Austin Occupational Medicine

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Case Report

Prevalence of Renal Impairment among Workers of a Paint Manufacturing Factory

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Received: September 12, 2016; **Accepted:** October 24, 2016; **Published:** October 25, 2016

Abstract

Introduction: Chronic Kidney Disease (CKD) is a major public health problem throughout the world. Adverse outcomes of chronic kidney disease can be prevented through early detection and treatment. Workers with a history of exposure to paints, glues, degreasing solvents, and cleaning solvents must be evaluated for renal impairment. Objective: To detect the prevalence of renal impairment among workers exposed to organic solvents as nephrotoxic substance.

Subjects and Methods: This is a analytical case control study conducted on all workers (n=181) of a paint manufacturing factory exposed to organic solvents during their work and 186 control individual never exposed occupationally to organic solvents and engaged in administrative tasks outside the factory. we evaluated their renal function using both routine renal function tests namely; serum urea, serum creatinine, estimated glomerular filtration rate in addition to urinary biomarkers; N acetyl-B-D glucosaminidase.

Result: The results of the study revealed statistically significant difference between the Urinary-N-Acetyl glucosaminidase activity (NAG index); (P-value<0.001) of the workers that exposed to organic solvents and their matched controls. The proportion of exposed workers that have abnormal NAG activity (53.6%) is higher than that in their matched controls (29.6%) and represent about two fold increase in the activity with high statistically significant difference (p-value<0.0001).

Conclusion: It appears that at least one of every two workers exposed to organic solvents in this factory has early renal impairment which couldn't be detected by the routine renal function tests.

Keywords: Chronic kidney disease; Renal impairment

Introduction

It is clear that an individual's likelihood of developing progressive Chronic kidney disease results from complex interactions between multiple genetic (none modifiable factors) and environmental factors (modifiable factors) [1]. Identification of the modifiable and controllable risk factors. eg. exposure to nephrotoxic substances such as organic solvents, is an important first step in understanding and hopefully, revering the increasing incidence of such disease [2]. Millions of workers are exposed to organic solvents worldwide at different workplaces. Depending on the vapor pressure of the individual solvents, workers may be exposed by inhalation. Exposure concentrations may be very high, at least for some procedures (e.g. cleaning). In addition, dermal exposure may contribute considerably to the overall exposure. Exposure may occur despite the use of protective clothing, because solvents may penetrate certain types of gloves or cloth. Solvent mixtures are frequently used. Therefore, effects may also be caused by combined exposures. Threshold limits in the air, established by several national and international institutions, enable control of a large number of solvents in air at the workplace [3]. Workers with a history of exposure to paints, glues, degreasing solvents, and cleaning solvents must be evaluated for renal impairment. Such patients may not know the risks of their exposure and may actually not understand the relationship between an exposure to kidney toxic solvent and the development of high blood pressure or in the worst case scenario the development of end-stage kidney failure [4]. Renal damage resulting from toxic exposure is progressive and will, if untreated, end in irreversible renal disease. There is, therefore, a need to develop a battery of tests for early detection of these effects [5]. As renal damage from solvent exposure may remain clinically silent for many years due to the large functional reserve capacity of the kidney, it is necessary to apply sensitive, reliable early indicators ("biomarkers of effect") to detect early effects and prevent further damage [6]. The aim of this study to detect the prevalence of renal impairment among workers exposed to organic solvents as nephrotoxic substance.

Subjects and Methods

Study design

Analytical, case control study

Study location

This study was implemented in one of the biggest factories manufacturing paints in Great Cairo, Egypt.

Citation: Hegazy IS, El-Raghi HA, Mohammed AM, Rizk SA, Badawy NA and Rashad HM. Prevalence of Renal Impairment among Workers of a Paint Manufacturing Factory. Austin Occup Med. 2016; 1(1): 1003.

Subjects

The study population consists of two groups:

Workers group (Exposed) composed of 181 industrial workers exposed currently to the organic solvents during their work in a paint manufacturing factory.

Case definition: All workers of the factory that exposed to organic solvents.

Were included in the study without any exclusion.

Control group (none exposed occupationally) consists of 186 of clerks engaged mainly in administrative tasks in organization away from the factory and haven't exposed occupationally to organic solvents neither currently nor in the past. They are matched with the workers group in number, sex and age group (5 year interval).

