REVIEW

Mercury exposure of gold mining workers in the northwest of Iran

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Abstract: Mercury exposure is a health concern in the occupational settings like gold mining and chloralkali industries and blood and urine levels of mercury are used as exposure indicators. In this study, blood and urine concentrations of mercury were determined using hydride generation atomic absorption spectrophotometery (HGAAS) in sixteen gold miners with neuropsychiatric symptoms. The patients treated with two chelating agents, dimercaprol and D-penicillamine. The mean serum mercury levels before and after chelation therapy were 208.14 $\mu g/L^{-1}$ and 10.50 $\mu g/L^{-1}$, respectively. The mean urinary mercury levels before and after chelation therapy were 134.70 $\mu g/L^{-1}$ and 17.23 $\mu g/L^{-1}$, respectively. The results of this study showed that there are significant differences between concentration of blood and urine mercury before and after intervention (p<0.005). There were no significant differences between in the biochemistry parameters of patients before and after treatment. This study indicated that the gold miners in the northwest of Iran had been exposed to high levels of mercury vapors [$Hg^{(0)}$].

Keywords: Dimercaprol, D-penicillamine, gold mining, mercury, Iran.

INTRODUCTION

Environmental and occupational exposure to heavy metals such as mercury, arsenic and lead are of significant health concern worldwide (Bartolucci *et al*., 2002). Such metals are known to target the mammalian organs such as central nervous system, gastrointestinal tract, cardiac and vascular system. Mercury is one of the most toxic metals found in three forms with different toxicities: elemental, inorganic and organic. Elemental form of mercury as vapor [$Hg^{(0)}$] is much more hazardous than the liquid form (Orloff *et al*., 1997). Mercury vapor exposure can occur from working in hazardous environments such as chloralkali industry, electrical control devices and from processing and extraction of gold, especially in developing countries (Mniszek 2001). Since heating in liquid mercury is the first step of purification of gold ore that is commonly carried out at the mining plants, a high mercury vapors can be found prevalently in the gold mining areas. To eliminate mercury in gold mining, before smelting, gold precipitates are heated to get rid of residuals of mercury (Drasch *et al*., 2001) and approximately, 3 to 5 million gold miners use mercury amalgamation to produce gold worldwide. Therefore these workers are in great risk of exposure to mercury, that needs to be prevented and treated (Eisler 2003).

Exposure to mercury can occur through several routes such as dermal, oral, and inhalation. In the case of vaporous mercury, inhalation of significant concentrations of mercury vapors during processing and extraction of gold is the main route of exposure. Inhalation of mercury vapors causes high blood concentration of mercury and can result in a variety of respiratory, neurologic, renal, immunologic, and reproductive disorders (Risher and Amler 2005).

Chelation therapy for the treatment of acute exposure to heavy toxic metals is accepted clinical and medical practice (George *et al*., 2004). Several chelators are available in medicine for treating toxicity of various forms of mercury and/or other metals with different efficacy. Improper use of chelators may generate unnecessary risk to the patients along with other potential risks such as binding to other divalent cations like zinc, copper, iron, chromium, manganese, and calcium that are essential for normal body function. Hence, to select the best chelators, it is important for attending physicians to know the route of exposure, side effects and route of excretion of the toxic metal. However, currently there is no unambiguous guidelines for physicians to identify the conditions in which chelation is either indicated or contraindicated.

Detection of mercury in biological samples such as blood and/or urine samples is a crucial diagnostic in assessing the levels of mercury contamination in environment and

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at workplaces (Ertas and Tezel 2004). This is important because of a need for distinguishing between mercury-induced symptoms from other agents that may cause similar manifestations or symptoms.

We investigated the role of mercury toxicity in inducing neuropsychiatric disorders. We studied the correlations between levels of mercury exposure to clinical neuropsychiatric manifestations in a group of sixteen men with clinical neuropsychiatric symptoms who worked in gold mines in the northwest of Iran.

MATERIALS AND METHOD

Subjects

A group of sixteen men, ranging in age from 25 to 56 years, worked in gold mining in the northwest of Iran. They were referred to the emergency department of Loghman Hakim Poison hospital and showed symptoms of neuropsychiatric manifestations like fatigue, insomnia, anorexia, and some had tremor of the fingers and impotency. Diagnosis of neuropsychiatric disorders was established by patients' physicians, based on the lack of any other diseases. High levels of mercury in blood and urine samples were detected by using hydride generation atomic absorption spectrophotometery (HGAAS).

