STUDY THE RENAL AFFECTION DUE TO SILICA EXPOSURE AMONG MARBLE CUTTING WORKERS

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Abstract:

Background: Silica (SiO_2), an abundant mineral found in sand, rock, and soil is an increasingly identified environmental nephrotoxin with fairly unique renal and systemic manifestations. **Aim:** To identify the relation between silica exposure among marble workers and renal diseases in order to early predict renal affection. **Materials & Methods:** This study was conducted in marble blasting area in El Maadi, in Cairo. The studied group included 25 workers in the marble blasting area. They were adult men aged between 18-42 years (26.5±7.8), working on the basis of 10 hours/day with one day off per week. A referent group of 40 males matched for age (that ranged from 21-41 yrs., 26.2±6.38), sex, socio-economic status, smoking habits selected from relatives of the Kasr Al Aini hospital patients, were also enrolled in our study. Each individual was subjected to detailed occupational and medical history taking and estimation of (A) Environmental air measure of SiO_2 : Using X-Ray Fluorescence Analysis at National Research Center , which demonstrates that silica in air is about 10 times exceeding the Egyptian standard for dust fall (B) Some biological analysis included renal urinary biomarkers . High-molecular-weight protein albumin (U.Malb), the low-molecular -weight protein α1-microglobulin (α 1 - M), urea and creatinine, urinary creatinine and the lysosomal enzyme N-acetyl-β-D-glucosaminidase (NAG). **Results:** Our results showed a statistically significant difference between the exposed and the control groups as regards different renal biomarkers as urinary albumin, serum creatinine, urinary creatinine, blood urea, NAG and α 1 microglobulin in urine. We illustrated a statistically significant positive correlation coefficient between duration of exposure to silica among the exposed group and urinary albumin, serum creatinine, N-acetyl-beta-D-glucosaminidase and α 1 microglobulin. We found also a statistically negative correlation coefficient between duration of exposure to silica among the exposed group and the urinary creatinine. We demonstrated a statistically positive significant correlation coefficient between the age of the workers and different investigations that indicates renal affection and we found also a statistically negative correlation coefficient between the level of serum creatinine and urinary creatinine. **Conclusion:** Our study demonstrated that occupational exposure to silica lead to subclinical signs of nephrotoxicity. Periodic tests as NAG and α 1 microglobulin in urine should be done to detect early renal affection. We should also insist that workers exposed to silica dust must wear protective equipment, and encourage engineering control to reduce the level of silica in air.

Key Words : Silica, renal affection, α 1 microglobulin, NAG , marble blasting

Introduction

Occupational exposure to heavy metals, organic solvents and silica is associated with a variety of renal manifestations. Silica (SiO2) is an abundant mineral found in sand, rock, and soil. Workers exposed to silica include sandblasters , miners, quarry workers, masons, marble and ceramic workers and glass manufacturers. The major environmental and occupational renal diseases include those related to lead, cadmium, chromium, mercury , arsenic, organic solvents and silica (Wedeen ,1997).

Silica (SiO2), an abundant mineral found in sand, rock, and soil is an increasingly identified environmental nephrotoxin with fairly unique renal and systemic manifestations. Approximately two million people are occupationally exposed to silica in the US. Of these individuals, 100 000 are at more than twice the recommended exposure limit determined by the National Institute for Occupational Safety and Health (NIOSH) (Steenland et al., 2001).

Workers in many occupations, particularly sandblasters, miners, quarry workers, masons, ceramic workers, marble workers and glass manufacturers are particularly at risk of silica toxicity (Rosenman et al., 2003) . In addition to the association between inhalation of silica and disabling lung disease that has been suspected for centuries and very well-recognized for many years, the renal implications of exposure to silica has also been increasingly described over the past two decades (Farzaneh et al., 2010).

Aim of the work

To identify the relation between silica exposure among marble cutting workers and renal diseases in order to early detection of renal affection .