Methods

Both workers and control groups were subjected to:

I. An interview to complete a questionnaire form

II. Full clinical examination: to evaluate the health status of the workers and their matched controls. General and abdominal examination were performed with emphasis on the signs of chronic renal disease (puffiness around eyes, lower limb edema, high blood pressure, etc…)

III. Laboratory investigations

a) Blood samples were collected from both exposed and their controls by sterile disposable syringes. Each sample was left to clot and centrifuged. The separated serum was used for estimation of routine Kidney function tests namely;

- **Serum urea** using the enzymatic method for determination of urea concentration in serum [7] with reference values 0.15-50mg/dl values above 50mg/dl have considered elevated.
- **Creatinine** using a colorimetric, alkaline picrate method (Jaffe) [8] with Reference values: 0.6-1.4mg/dl for males. Values above 1.4mg/dl have considered elevated. High performance diagnostic reagent kits had been used for determination of Serum urea and creatinine in this study.
- **The glomerular filtration rate** (GFR) was calculated individually for each person using Modification of Diet in Renal Disease (MDRD) formula that recommended by NKF-K/DOQI clinical practice guidelines. This formula depends on 4 variables (serum creatinine, age, gender and race) Estimated GFR = 186 X (serum creatinine)$^{-1.154}$ X (age)$^{-0.203}$ X (0.742 if female) X (1.212 if African American).

b) Urine samples in sterile labeled containers were collected in the morning from all individuals then centrifuged to remove insoluble salts and debris. Aliquots were stored at -20°C for the estimation of the early markers of renal damage namely;

- N-acetyl-β-D glucosaminidase (NAG) using the colorimetric method [9] with normal reference values 4.2±1.2mU/mg of urinary creatinine. Because NAG activity is known to vary with age and diuriesis; hence, a NAG index (ratio of NAG activity to urinary creatinine) was calculated to minimize variability [10]. A commercial kits (FAR NAG kit) for colorimetric determination of N-Acetyl-B-D-Glucosaminidase in urine and in serum manufactured by FAR srl via Fermi. The early markers were determined only for 125 exposed worker and 128 of their matched controls selected randomly due to financial causes.

Important calculations used in this study

- **Body Mass Index:** Anthropometric measurements were performed (weight and height) and the body mass index (BMI) was calculated as the individual's body weight divided by the square of his height (kg/m^2) [11].
- **Mean Arterial Pressure (MAP):** the average blood pressure in single cardiac cycle in an individual was calculated using the following formula: MAP = [(2 x diastolic) + systolic] divided by 3 [12]. MAP from 70 to 110 mmHg is considered normal.
- **Blood Pressure:** The blood pressure was measured by maintaining the arm-cuff position at the heart level during rest in seated position. Two readings were taken (1-2min interval) and the mean value of the two measurements was used. The blood pressure was measured by auscultation method using mercury sphygmomanometer [13].

Important definitions used in this study

- **Hypertension:** defined in the study by personal history of hypertension and/or use of anti-hypertensive drugs.
- **Diabetes:** is defined in this study by a personal history of diabetes mellitus and/or diabetic medication usage.

Statistical Analysis

The collected data, the clinical and laboratory results have been computerized and coded using SPSS version 20.0 software and statistically analyzed. Data were expressed as mean values ± Standard Deviation (SD). Ranges, frequency of distributions were estimated for quantitative variables. The mean of quantitative variables of the two comparable groups (exposed group and control group) was compared using the Independent-Samples Student's t-test. The significance of differences between proportions was tested by the Chi-square test (χ^2). The correlations between individual variables were tested using Pearson correlation coefficient (r) Values ≤ 0.05 were considered statistically significant. Multivariate logistic regression analysis used to detect the odds ratio of the outcome in response to certain variable with adjustment of the other cofounders (CI =95%).

Results

A total number of studied exposed group (n=181) are males. Their mean age is 42±10.7 and age range (21-59) years old. Most of them are married (88.4%). The exposed workers that have either basic education or less form a great bulk in the factory (40.5%). About two fifth of the workers are currently tobacco smokers (45.3%). About one fourth of the workers smoke shisha occasionally (24.2%). No other special smoking habits have been recorded.

