Impact of occupational exposure to elemental mercury on some antioxidative enzymes among dental staff

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Impact of occupational exposure to elemental mercury on some antioxidative enzymes among dental staff

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Abstract

Objectives: The aim of this study is to investigate the effect of elemental mercury exposure on renal function and antioxidative enzymes activity as a possible mechanism of renal affection among dental staff. Methods: This study was performed on a group of dental staff exposed to elemental mercury (N=32) and matched control group (N=37). Urinary and blood level of mercury, albumin α1 microgloblin in urine, glutathione peroxidase and superoxide dismutase blood level were measured for the exposed and control group. Results: Compared to the control group, urinary and blood mercury were significantly higher in the exposed group. Glutathione peroxidase and superoxide dismutase activities in blood were significantly decreased and were negatively correlated with duration of work. Conclusion: Oxidative stress is an important molecular mechanism for renal dysfunction in mercury exposure, manifested by decreased activities of antioxidant enzymes.

Keywords

Dental staff, elemental mercury, glutathione peroxidase, renal affection, superoxide dismutase

Introduction

Oxidative stress is an important molecular mechanism for kidney injury in mercury toxicity. Some studies have shown increased indices of lipid peroxidation and changes in the activities of antioxidant enzymes in laboratory animals exposed to mercury (Augusti et al., 2007; Bano and Hasan, 1989; Miller et al., 1991; Seppänen et al., 2004; Stohs and Bagchi, 1995). Another experimental study elicited nephrotoxicity and oxidative damage by improving antioxidant defense, tissue integrity, and energy metabolism (Khan et al., 2009; Stankiewicz and Skrzydlewska, 2003).

The role of the kidneys in the excretion of toxic substances from the body means that the kidneys are a target organ for many toxic substances and renal effects have been used as an early indicator of environmental exposure to many heavy metals and solvents (De Burbure et al., 2003; El-Safty et al., 2002; Ritchie et al., 2004) but the long-term effects on this organ have not yet been determined with certainty.

Exposure to mercury has been known to adversely affect human health (Langworth et al., 1997; Trzcinka-Ochocka et al., 2007; Zolfaghari et al., 2007). However, the results of epidemiological studies among dental workers occupationally exposed to mercury are inconsistent concerning renal function.

The property of mercury to amalgamate with other metals is used to create a material for filling teeth. This material remains the cheapest and most efficient in tooth restoration. From the nephrotoxicity point of view, dental amalgam is an unsuitable filling material, as it may give rise to mercury toxicity. Mercury levels in blood and urine are good markers of such toxicity. In exposure conditions, renal damage is possible and may be assessed by urinary excretions of albumin, NAG, and gamma-GT (Apostoli et al., 2002; Jarosińska et al., 2008; Mortada et al., 2002).

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On the basis of experimental studies (Augusti et al., 2007; Singh et al., 2003; Zwolińska et al., 2004), the role of oxidative stress and its relation to renal dysfunction-induced nephrotoxicity has been discussed, however, the precise mechanism underlying mercury-induced renal damage in human due to oxidative stress is not studied in detail.

So the aim of this research is to detect the relationship between elemental mercury exposure and oxidative stress by measuring the activities of some antioxidant enzymes glutathione peroxidase (GPx) and superoxide dismutase (SOD). And to verify the mercury effect on antioxidative enzymes activities as a possible mechanism of renal affection among dental staff.

Participants and Methods

Study Population

This study was performed on an exposed and a control group. The exposed group consisted of 32 individuals of dental staff exposed to elemental mercury, comprising of 20 nurses (7 males and 13 females) and 12 dentists (8 males and 4 females). Dental staff were all affiliated to the department of pediatric dentistry, Faculty of Oral and Dental Medicine, Cairo university.

Control group consisted of a total of 37 individuals (17 males and 20 females) selected from other departments at the same hospital, not exposed to elemental mercury, matching the exposed group as regards age, gender, socioeconomic status and special habits of medical importance.

Prior to this study, approval of the pediatric dentistry department chairman was obtained. A consent to share in the study and an approval to give blood samples from each individual were obtained after explaining to them the aim and importance of the study. Strict confidentiality was observed throughout sample collection, coding, testing, and recording of the results. Participants were allowed to obtain copies of the results.