Subjects and Methods

This study was conducted in marble blasting area in El Maadi, in Cairo. The study was accomplished during the months of April amd May 2012. The studied group comprised 25 workers in the marble blasting area. They were adult men aged between 18-42 years (26.5 ±7.8), working on the basis of 10 hours/day with one day off per week. None of the workers used any protective equipment during working hours. A referent group of 40 males matched for age (that ranged from 21-41 yrs., 26.2±6.38), sex, socio-economic status, smoking habits selected from relatives of the Kasr Al Aini hospital patients, were also enrolled in our study. The study protocol was first approved by the Ethics Committee of Occupational and Environmental department ethical committee , KasrAl Ainy Hospital, Faculty of Medicine, Cairo University. Prior to this study, a written consent to share in the study and an approval to give blood and urine samples from each individual were obtained after explaining to them the aim and importance of the study. During the study, ethical guidelines of good clinical practices (GCPs) and strict confidentiality was observed throughout sample collection, coding, testing, and recording of the results, during the study. The following investigations were performed after taking individual consent.

(A) Environmental air measure of SiO_2 :

It was done by dust fall jars (collectors). The collectors are cylindrical glass jars 17 cm. in height, 9.5 cm. in diameter, half filled with distilled water, and mounted on iron tripods, the height of which is about 50 cm., to avoid overturning by strong winds and the collection of dusts picked up by winds from the underlying surface (Esmat, 1982).

Using X-Ray Fluorescence Analysis at National Research Center , Analysis and consulting unit. SiO2 was 170 mg/gm of dust sample Precipitation rate was 151.52 gm/m2 / 30 days and Rate of precipitation (dust fall rate) 151.52 gm/m2. month (30 days). According to the Egyptian Standard (year 1971) for dust fall rate, it varies from 7 gm/ m2.month for residential areas to 14 gm/m2. month for industrial areas (Egyptian ministry, 1971). So, it is about 10 times exceeding the Egyptian standard for dust fall.

It was analyzed by X-Ray Fluorescence (XRF).

The instrument is: Axios, WD- XRF Sequential Spectrometer.

It is done in NRC (National Research Center) XRF lab. Two samples were prepared from each specimen after reaching fine powder form. One is fused bead sample, and the other is pressed powder sample.

Results: SiO2 conc. in the sample was 17.32%

SiO2 = 170 mg/gm of dust sample

Rate of precipitation (dust fall rate) = 151.52 gm/m2. month (30 days

According to the Egyptian Standard (year 1971) for dust fall rate, it varies from 7 gm/ m2.month for residential areas to 14 gm/m2. month for industrial areas (Egyptian ministry, 1971). So, it is about 10 times exceeding the Egyptian standard for dust fall.

Another environmental sample was collected on a filter paper actively by air pump for one hour. Another filter paper was used as a control sample. The coating and the control samples were analyzed by thin film X-ray diffraction. The instrument is: X pertpro. Panalytical Cu k α with secondary monochromator Kv:45, ma:40, Holland

Sample analysis revealed that it contains: calcite CaCO3 and dolomite Ca Mg (CO3)2.

Sample preparation:

The samples were arrived to NRC XRF lab as stone peaces; they were crushed then grind in Herzog mill to rich fine powder (it feels like flour when rubbed between the fingers). Two sample were prepared from each specimen. One pressed powder samples prepared in order to measure the trace elements, the other one fused bead were prepared in order to measure the major elements.

Quantitative Analysis:

Main Constituents	Wt%
SiO_2	17.32
Al_2O_3	3.94
Fe_2O_3	2.61
MnO	0.06
CuO	0.04
ZnO	0.02
MgO	2.26
CaO	24.68
K_2O	1.21

(B) Renal urinary biomarkers including the high-molecular-weight protein albumin (U.Malb). Random urine sample was used, volume between 1-10 ml, taken in plastic urine container (not acidified). Patients were instructed to empty their bladders then drink a large glass of water and then we collected the urine samples from them within one hour at KasrAl-Aini (Occupational and environmental department). The samples were kept in the refrigerator till transferred to the lab. (C)The low-molecular-weight protein α1-microglobulin (α1 - M) . (D) Urea and creatinine. (E) Urinary creatinine. (F) The lysosomal enzyme N-acetyl-β-D-glucosaminidase (NAG) .