The range of duration of exposure to organic solvents was (1-

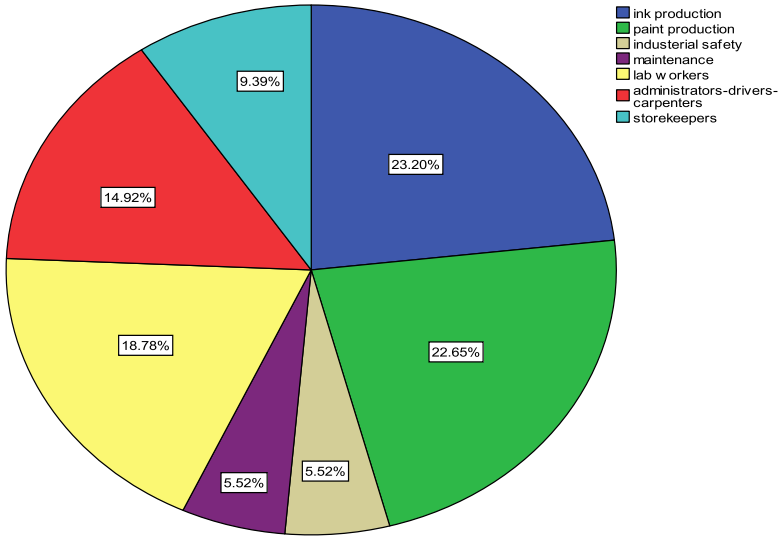

Figure 1: Pie chart shows working activities in the paint manufacturing factory.

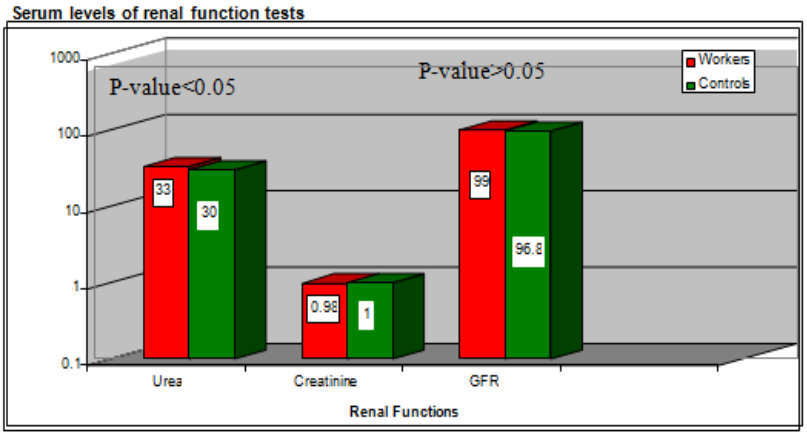

Figure 2: Bar chart shows comparison between the serum levels of renal function tests of exposed workers and control group.

42) years with mean duration (17.3±11.4) years. The workers in the factory are exposed during their work daily to mixture of organic solvents; 5 days weekly for 8 hours daily. It was observed that 52.5% of the workers (n=95) are using the Personal Protective Equipment (PPE) regularly while 47.5% (n=86) always didn't use PPE. The workers group was matched in age with 186 employers engaged in administrative tasks outside the factory. Statistically significant difference (P-value = 0.016) in the smoking pattern of workers when compared to their matched controls. About half of the workers are currently smokers (45.3%) compared with (38.2%) among controls.

Figure 2 represents statistically insignificant differences in mean values of routine renal function tests between the workers group and their controls.

Table 1 reveals that the control group is matched in age with the workers (P-value =0.2). There is a statistically significant difference (p-value<0.0001) between the exposed workers (31±5.7) and their matched controls (27.6 ±4.6) in mean values of body mass index as well as in systolic blood pressure with higher mean values among the workers group (123.6±15.8 mmHg).

Table 2 clarifies the statistically significant higher (P-value<0.0001) mean rank of the Urinary-N-Acetyl glucosaminidase (NAG index) among the workers that exposed to organic solvents when compared to their matched control.

Table3 Shows that the proportion of exposed workers that have abnormal NAG activity (53.6%) is higher than that in their matched controls (29.6%) with high statistically significant difference (p-value<0.0001).

Table 4 Shows the significant association between the occupational exposures to organic solvents after adjustment of age, smoking status, hypertensive state, diabetic state and the body mass index (OR=0.4&P-value<0.0001).

Discussion

The organic Solvents represent an important group of environmental pollutants to which people are exposed daily in the household settings and workplace. They are present as ingredients in

Table 1: Statistical comparison between the exposed workers and their matched controls in respect to some personal and medical factors.