Methods

The study population was subjected to a specially designed detailed questionnaire including medical history, personal, present, past, family and occupational history.

The exculsion criteria for both groups necessitate that there is no history of occupational exposure to nephrotoxic substances, no history of renal diseases, diabetes mellitus, no evidence of hematuria, pyuria, glycosuria, and urinary tract infections.

The exposed group fulfilled the inclusion criteria that necessitate working with amalgam on daily basis during at least 2 years, at least 4 hours per day.

Laboratory Investigations

Blood was collected in metal-free polyethylene tubes. The blood samples were centrifuged at 1500*g* for 20 minutes at 5°C. Packed erythrocytes and plasma were then separated. All the samples were stored at −80°C until analyzed. Also urine samples (25 mL) were collected and stored at −80°C.

Measurement of mercury level in urine (U-Hg) and blood (B-Hg). The samples were wet digested with nitric and perchloric acids (5:1) at 25-35°C. Then the samples were filtered through Whatman Ashless Filter Paper, and added to bi-distilled water to total amount of 10 mL. The mercury content was determined in wet digested samples by a cold vapor atomic absorption technique using mercury evaporation kit. All chemicals used in analysis were of analytical grade. Calibration standard (CAL): A solution was prepared from the dilution of stock standard solutions. Mercury Hollow Cathode Lamp was used. Absorption Cell-Standard spectrophotometer cells 10-cm long having quartz windows also was used.

As for blood mercury, concentrations were estimated in μg/L and expressed as means of total mercury in blood, considering the plasma and erythrocyte ratio (2/3). As regards urinary mercury, it was corrected according to urinary creatinine and was expressed in μg Hg/g creatinine.

Assessment of renal function. Quantitative analyses of proteins in urine were performed using a Behring BN II nephelometer (Schotters et al., 1988). Glomerular renal function was assessed by determining albumin in urine, while tubular renal function was assessed by determining α1 microgloblin in urine. The protein concentrations in urine were expressed per gram of creatinine. Creatinine in urine was on a Roche/Hitachi 917 automated biochemical analyzer.

Determination of GPx activity blood level. Blood was collected using EDTA as anticoagulant and centrifuged at 1000 *g* for 10 minutes. The white buffy layer formed of leucocytes was then removed and discarded. Erythrocytes were lysed in 4 volumes of ice-cold HPLC-grade water then centrifuged at 1000 *g* for

Table 1. Mean ± SD of mercury in urine, mercury in blood, superoxide dismutase, glutathione peroxidase in blood and albumin α_1 microgloblin, in urine between exposed and control group

	Exposed	Control		
Value	*N* = 32	*N* = 37	*t*-Test	*p* Value
Mercury in urine[a]	10.02 ± 1.36	4.74 ± 0.84	19.67	**<0.001**
Mercury in blood[b]	7.74 ± 1.03	4.79 ± 0.84	13.59	**<0.001**
Superoxide dismutase[c]	240.03 ± 34.90	415.44 ± 44.63	-17.9	**<0.001**
Glutathione peroxidase[d]	18.66 ± 2.07	30.10 ± 4.26	-13.80	**<0.001**
Albumin in urine[e]	1.24 ± 0.65	0.55 ± 0.26	5.91	**<0.001**
α_1 microgloblin[f]	1.70 ± 0.72	0.70 ± 0.17	8.22	**<0.001**

[a]Mercury in urine (U-Hg): μg Hg/gm creatinine.
[b]Mercury in blood (B-Hg): μg/L.
[c]Superoxide dismutase (SOD):μg/L
[d]Glutathione peroxidase (GPX):μg/L
[e]Albumin in urine: gm/creatinine.
[f]α_1 microgloblin in urine: gm/creatinine.

15 minutes at 4°C. Supernatant erythrocyte lysate collected was analyzed.

The Cayman glutathione peroxidase assay kit was used to measure all the glutathione-dependent peroxidases in plasma and erythrocyte lysate indirectly by a coupled reaction with glutathione reductase (GR). The oxidized glutathione produced upon reduction of hydroperoxide by GPx was recycled to its reduced state by GR and NADPH. The oxidation of NADPH to $NADP^-$ was accompanied by decrease in absorbance at 340 nm which was directly proportional to the GPx activity in the sample (Ursini et al., 1985).

