometric Measurements

Spirometry was done by a portable computerized spirometer (Spirolab II) designed for ambulatory spirometry measurements. All the measured values were expressed as percentages from predicted values.

The apparatus was fed first with serial number, age, sex, height, and race of the subject according to the American Thoracic Society criteria (two readings of FEV_1 and FVC should not differ by more than 5% or 100 mL).[8] The test was done in the sitting position and the subject was told in simple words about the procedure and principals of the test. After applying a nasal clip, the subject was connected to the apparatus via the mouth piece which was changed for each worker. For each participant FVC, FEV_1, FEV_1/FVC, and forced expiratory flow between 25% and 75% of FVC (FEF_{25-75}) were recorded.

Electrophysiological Study

Electromyography (EMG) of the distal upper and lower limbs of participants was done at Neuropsychiatry Department, Menoufiya University Hospital with a Viking Quest apparatus (Neurocare Group, USA) by a neuropsychiatric (one of the authors).

Urinary Hippuric Acid Concentration

Mid-stream urine sample (10–20 mL) was obtained from the exposed group at the end of the work shift and from all unexposed participants. All samples were collected using a sterile plastic container with a number marked by a sticker on the cover of the container and transported as quickly as possible to avoid the damage associated with storage.

The analysis of urinary hippuric acid

(HA) were carried out in a commercial diagnostic laboratory (Saridar Laboratory, El-Dokki, Cairo, Egypt). Samples were transported to the laboratory at or below 8 °C and processed within 12 hours of collection. Urine was analyzed according to Lof, *et al*,[9] with 2-methylhippuric acid as an internal standard. A high-performance liquid chromatography (HPLC) system (Hewlett-Packard Model 1050 equipped with a Lichrospher 100 RP-100 [5 µm] pre-packed column) with a UV detector (240 nm) was used for the analysis. Results were considered positive if the measured urinary HA was ≥0.31 g/g creatinine.[5]

Data Management

Data were analyzed by SPSS ver 13. *Student's t* test was used for comparison of means between the two groups. χ^2 or Fisher exact test was used to study the probable association between categorical variables. A p value <0.05 was considered statistically significant.

Results

The mean±SD age of exposed workers and unexposed participants was 28.8±8.5 and 28.6±7.9 years, respectively (p=0.903).

In the exposed group, the frequencies of cough, asthmatic attach, paresthesia, abnormal EMG findings, positive urinary HA and abnormal spirometric changes were significantly higher than those in unexposed group (Tables 1 and 2).

There was no significant difference between the exposed and unexposed groups in terms of manifestations of motor diseases. The frequencies of superficial and deep sensations were also not significantly different.

There was a significant lower mean FEV_1% among the exposed than unexposed group (Table 2).

The mean values of spirometric measurements were significantly lower among smoker workers than non-smokers (Table 3). The frequencies of abnormal EMG findings, positive urinary HA, and abnormal spirometry were also significantly higher in those who worked for ≥5 years than those who did not (Table 4). Among the exposed group, there was a significant negative correlation between the duration of employment and FEV_1% (r=0.51, p<0.05), FVC% (r=0.47, p<0.05); there was also a significant positive correlation between duration of employment and abnormal EMG findings (*Spearman's* ρ=0.6, p<0.001) and positive urinary HA (*Spearman's* ρ=0.62, p<0.001).

Table 2: Paraclinical parameters measured in exposed and unexposed groups.

Parameter	Participants		RR (95%CI)
	Exposed (n=50)	Unexposed (n=50)	
Mean±SD FVC%	85.0±10.7	86.8±0.1	–
Mean±SD FEV_1%	76.3±8.7*	87.6±12.9	–
Mean±SD FEV_1/FVC%	93.0±11.5	97.7±19.2	–
Mean±SD FEF_{25-75}%	91.1±8.2	93.4±8.5	–
Abnormal EMG, n (%)	10 (20)	2 (4)	5 (1.15–21.68)
Positive urinary HA, n (%)	22 (44%)	5 (10)	4.4 (1.81–10.7)
Abnormal spirometry, n (%)	15 (30%)	4 (8)	3.75 (1.34–10.51)

*Significantly (p<0.05) different from the unexposed group.
HA: Hippuric acid

Discussion

In this study, cough and asthmatic at-

Table 3: Paraclinical parameters measured in smoker and non-smoker exposed workers (n=50)

Parameter	Smokers (n=15)	Non-smokers (n=35)	p value
Mean±SD FVC%	81.1±14.0	89.8±8.1	<0.001
Mean±SD FEV_1%	79.9±17.3	94.0±5.8	<0.001
Mean±SD FEV_1/FVC%	100.9±18.3	106.1±5.8	<0.05
Mean±SD FEF_{25-75}%	90.1±9.2	92.4±9.2	NS
Abnormal spirometry, n (%)	8 (53)	2 (6)	<0.001
Abnormal EMG, n (%)	6 (40)	4 (11)	<0.05
Positive urinary HA, n (%)	8 (53)	14 (40)	NS

NS: Not significant; HA: Hippuric acid

tacks—as chest complaints—were more prevalent in the exposed than unexposed (RR: 4, 95% CI: 1.63–9.82; RR: 5.5, 95% CI: 1.82–23.56, respectively). There were also a significantly lower mean FEV_1 and a significant higher frequency of abnormal spirometric findings among the exposed than unexposed group. These observations were in accord to what reported by Tarlo, *et al*,[10] who mentioned that exposure to work place air pollutants can negatively affect the respiratory system. Furthermore, Todd, *et al*,[11] reported that adverse health effects experienced by footwear and equipment factory workers (in the form of cough and neurological manifestations) were associated with occupational exposures to volatile organic solvents and water-based adhesives. Moreover, Cakmak, *et al*,[12] stated that chronic exposure to solvents (including toluene) had an adverse effect on respiratory system during their study on 1091 gun factory workers. Xu and Christiani,[13] reported that occupational exposure to organic solvents, mostly isocyanates, may result in obstructive spirometric results, particularly when combined with dust.