Variable (mean±SD)	Workers (n=181)	Control group (n=186)	t-value	p-value
Age	42±10.7	40±10	1.27	0.2
Body mass index (BMI)	31±5.7	27.6 ±4.6	6.1	<0.0001
Systolic blood pressure	123.6±15.8	118.4±15.4	3.1	0.002
Diastolic blood pressure	74.9±9.4	75±9	-0.16	0.8
Mean arterial blood pressure (MAP)	91±10.6	89.5±10.4	1.4	0.1

N.B. no signs or symptoms of renal impairment have been detected among both studied groups.

Table 2: Statistical comparison between the renal function tests of workers and control groups.

Renal function test	Workers group (n=125)	Control group (n=128)	p- value*
Urinary-N-Acetyl glucosaminidase (NAG index) (mu/mg Cr)	9.9±14.2(153.7)	4.9±8.2(100.9)	<0.0001

Data are presented as Mean ±SD and Mean rank of Mann-Whitney U test
*P-value of Mann-Whitney U test.

Table 3: Distribution of NAG activities among the exposed workers and their controls.

Renal biomarker	Cut off value	Frequency of abnormal values				Pearson Chi-Square test
		Workers group (n=125)		Control group (n=128)		
		f	%	*f*	%	
Urinary NAG index* Normal Elevated	5.4 mu/ mg cr.	58 67	46.4 53.6	89 38	70.4 29.6	X^2=14.8 df=1 p-value<0.0001

paints, varnishes, lacquers, glues, adhesives, degreasers, cleaners and in the production of dyes, polymers, plastics, textiles, printing inks, agricultural products and pharmaceuticals [14]. Organic solvents are present also in detergents (citrus terpenes), in perfumes (ethanol), home deodorizers, toothpaste (formaldehyde), carpets cleaners, nail polish removers, bathroom cleaners and glue solvents (acetone, methyl acetate, ethyl acetate), in dry cleaning (e.g. tetrachloroethylene), paint thinners (e.g. toluene, turpentine), in spot removers (e.g. hexane, petrol ether), furniture oils, shoe care products [15].

The results of the studies performed to study the effect of exposure to organic solvents on kidney in workers occupationally exposed to organic solvents over the last twenty years are contradictory, tubular, glomerular, or no effects were found [16]. This case control study was carried out in one of the biggest factories manufacturing paint in Egypt. The study was conducted on two groups of individuals; workers group (n=181) and control group (n=186). There are 7 working groups constitute the main working bulk in the factory. Paint production and ink production workers represent 46.1% (n=83). Laboratory workers represent 18.8% (n=34) while storekeepers, industrial safety and maintenance workers represent 20.4% (n=37). Clerks, carpenters and others represent 14.9% (n=27) as shown in (Figure 1). The health risk of exposure to organic solvents depends on the specific solvent and on the level of exposure to the solvent. Solvents differ in their potency to harm health [17]. The results of our study showed statistically significant difference between the workers that exposed to organic solvents and their matched controls in serum urea levels (P-value=0.004). The mean serum urea level of the workers (33±9.6 mg/dl) was higher than that of their matched controls (30±7.9

Table 4: Associations of occupational exposure to organic solvents with risk of renal impairment compared to controls presented as adjusted odds ratios.

	NAG Index	
Variable	Adjusted OR (95%CI)	p-value
Exposure to organic solvents	0.4	<0.0001
Age (years)	1	0.09
Smoking (yes/no)	1.1	0.5
Hypertension (yes/no)	0.6	0.3
Diabetes (yes/no)	0.3	0.06
BMI (kg/m^2)	1	0.2