Instrumentation

Levels of blood and urine mercury were detected by cold vapor- atomic absorption technique. Mercury evaporation kit (VGA-77) was used at a Varian Model AA240FS atomic absorption spectrometer.

Reagents

All analytical grade reagents were purchased from Merck Darmstadt. Deionized (18.2MΩcm_1) water was used throughout the experiments, obtained from lab water purification system (USF ELGA maxima HPLC made in UK).

Sample collection

Prior to use and to eliminate any contamination, all plasticwares were submerged overnight in 20% nitric acid, rinsed thoroughly with deionized water and dried in incubator at 40°C and 24h. Urine samples were collected and stored at 4°C prior to analyses.

Determination of mercury in whole blood

One mL of whole blood was mixed with 4 mL of a mixture 70% (w/w) each of nitric acid, perchloric acid and sulfuric acid respectively 2:1:1. This mixture was warmed at 45oC for 60 minutes then heated at 90^{o}C for at least 60 minutes until the brown fumes eliminated and remaining golden yellow liquid. Mercury cation was reduced to metallic form by stannous chloride 25% (w/v) in a hydrochloric acid 20% (v/v).

Determination of mercury in urine

Polyethylene containers were used to collect urine samples. Collected urine samples were centrifuged at 3000g for 10 min and the supernatants were analyzed. All analyses were performed using the hydride generation-atomic fluorescence.

Treatment

The first step in treatment process is eliminating the source of exposure. All patients were hospitalized for five days. They were treated with Dimercaprol 250 mg IM every 6 hours for 3 days, and an additional two days with same dose every 12 hours. D-penicillamine 250 mg was given orally 3 times a day for 15 days, along with vitamin B6 in an outpatient setting.

RESULTS

In this study, sixteen gold miners with neuropsychiatric symptoms were recruited. Urine and blood samples from patients were collected and analyzed for total mercury concentration before and after treatment. Mean of mercury levels in serum and urine samples before treatment were 197.88±131.842µg/ L^{-1} (10 to 390) and 122.50±51.575µg/ L^{-1} (40 to 200), respectively (table 1). These levels were significantly higher than reference range of mercury in serum (0.6-59 µg/L^{-1}) and urine (5-20 µg/L^{-1}). Interestingly, few patients had normal levels of serum mercury but 100% of patients had significantly higher mercury levels in the urine. Patients were treated with metals chelators dimercaprol and D-penicillamine as elaborated in materials and methods. Three months after beginning of treatments, urine and blood samples were collected for measuring mercury levels. Mean of post-treatment mercury levels in blood and urine reduced to 9.56±4.13µg/ L^{-1} and 16.12±7.94µg/ L^{-1}, respectively that was significantly lower than pre-treatment levels (p<0.001).All patients after treatment showed serum and urine mercury levels within normal limits. Abdominal, kidney and liver sonograms in all patients were normal and there were no significant differences in the biochemistry panel before and after treatment (table 1).

DISCUSSION

Exposure to mercury vapor in gold mining is an occupational hazard and has been reported in several publications in different areas of the world. Despite many gold mining plants, there is no report of levels of mercury in body fluids of gold miners in Iran. The poor occupational conditions and the continuous activity of gold miners justify biological monitoring of mercury exposure. Based on IPCS, mercury levels in body fluids such as serum and urine are used as indicators for recent, constant, and long-term exposures. Inhalation of mercury vapor and to a lesser extent absorption from skin result in elevation of mercury levels in serum. Our data shows that

in neuropsychiatric patients serum mercury level was not high in all cases but 100% of patients had elevated urine mercury levels. This indicates the importance of urine mercury level in diagnosis of mercury toxicity in patients with neuropsychiatric manifestations. Oxidization of mercury vapor [$Hg^{(0)}$] by catalase enzyme results in divalent ionic mercury [$Hg^{(II)}$], and excretion in the urine (IPCS 1991). Considering that the level of inorganic form of mercury in urine is elevated much slower than blood mercury level, it is reasonable to conclude that blood mercury level can be utilized as an indicator of recent exposure whereas urinary level of mercury to be exploited as an indicator of chronic exposure to mercury vapor [($Hg^{(0)}$] (Barregard 1993).