Determination of superoxide dismutase activity (SOD) blood level. SOD Assay Kit-WST allows very convenient SOD assaying by utilizing Dojindo's highly water-soluble tetrazolium salt, WST-1 (2-(4-Iodophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfophenyl)-2H-tetrazolium, monosodium salt) that produces a water-soluble formazan dye upon reduction with a superoxide anion. The rate of the reduction with O_2 are linearly related to the xanthine oxidase (XO) activity and is inhibited by SOD. Therefore, the 50% inhibition activity of SOD or SOD-like materials can be determined by a colorimetric method (Ukeda et al., 1997).

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 less than 0.005 were considered statistically significant and highly significant, respectively.

Results

The study population consists of exposed and control groups. The exposed group consisted of 32 dental staff 20 nurses (62.5%; 7 males and 13 females) and 12 dentists (37.5%; 8 males and 4 females working in department of pediatric dentistry). Their mean age was 43.23 ± 10.75 years ranging from 28 to 67 years. Mean duration of exposure was 17.18 ± 5.93 years ranging from 8 to 24 years. The mean age of the control group were 41.33 ± 10.78 years, ranging from 25 to 66 years, showing no statistically significant difference when compared with exposed group.

The mean value of measured creatinine corrected urinary mercury (U-Hg) among exposed dental personnel (10.02 ± 1.36 μg Hg/gm creatinine) was statistically significantly higher than that of the controls (4.74 ± 0.84 μg Hg/gm creatinine) $p < 0.001$; Table 1.

Estimation of total mean value of blood mercury showed significantly higher levels among the exposed dental personnel compared to their controls (7.74 ± 1.03 versus 4.79 ± 0.84 μg/L) $p < .001$; Table 1.

The indicators of renal function as albumin and α_1 microgloblin in urine were significantly elevated at level $p < 0.001$ (Table 1) in exposed dental staff compared with control group.

Table 2. Correlation coefficient® between duration of exposure to mercury and each of mercury in urine (U-Hg), mercury in blood (B-Hg), superoxide dismutase (SOD) and glutathione peroxidase (GPX) among exposed workers.

	U-Hg	B-Hg	SOD	GPX
Duration of exposure	r = 0.403 p < 0.05	r = 0.436 p < 0.05	r = -0.407 p < 0.05	r = -0.656 p < 0.001

Table 3. Correlation coefficient® between duration of exposure to mercury and each albumin and α microgloblin in urine among exposed workers

	Albumin in urine	α_1 microgloblin in urine
Duration of exposure	R = 0.823	r = 0.838
	p < 0.001	p < 0.001

The mean value of GPx and SOD activities in blood were statistically significantly decreased ($P < 0.001$ Table 1) in exposed dental personnel compared with control group.

Correlation between different variables revealed positive significant correlation between duration of work exposure to elemental mercury among dental professional and both U-Hg and B-Hg ($r = .40$, $p < 0.05$ $r = 0.436$ $p < 0.05$ respectively; Table 2).

There is a statistically significant negative correlation between duration of work exposure to elemental mercury and both GPx and SOD ($r = -0.656$ $p < 0.001$; $r = -0.407$ $p < 0.05$, respectively; Table 2).

A significant positive correlation between duration of work exposure to elemental mercury among dental professional and both albumin and α_1 microgloblin in urine ($r = 0.823$, $p < .001$; $r = .838$ $p < .001$, respectively; Table 3).

A positive significant correlation between U-Hg (mercury in urine) and each of B-Hg (blood mercury), albumin and α_1 microgloblin in urine ($r = 0.644$, $p < .001$; $r = 0.387$, $p < 0.05$; $r = 0.452$; $p < 0.05$, respectively, Table 4).

A statistically significant negative correlation were between U-Hg (mercury in urine) and both GPx and SOD activities in blood $r = -0.668$, $p < .001$, $r = -0.670$, $p < 0.001$; respectively; Table 4.