Blood sample collection:

From each subject, 10 cc of blood were taken through a vein puncture using a dry plastic disposable syringe under complete aseptic condition. Three cubic centimeters of blood were taken into a clean tube containing anticoagulant for determination of urea level in blood. The remaining 7 cc of blood were kept in a tube and allowed to clot then centrifuged for separation of the serum for determination of the following biochemical parameters using Hitashi (911) auto analyzer: i-Kidney function test as creatinine. All Samples were transported to The Biochemistry department at The National Research Centre, Dokki to be analyzed.

Urine sample collection:

A urine sample was collected from each subject, in a sterile container. All subjects washed their hands with soap and water prior to sample collection to avoid contamination.

All investigations were done at The Biochemistry department at The National Research Centre, Dokki.

Statistical analysis

Data obtained from the study was coded and entered using the statistical package SPSS version 16. The mean values, standard deviation (SD) and ranges were then estimated for quantitative variables, as for the qualitative variables, the frequency distribution was calculated. Comparisons between exposed and control groups were done using the independent simple t-test. The correlations between individual variables were calculated using Pearson correlation coefficient. P values less than 0.05 and 0.001 were considered statistically significant.

Results

Our results showed a statistically significant difference between the exposed and the control groups as regards different renal biomarkers as urinary albumin, serum creatinine, urinary creatinine, blood urea, NAG and α 1 microglobulin in urine (Table 1). There was no statistically significant difference between the exposed and the control groups as regards the smoking habit .We illustrated a statistically significant positive correlation coefficient between duration of exposure to silica among the exposed group and urinary albumin, serum creatinine, N-acetyl-beta-D-glucosaminidase and α 1 microglobulin. We found also a statistically negative correlation coefficient between duration of exposure to silica among the exposed group and the urinary creatinine (Table 2). We demonstrated a statistically positive significant correlation coefficient between the age of the workers and different investigations that indicate renal affection as albumin in urine, serum creatinine, blood urea, NAG and α-1 microglobulin (Table 3), and we found also a statistically negative correlation coefficient between the level of serum creatinine and urinary creatinine (Table 4). Environmental study showed that SiO_2 conc. in the sample was 17.32% .

SiO_2 = 170 mg/gm of dust sample

Rate of precipitation (dust fall rate) = 151.52 gm/m2. month (30 days). According to the Egyptian Standard (year 1971) for dust fall rate, it varies from 7 gm/m2.month for residential areas to 14 gm/m2. month for industrial areas (Egyptian ministry, 1971).So, it is about 10 times exceeding the Egyptian standard for dust fall.

Table (1): Comparison between the exposed group to silica and the control group as regards different investigations:

	Exposed group N:25		Control group N:40		t test	P value
	Mean	±SD	Mean	±SD		
Age	34.48	±12.14	35.65	±11.75	-0.38	> 0.05
Albumin in urine (0-8)mg/dl	31.20	±14.15	4.57	±2.50	11.65	**⋆<0.05**
Serum creatinine (0-1.4)mg/dl	1.4	±0.59	0.87	±0.20	5.13	**⋆< 0.05**
Blood urea < 40 mg/dl	49	±22.13	19.5	±10.22	7.29	**⋆<0.05**
Urinary creatinine (30-400)mg/dl	166.8	±100.84	227.95	±64.76	-2.98	**⋆< 0.05**
NAG 1-4 U/gmcreatinine	17.12	±9.38	3.30	±1.09	9.26	**⋆< 0.05**
α 1 microglobulin < 15 mg/gmcreatinine	34.88	±15.18	9.97	±3.93	9.89	**⋆< 0.05**

⋆ **Statistically significant p <0.05**

Table (2): Correlation coefficient between duration of exposure to silica dust among the exposed group and different investigations

	r	P value
Albumin in urine	0.862	**< 0.05⋆**
Serum creatinine	0.857	**< 0.05⋆**
Blood urea	0.679	**< 0.05⋆**
Urinary creatinine	-0.72	**< 0.05⋆**
NAG	0.824	**< 0.05⋆**
α 1 microglobulin	0.895	**< 0.05⋆**