mg/dl). Statistically insignificant differences were observed in mean values of both serum creatinine and glomerular filtration rate in both studied groups as illustrated in (Figure 2). It is clear that serum creatinine and other routine markers are not very sensitive and are generally only raised when acute renal injury or chronic renal injury is well established [18]. Measurement of certain enzymes such as N-acetyl-β-(D)-glucosaminidase has been used in both animals and man for many years to provide insight into the onset of renal injury. Bazzi, 2002 [19] reported an increase in the urinary excretion of N-acetyl-glucosaminidase (NAG) in subjects exposed to substances toxic for renal tubular cells such as organic solvents. This statement is supported by our results where we found statistically significant difference in the Urinary-N-Acetyl glucosaminidase activity (NAG index); (P-value<0.0001); between the workers that exposed to organic solvents and their matched controls with higher mean ranks among the workers group (Table 2). This may be due to the dysfunction of tubular epithelial cells induced by increased traffic of proteins in the tubular lumen [19]. We found also that the proportion of exposed workers that have abnormal NAG activity (53.6%) is significantly higher than that in their matched controls (29.6%); (p-value<0.0001) as presented in (Table 3). High blood pressure is one of the risk factors of the development of renal disease and is one of the most common leading causes of kidney failure, also called End-Stage Renal Disease (ESRD). Every year, high blood pressure causes more than 25,000 new cases of kidney failure in the United States [20]. The Mean Arterial Pressure (MAP) is a term used in medicine to describe an

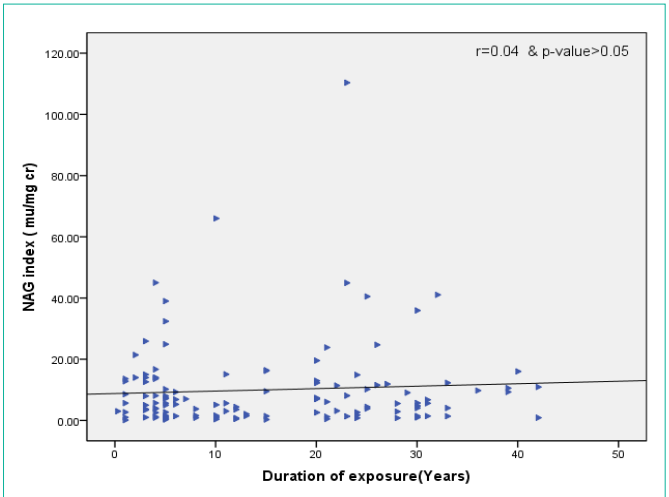

Figure 3: Shows insignificant correlation between NAG activity and the duration of exposure of workers to organic solvents.

average blood pressure in single cardiac cycle in an individual. It is believed that a MAP that is greater than 60 mmHg is enough to sustain the organs of the average person. MAP is normally between 70 to 110 mmHg. If the MAP falls significantly below this value for an appreciable time, the end organ will not get enough blood flow, and will become ischemic [21]. Statistical comparison between the mean blood pressure of the workers group and their matched control group revealed matching between the two groups (p-value=0.1) and both of them were within normal range (91±10.6 mmHg) in workers and (89.5±10.4 mmHg) in controls. Diabetes causes 9.1 to 29.9 percent of the cases of ESRD in various developing countries, and hypertension leads to 13 to 21 percent of the cases [22]. Since 2003, a substantial number of clinical and experimental data concerning the adverse renal effects of smoking have been published [23]. On the other hand obesity may play an important role in the development of chronic kidney disease thus it is considered one of the important renal risk factors [24]. Based on the previous facts, we studied the association between the renal impairment; as defined by increased NAG activity; and the exposure of workers to organic solvents after adjustment of the smoking, diabetic, hypertensive state and BMI of the workers as confounding factors. Statistically significant association was observed between the NAG activity and their occupational exposure to organic solvents (OR=0.4 & P-value<0.0001) as shown in (Table 4). No correlation was observed between the duration of exposure of workers to organic solvents and their level of NAG activity (p-value>0.05) as illustrated in (Figure 3). This finding may be explained by referral of some workers to administrative tasks in the same workplace due to seniority or due to health state, leading to less exposure to organic solvents than other workers. This explanation is in agreement with Price RG, 1992 [25] who reported that the NAG activity remains high during active disease or a sustained toxic exposure but falls to normal levels on recovery or removal of the toxin. It appears that one of every two workers exposed to organic solvents in this factory has early renal impairment which couldn't be detected by the routine renal function tests either during the study or during the annual routine investigations for the workers. This finding may highlights the importance for introduction of early renal biomarkers in the routine annual follow up of workers in the paint manufacturing factories for early detection of the renal impairment.

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Austin Occup Med - Volume 1 Issue 1 - 2016
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Citation: Hegazy IS, El-Raghi HA, Mohammed AM, Rizk SA, Badawy NA and Rashad HM. Prevalence of Renal Impairment among Workers of a Paint Manufacturing Factory. Austin Occup Med. 2016; 1(1): 1003.