Table: Laboratory findings

	Group	N	Mean	Std. Deviation	*p* value
Serum (Hg)	Pretreatment	16	197.88	131.842	0.001
	Posttreatment	16	9.56	4.131	
Urine (Hg)	Pretreatment	16	122.50	51.575	0.001
	Posttreatment	16	16.12	7.940	
D.B.	Pretreatment	16	0.4125	0.09574	0.068
	Posttreatment	16	0.4000	0.16330	
T.B.	Pretreatment	16	1.8438	0.16721	0.005
	Posttreatment	16	1.9812	0.47919	
Cr	Pretreatment	16	0.9938	0.22051	0.350
	Posttreatment	16	0.9562	0.26575	
BUN	Pretreatment	16	14.1250	2.02896	0.022
	Posttreatment	16	15.0000	3.70585	
Na	Pretreatment	16	1.3569E2	3.04891	0.276
	Posttreatment	16	1.3500E2	3.68782	
K	Pretreatment	16	3.9687	0.24144	0.152
	Posttreatment	16	4.1500	0.34448	
AST	Pretreatment	16	20.2500	2.84019	0.061
	Posttreatment	16	22.0625	4.56755	
ALT	Pretreatment	16	27.3125	3.80734	0.075
	Posttreatment	16	27.3125	5.62991	

Direct Billirobine (D.B.), Total Billirobine (T.B.) Ceratinine (Cr), Blood Urea Nitrogen (BUN), Serum Sodium (Na), Serum potassium (K), Alanine transaminase (ALT), Aspartate transaminase (AST), Reference range of mercury; (Urine Hg 5-20 µg/lit, Serum Hg 0.6-59 µg/lit)

In normal population and in the absence of consumption of methyl mercury contaminated fish, mean concentration of mercury level in serum is approximately 5-10 $\mu g/L^{-1}$ (IPCS 1991). However, the level of serum mercury in employers of certain workplaces varies from 20 to 100 $\mu g/L^{-1}$ (Schutz *et al*., 1994). In another study, elevated mercury levels were found in blood and urine samples of patients who worked in the amalgam extraction salons (Bose-O'Reilly *et al*., 2008). The urine samples of workers burning amalgam have shown mercury levels as high as 400 $\mu g/L^{-1}$. These levels of mercury are indicative of chronic exposure to mercury sources.

The acceptable and the most common treatment for decontaminating toxic metals is chelation therapy. There are several chelating agents that can bind to mercury and facilitate its elimination through the urine (Risher and Amler 2005). Among the best chelating agents that are used to remove mercury from the body, D-penicillamine and Dimercaprol have been used commonly (George *et al*., 2004). Meso-2,3-dimercaptosuccinic acid (DMSA) and 2,3-dimercapto-1-propanesulfonic acid (DMPS) have also been used to treat acute inorganic mercury poisoning, however, there is no report to demonstrate that these chelating agents may have clinical benefits in patients with poisoning from elemental mercury vapor (Bluhm *et al*., 1992; Sandborgh Englund *et al*., 1994). DMSA is approved by FDA only for treating mercury poisoning in children. Although recommended by few physicians for treating mercury poisoning, Glutathione and N-acetylcysteine (NAC) have been reported to have side effects such as elevation of mercury levels in kidneys and brain (Rooney 2007). Several studies have reported possible adverse responses following administration of Dimercaprol and D-penicillamine (Boscolo *et al*., 2009) but in our treatment process, no adverse effect was reported by or detected in any patients. Patients' symptoms of insomnia, irritation, excitement, agitation, weakness, tremors in the hands and fingers and reduced libido were reduced during and abolished by end of the treatment protocol, indicating that they were cured completely. A significant differences between pre-treatment and post-treatment mercury levels in urine and blood samples was seen ($p<0.001$), demonstrating the efficacy of the interventions (table 1). The main advantages of our protocol for treatment of mercury poisoning were using low doses of medicines and a short period of therapy. Further studies are warranted to confirm our data and to elucidate the extent of exposure to mercury in northwest of Iran.

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