Discussion

Mercury is well-known to be absorbed by the body following inhalation, with numerous occupational studies showing air levels to be correlated with internal doses estimated by urinary mercury excretion (Farahat et al., 2009; Heyer et al., 2008; Levy, 1995; Mortada et al., 2002). There is much controversy about the safety of dental amalgam as it has been demonstrated to pose occupational risks to dental practitioners and their assistants

In the current study, the mean concentration of U-Hg mercury among dental workers were higher than their control (Table 1), this is in accordance with the results reported by several studies (Jarosińska et al., 2008; Mortada et al., 2002; Ritchie et al., 2004). The significant elevation of urinary mercury levels in the current study in exposed dental staff can be explained on the basis of lack of awareness regarding their occupational risks, such as lack of wearing gloves and masks all the time during manual handling of mercury amalgam. Contaminating the room air from careless behavior as expressing excess mercury from mercury amalgam and during routine removal of old amalgam fillings with high-speed rotary instruments, lack of hygiene measures as proper exhaust ventilation.

However, Trzcinka-Ochocka et al. (2007) in their study aimed at assessing the effect of exposure to mercury (Hg) vapor from amalgam fillings among dental surgery staff in a city of Poland. They reported that there was no statistically significant differences in the mean of urinary Hg concentrations between the study and control groups. Better work hygiene measures when handling amalgam fillings and use of alternative materials for dental fillings are factors accounting for the different results between our study and theirs. As the blood level of mercury B-Hg among dental workers were higher than their control

Table 4. Correlation coefficient® between mercury in urine (U-Hg) and each of mercury in blood (B-Hg), superoxide dismutase (SOD), glutathione peroxidase (GPX) and albumin and α_1 microgloblin in urine among exposed workers

B-Hg	SOD	GPX	Albumin in urine	α_1 microgloblin in urine	
U-Hg	r = 0.644 p < 0.001	r = −0.670 p < 0.001	r = −0.668 p < 0.001	r = 0.387 p < 0.05	r = 0.452 p < 0.05

Table 5. Mean ± SD of duration of exposure to elemental mercury among exposed group

	Mean	SD	Range
Duration of exposure[a]	17.18	5.93	8-24

[a] Duration of exposure in years.

(Table 1), this is in agreement with the results reported by (Farahat et al., 2009; Mortada et al., 2002); however, in another study by Apostoli et al. (2002), who detected the concentrations of U-Hg and B-Hg in 3 different groups: 122 workers exposed, 18 workers formerly exposed and 196 subjects not occupationally or environmentally exposed to mercury, found that B-Hg values were similar in the three groups, this may be due to longer duration of exposure in our study than theirs.

In our study, there is a statistically significant positive correlation between duration of exposure and both U-Hg and B-Hg (Table 2), this is in resemblance with the results of Herber et al., 1988; Ritchie et al., 2004; Trzcinka-Ochocka et al., 2007; however, it did not agree with Kobal et al. (2004); in their study of retired miners, they reported a significant negative correlation between U-Hg concentration and duration of time after exposure.

Dental amalgam filling contains about 50% elemental mercury, possible health effects as renal dysfunction have been discussed in some studies (Bates, 2006; Brownawell et al., 2005; Levy,1995; Mackert and Berglund, 1997). However in the field of dental practice, mercury emitted from dental amalgam and possible health effects among dental professional have not been studied in detail.

In this study, antioxidant activities GPx and SOD activities in blood were determined in an attempt to find out whether the effect of long term exposure to mercury from dental amalgam induce renal dysfunction in dental professionals. The detoxification process for heavy metals involves reduced glutathione (GSH), metallothioneins and interactions with other elements such as selenium and its antioxidative selenoenzymes, e.g. glutathione peroxidase (GSH-Px).

SOD is an enzyme used extensively as a biochemical indicator of pathological states associated with oxidative stress (Perrin-Nadif et al., 1996).

Numerous studies have indicated that mercury can promote lipid peroxidation in laboratory animals exposed to mercury through free radical generation and interaction with antioxidative enzymes activities (Bulat et al., 1998; Jadhav et al., 2007; Kobal et al., 2004; Patrick, 2002; Seppänen et al., 2004). However, the precise mechanism underlying mercury induced renal damage in human due to these activities are not studied in detail.

In the current study, the concentrations of GPx and SOD activities in blood of exposed group were significantly lower ($p < 0.01$) than in controls, Table 1. Our findings are in agreement of Bulat et al. (1998), who found increased lipid peroxidation in erythrocytes of workers occupationally exposed to elemental mercury. And they postulated that this exposure leads to decreased activity of GPX and SOD in erythrocytes.