⋆ Statistically significant p <0.05

Table (3): Correlation coefficient between age of the exposed workers and different investigations

	r	P value
Albumin in urine	0.835	**< 0.05⋆**
Serum creatinine	0.873	**< 0.05⋆**
Blood urea	0.672	**< 0.05⋆**
Urinary creatinine	-0.758	**< 0.05⋆**
NAG	0.780	**< 0.05⋆**
α 1 microglobulin	0.885	**< 0.05⋆**

⋆ Statistically significant p <0.05

Table (4): Correlation coefficient between serum creatinine and urinary creatinine among the exposed workers

	r	P value
Urinary creatinine	-0.904	**< 0.05⋆**

⋆ Statistically significant p <0.05

Discussion

Crystalline silica is classically associated with the inhalational occupational disease called silicosis . In our work we studied the association between silica exposure and the development of renal abnormalities. Renal urinary biomarkers that proved most useful to define defects on various parts of the nephron include the following: high-molecular-weight protein, albumin for evaluating glomerular integrity; low-molecular-weight protein; α1-microglobulin (α 1 - M) for assessing tubular protein reabsorption, and the lysosomal enzyme N-acetyl-β-D-glucosaminidase (NAG) to indicate tubular injury (Mueller et al.,1997) . Our study demonstrated that occupational exposure to silica showed a statistically significant difference between the exposed and the control groups as regards different renal biomarkers as urinary albumin, serum creatinine, urinary creatinine, blood urea, NAG and α 1 microglobulin in urine as shown in (table1), and these results are in accordance with (Vupputuri et al., 2012) who reported that occupational exposure to silica may be associated with chronic kidney disease and they also reported the statistically significant differences between workers exposed to silica and the control group as regards the same investigations.

EL-Safty and her co –workers (2003) studied subclinical nephrotoxicity caused by smoking and occupational silica exposure among Egyptian industrial workers. They mentioned that silica exposure resulted in glomerular-type proteinuria with significant elevation of urinary albumin. Hotz and his colleagues (1995) found an increase in the urinary excretion of albumin, transferrin, retinol-binding protein and N-acetyl-beta-D-glucosaminidase in the exposed group to silica and the prevalences of pathological findings were also detected in this group. They also strongly suggested that occupational exposure to silica may lead to subclinical renal effects after less than 2 years and in the absence of silicosis. N-acetyl-beta-D-glucosaminidase is a high molecular-weight lysosomal enzyme found in many tissues of the body. It cannot pass into glomerular ultrafiltrate due to its high molecular weight. However, this enzyme shows high activity in renal proximal tubular cells, and leaks into the tubular fluid as the ultrafiltrate passes through proximal tubules. When proximal tubular cells are injured due to any disease process including glomerular proteinuria, nephrolithiasis, hyperglycemia, interstitial nephritis, transplant rejection or nephrotoxic agents such as antibiotics, antiepileptics, silica or radiocontrast agents, its urine level increases and thus is used as a reflection of proximal tubular cell necrosis (Kavukcu et al., 2002). EL-Safty and her co-workers (2003) stated that data from studying functional and structural integrity of proximal tubules in their study suggested renal proximal tubular damage . Sherson and Jorgensen(1989) studied morphologic changes in kidneys of patients after silica exposure under light and electron microscopy and found that tubular alterations were confined to proximal convoluted tubules. Other researchers also demonstrated an increased urinary excretion of albumin, transferrin, retinol-binding protein and N-acetyl-beta-D-glucosaminidase , α 1 microglobulin in the exposed group to silica (Mwangi et al., 2009). Ng and his colleagues (1993) reported that exposure to silica had glomerular and proximal tubular dysfunction evidenced by increased urinary excretions of albumin, alpha-1-microglobulin (AMG), and beta-N-acetyl-glucosaminidase (NAG). The investigation was replicated in a group of granite workers .