Table 4: Paraclinical parameters measured in exposed workers with duration of employment <5 years vs. ≥5 years

Parameter	Duration of employment		p value
	<5 years (n=24)	≥5 years (n=26)	
Abnormal EMG, n (%)	0 (0)	10 (39)	<0.001
Positive urinary HA	4 (17)	18 (69)	<0.001
Abnormal spirometry, n (%)	1 (4)	14 (54)	<0.001

HA: Hippuric acid

In this study, parasthesia—a symptom of polyneuropathy—was significantly more frequent among the exposed than unexposed group (RR: 5.5, 95% CI: 1.28–23.56). Furthermore, a significantly higher prevalence of abnormal EMG was observed in the exposed than unexposed group. These results were in agreement with report of Wang, *et al*,[14] who found that paresthesia (42%) and burning sensations in toes and fingers (36%) were the main clinical manifestations of n-hexane polyneuropathy among workers in press proofing in Taipei. Also, Jovica *et al*,[15] revealed that combined exposure to organic solvents including toluene, white spirit, butyl acetate, ethyl acetate and xylene, in the manufacturing of paint, cartridge and lacquer industry, was associated with significant reduction in EMG activities in the exposed (18%) than unexposed group (2%). Also, Kararizou, *et al*,[16] who conducted a study to investigate the causes of polyneuropathy in teenagers found that toxic polyneuropathy (22%) was the second common cause of neuropathy in teenagers. Moreover, Beer, *et al*,[17] reported that chronic exposure to various or-

ganic solvents or other exposures would lead to different patterns of cognitive disturbance.

This study revealed a significantly higher prevalence of positive urinary HA among the exposed than unexposed group (RR:4.4, 95% CI: 1.81–10.7). This result was in accord to findings of Heuser, *et al*,[18] and Jovica, *et al*,[15] who reported that urinary HA—as an indicator of peripheral neuropathy—was significantly higher in workers exposed to organic solvents mainly toluene. Ismet, *et al*,[5] mentioned that the value of urinary HA—as a marker for toluene exposure—in glue sniffers was 73 fold higher than in the controls.

We found that smokers had a significantly lower mean value of spirometric measurements. This finding was in agreement with Meredith, *et al*,[19] who reported that smoking and atopy may increase the likelihood of development of obstructive spirometric measurement and occupational asthma—mainly due to toluene diisocyanates.

In the current study, with increasing duration of employment, there was a significant increase in the abnormal spirometric measurements. However, no association was found between smoking and urinary excretion of HA in workers. This was in parallel with findings of Elisa and José,[20] who conducted a study to establish the reference values for urinary HA, and to evaluate the impact of age, gender, alcohol, and tobacco on these values in a population unexposed to toluene. They concluded that there were no association between urinary HA excretion and smoking and alcohol consumption.

We found a significant positive correlation between duration of employment and EMG activities which was in agreement with Stetkaiova, *et al*,[21] who conducted a study to evaluate possible subclinical impairment of the nervous system due to occupational exposure to toluene and styrene. They also found an increasing trend in the frequency of abnormal EMG findings with increased duration of exposure to toluene and styrene (17%).

We also found a significant positive correlation between duration of employment and occupational asthma, as evidenced by lower spirometric measurements. This observation was in keeping with Sim and Dong,[22] who studied the prevalence of isocyanate-induced asthma in workers and concluded that 40% of isocyanate-induced asthma occurs after a long latency period ranging from 30 to 132 months. Other studies also reported that the higher the duration of exposure to toluene diisocyanates, the greater the adverse effect on respiratory system.[19,23]

Based on what we found, we should aim at raising the awareness and knowledge of workers of bone glue factories about the hazards of their job. Pre-employment medical examination for workers in this industry should exclude those with respiratory or neurological manifestations which may be exacerbated

TAKE-HOME MESSAGE

- Occupational exposure to low molecular weight agents such as isocyanates which cause occupational lung disease, is common in bone glue industry.
- In those working in bone glue factory, the frequencies of cough, asthmatic attach, paresthesia, abnormal EMG findings, positive urinary hippuric acid and abnormal spirometric changes were significantly higher than those in unexposed group.
- Duration of employment is an imporatant predictor for the severity of occupational asthma.

by working in this industry. Spirometry and neurological examination and EMG should be included in the periodic medical examination of exposed workers for early detection of respiratory and neurological disorders. Keeping accurate health records of workers are of paramount importance so that those at risk can be monitored and if necessary moved to another position. Measurement of urinary HA is also a useful indicator of the nerve conduction abnormalities and should be measured periodically for these workers. Using personal protective devices, especially masks, during work as well as care for personal hygiene to get rid of fumes and dust in the hands and clothes must be emphasized. Establishing policies on prohibition of smoking in the workplace, establishing incentives to discourage smoking, offering smoking cessation courses, and providing literature on the harmful effects of cigarette smoking to workers and employees are also important.

Conflicts of Interest: None declared.

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