Our study is in resemblance to the results of Kobal et al. (2008), who studied the potential effects of remote long-term intermittent occupational elemental Hg vapour exposure on erythrocyte glutathione levels and some antioxidative enzyme activities in ex-mercury miner, in period after exposure. They found significantly lower reduced GSH level ($p < 0.05$) determined in group of retired miners; however, there were no differences in mean total reduced GSH, oxidized disulphide glutathione (GSSG) concentration levels, and GSH/GSSG ratio between miners and controls were found. Also a positive correlation between GSSG and present U-Hg excretion ($r = 0.41$, $p = 0.001$) in the whole group of ex-mercury miners was observed. On the other hand, our study shows a statistically significant negative correlation between U-Hg (mercury in urine) and both GPx and SOD activities in blood, Table 4. This can be explained by the fact that our workers are still working but Kobal's workers were retired.

According to Kobal et al. (2008), the moderate but significantly increased GSH level, GR and catalase (CAT) activity in erythrocytes in the subgroup of miners observed in the period after exposure to Hg could be an inductive and additive response to maintain the balance between GSH and antioxidative enzymes in interaction with the Hg body burden accumulated during remote occupational exposure, which does not represent a severely increased oxidative stress.

The kidneys are one of the main target organs for elemental mercury, which accumulates in the kidneys, some studies have shown this effects (El-Safty et al., 2003; Franko et al., 2005). However, in occupational field, the long-term effects of elemental Hg on the kidneys have not been studied in detail.

According to Roels et al. (1999), successful prevention of renal diseases induced by occupational or environmental exposure to toxic metals such as mercury relies on the capability to detect nephrotoxic

effects at a stage when they are still reversible or at least not yet compromising renal function.

The knowledge of dose-effect/response relations has been useful to control nephrotoxic effects of these metals through a 'biological monitoring of exposure approach.' Chronic occupational exposure to inorganic mercury (mainly mercury vapor) may result in renal alterations affecting both tubules and glomeruli (Mortada et al., 2002).

In this study, the indicators of renal function as albumin and α_1 microgloblin in urine were significantly elevated at level $p < 0.001$ (Table 1) in exposed dental personnel compared with control group. This is in agreement with Franko et al. (2005), who found significantly elevated albumin, IgG and α_1 microgloblin in urine of exposed miners of Idrija mercury mine when compared to unexposed group. This is not in agreement of Langworth et al. (1997), who found no difference between the exposed and control group in urinary excretion of albumin and urinary activity of the tubular enzyme *N*-acetyl-beta-glucose-aminidase of mercury exposure in the dental professional in Sweden.

In the current study, a significant positive correlation between duration of work exposure to elemental mercury among dental professional and both albumin and α_1 microgloblin in urine ($r = 0.823$, $p < 0.001$; $r = 0.838$ $p < 0.001$ respectively; Table 3). This is concomitant with the study of Franko et al. (2005). So, determination of urine proteins as markers of early subclinical renal damage may be useful in monitoring occupational exposure to mercury vapours, especially in the group of workers with higher values of urine mercury concentrations.

Although, Table 4 shows, a positive significant correlation between U-Hg (mercury in urine) and each of albumin and α_1 microgloblin in urine ($r = 0.387$, $p < 0.05$; $r = 0.452$ $p < 0.05$, respectively). However, none of our study subjects has clinical evidence of renal damage.

From this study, we conclude that dental staff exposed to elemental mercury showed higher levels of urinary and blood mercury compared with their control group. We also concluded that oxidative stress is an important molecular mechanism for renal dysfunction in mercury toxicity among dental staff, this manifested by decreased activity of GPX and SOD. Further studies are warranted to investigate the mercury role on renal function in exposed workers.

American Dental Association (ADA) has recognized the importance of observing proper mercury hygiene practices for the safety of dental professionals. In 2003, the ADA Council on Scientific Affairs adopted mercury hygiene recommendations to provide guidance to dentists and their staff members for safe handling of mercury and dental amalgam. Also, they described office engineering considerations and hygiene recommendations to be used during preparation and placement of dental amalgam restorations.

So, we recommend safe handling of amalgam, as a source of mercury, in the training of dentists and their assistants. Also, good and proper ventilation is a must at place of working. We also recommend 1-year follow-up to find out the effects of implementation of hygienic measurements on mercury levels in blood and urine of dental staff and their affection on renal function and antioxidants enzymes.

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