To exclude the effect of smoking on the kidney affection, we demonstrated in our work that there was no statistically significant difference between the exposed and the control groups as regards the smoking habit . Rabi and his colleagues (2010) suggested that heavy cigarette smoking increases the risk of chronic kidney diseases overall and particularly classified as hypertensive nephropathy and diabetic nephropathy.

In our work, we illustrated a statistically significant positive correlation coefficient between duration of exposure to silica among the exposed group and urinary albumin, serum creatinine, N-acetyl-beta-D-glucosaminidase and α 1 microglobulin, we found also a statistically negative correlation coefficient between duration of exposure to silica among the exposed group and the urinary creatinine as shown in (table 2). In contrary to our results Mwangi and his co-workers (2009) said that no correlation was observed between work duration and renal indicators for affection and the reason for that is unclear. Rabiti and his colleagues (1999) reported also that exposure to silica dust among ceramic workers is associated with nephrotoxic effects and the risk was higher among subjects with < 20 years since first employment than among those employed > 20 years. In accordance with our results , Hotz and his colleagues (1995) reported that occupational exposure to silica may lead to subclinical renal effects after less than 2 years and in the absence of silicosis and these effects increased with duration of exposure . NG and his co-workers (1993) found that low molecular weight proteinuria and enzymuria were significantly correlated with duration of exposure in the high but not the low exposure group. These increases were most pronounced in those with 10 or more years of heavy exposure.

In our study , we demonstrated a statistically positive significant correlation coefficient between the age of the workers and different investigations that indicate renal affection as albumin in urine, serum creatinine, blood urea, NAG and α-1 microglobulin as shown in (table 3). We found also a statistically negative correlation coefficient between the level of serum creatinine and urinary creatinine and these findings illustrated in (table 4) . Vearrier and Greenberg (2011) found that advanced age increased the risk of renal and other health affection of miners exposed to silica. Ng and his co-workers (1992) are also in accordance with our findings as they reported that the possible human nephrotoxicity of silica has often been suggested by previous reports about clinical studies of silicotic patients. Urinary excretions of albumin, alpha-1-microglobulin (AMG), and beta-N-acetyl-glucosaminidase (NAG) were measured in 33 male workers exposed to silica (mean duration of employment 16 years) and 19 male age matched non-exposed subjects with no history of primary or secondary renal diseases. Significantly higher urinary excretions of albumin and AMG were found in the workers exposed to silica. These findings suggest that prolonged exposure to silica with increased age of the workers is associated with chronic irreversible nephrotoxicity in exposed workers. We found in our work a statistically significant negative correlation between serum and urinary creatinine among the exposed workers as shown in (table 4). The urine creatinine level is generally compared with the level of creatinine in blood, to find out how well the kidneys are functioning. Low urine creatinine levels is not a cause of concern, if the level of creatinine in blood is normal. If the level of creatinine in urine is high, compared to blood creatinine level, it can mean that the kidneys are healthy and working efficiently. On the other hand, if the level of creatinine in urine is low, but the creatinine level in blood is high, then it could indicate a problem with the kidneys. (Bora, 2011). Abnormal results of urinary creatinine are nonspecific, but may be due to renal affection and the level of urinary creatinine is inversely related to serum creatinine (Landry and Bazari, 2011). These findings are in accordance with our results.

Conclusion

Our study demonstrated that occupational exposure to silica lead to subclinical signs of nephrotoxicity, and this effect related to the duration of exposure and the age of workers that gives us the attention to do periodic tests as NAG and α 1 microglobulin in urine to detect early renal affection and put a good precautions to avoid manifest renal diseases. We should also insist that workers exposed to silica dust must wear protective equipment. Also we recommended to reduce the exposure level of silica in air and reduce working hours. NAG and α 1 microglobulin in urine have superior sensitivity and detect renal affection earlier than serum creatinine, enhancing the ability to demonstrate the benefit of kidney-protective strategies.

References

1. Bora C (2011): Low creatinine levels in urine http://www.buzzle.com/articles/low-creatinine-levels-in-urine.html.
2. Egyptian Ministry of Public Health (1971): Order no 470 for the year 1971.
3. EL-Safty A, Gadallahb M, Shoumanb A E and Nessimb D E (2003): Subclinical nephrotoxicity caused by smoking and occupational silica exposure among Egyptian industrial workers. Archives of Medical Research 34 (5) : 415–42.
4. Esmat A A (1982) : Ph. D. “Physiological studies on the contamination and toxicity of some plants by certain heavy metals”.
5. Farzaneh MR, Jamshidiha F and KowsarianS (2010): Inhalational lung disease. The International Journal of Occupational and Environmental Medicine; 1(1):11-20.
6. Hotz P, Gonzalez-Lorenzo J, Siles E, Trujillano G, Lauwerys R and Bernard A (1995):Subclinical signs of kidney dysfunction following short exposure to silica in the absence of silicosis. In :Nephron. 1995;70(4):438-42.
7. Kavukçu S, Soylu A and Türkmen M (2002):The clinical value of urinary N-acetyl-beta-D-glucosaminidase levels in childhood age group.Acta Med Okayama.;56(1):7-11.
8. Landry DW and Bazari H (2011): Approach to the patient with renal disease. In: Goldman L, Schafer AI, eds. Cecil Medicine. 24th ed. Philadelphia, Pa: Saunders Elsevier:chap 116.
9. Mueller P W, Lash L H, Price R G, Stolte H, Gelpi E, Maack T and Berndt W O (1997): Urinary biomarkers to detect significant effects of environmental and occupational exposure to nephrotoxins. Categories of tests for detecting effects of nephrotoxins. Renal Fail, 19: 505–521.
10. Mwangi DM, NjagiLJ ,Mcligeyo SO, Kihoro JM, Ngeranwa JJN, Orinda GO and Njagi ENM (2009):Subclinical nephrotoxicity associated with occupational silica exposure among male Kenyan industrial workers . In :East Afr Med J. ;86 (5):244-50.
11. Ng TP, Ng YL, Lee HS, Chia KS and Ong HY (1992):A study of silica nephrotoxicity in exposed silicotic and non-silicotic workers.In : Br J Ind Med.;49(1):35-7.
12. Ng TP, Lee HS and Phoon WH (1993): Further evidence of human silica nephrotoxicity in occupationally exposed workers. In: Br J Ind Med. 1993;50(10):907-12.
13. Rabi Y, Habib H, Ayham L, Radwan A, Leon V, George A, Nader K, Saleem A, Saeed A and Sami A (2010):Association between smoking and chronic kidney disease: a case control study, online at: http://www.biomedcentral.com/1471-2458/10/731.
14. Rapiti E, Sperati A, Miceli M, Forastiere F, Di L, Cavariani F, Goldsmith D F, and Perucci C

A(1999): End stage renal disease among ceramic workers exposed to silica:Occup Environ Med.; 56(8): 559–56.

15. Rosenman KD, Reilly MJ and Henneberger PK (2003): Estimating the total number of newly-recognized silicosis cases in the United States. Am J Ind Med;44(2):141-7.
16. Sherson D and Jorgensen F (1989):Rapidly progressive crescenteric glomerulonephritis in a sandblaster with silicosis, In: Br J Ind Med, 46 : 675–676.
17. Steenland K, Sanderson W and Calvert GM (2001): Kidney disease and arthritis in a cohort study of workers exposed to silica. Epidemiology;12(4):405-12.
18. Vearrier D and Greenberg MI (2011): Occupational health of miners at altitude: adverse health effects, toxic exposures, pre-placement screening, acclimatization, and worker surveillance. In :ClinToxicol (Phila); 49 (7): 629-40.
19. Vupputuri S, Parks CG, Nylander-French LA, Owen-Smith A, Hogan SL and Sandler DP (2012): Occupational silica exposure and chronic kidney disease, In :Ren Fail;34(1):40-6.
20. Wedeen RP (1997): Occupational and environmental renal disease. Semin Nephrol;17(1):46-53.