Potential Kidney Effects in Ex-Miners of the Idrija Mercury Mine Exposed to Elemental Mercury and Silica Dust

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Abstract: Increased mortality from kidney disease was observed in miners exposed to crystalline silica and elemental mercury (Hg°) in the Idrija Mercury Mine. The objective of this study was to evaluate certain biological markers of potential nephrotoxicity in miners with remote occupational exposure to Hg° and silica dust. 49 ex-miners and 56 age-matched controls were included in the study. The markers of nephrotoxicity were evaluated as a urinary protein of high and low molecular weight (albumin and a1-mglobulin) and N-acetyl-b-D-glucosaminidase enzyme activity (NAG). Past occupational exposure of miners to Hg° was evaluated using biological indices of exposure. The U-Hg levels obtained during past exposure varied from 50 to 122 mg/L. 75% of all observed miners were co-exposed to silica dust. No differences in background exposure to Cd and Pb were observed between the two groups. Slight increases in urinary albumin (p=0.041) and a1-mglobulin (p=0.025) were observed in ex-miners. The magnitude of observed levels of glomerular and tubular proteins represents no clinically significant alteration of renal function. The role of background exposure to Pb and Cd and some other confounders cannot be ruled out.

Key words: elemental mercury, silica, occupational exposure, nephrotoxicity

INTRODUCTION

Increased mortality from kidney disease was observed in miners exposed to crystalline silica (SiO_2) and elemental mercury (Hg°) in the Idrija Mercury Mine (BOFFETTA ET AL., 2001). The potential nephrotoxicity of silica and Hg° is well known (NG ET AL., 1993; HOTZ ET AL., 1995; BUCHET ET AL., 1980; ROELS ET AL., 1978, BARREGÅRD ET AL., 1988; KOBAL ET AL., 2000; WHO 2003).

The long-term effect of Hg° occupational exposure on kidney function has been evaluated in some studies (ELLINGSEN ET AL., 1993; KOBAL ET AL., 2001; KOBAL ET AL., 2002). After the cessation of silica dust exposure, the persistence of kidney effects was reported (NG ET AL., 1992). The aim of the present study was to re-evaluate our previous studies and to test the potential possibility of past co-exposure to Hg° and silica dust being associated with the long-term effects on kidney function in ex-mercury miners.

SUBJECTS AND METHODS

After the application of exclusion criteria, 49 ex-miners and 56 age-matched controls were included in the study. The control group was selected from mercury and silica dust-free works, and the ex-mercury miners' group was selected from the Idrija Mercury Mine. Ex-mercury miners were studied in the period after the cessation of exposure to Hg° and silica dust. It was established from medical examination data that the controls and ex-mercury miners (1) did not have kidney disease or any disease likely to impair kidney function (diabetes, gout), (2) did not regularly consume drugs with potential nephrotoxicity (analgesics, lithium), (3) had concentrations of lead in blood below 250 μg/L and cadmium in urine below 2 μg/g creatinine. Those subjects with urinary creatinine concentrations below 0.3 g/L or above 3.0 g/L and urinary pH values higher than 8.0 were excluded. Large-size chest radiographs of all ex-miners were made during medical examinations, and no cases of radiological silicosis were established. The impact of miners' past occupational exposure to Hg°, silica dust, background cadmium (Cd) and lead (Pb), as well as their present urine mercury (U-Hg) and some markers of nephrotoxicity as a urinary protein of high and low molecular weight (albumin and α1-μglobulin) and N-acetyl-β-D-glucosaminidase enzyme activity (NAG) were evaluated. Past occupational exposure of miners to Hg° was evaluated using biological indices of exposure. Miners' underground exposure to silica dust was defined by years of exposure. Ore deposits were made of different rocks with 2.5 – 71 % SiO_2. Total mercury in urine was determined by CVAAS. Urine albumin and a1-mglobulin levels were assessed by immunonephelometry. The catalytic activity of NAG (EC 3.2.1.30) was estimated by means of a colorimetric assay (Roche). Cadmium and lead in whole blood were determined using graphite furnace atomic absorption spectrometry - GFA on SpectrAA 800 Zeeman (Varian, Australia).

Data analyses were evaluated by the application of analyses of variance, Pearson's correlation coefficient (ANOVA Software) and machine learning methods – regression trees (QUINLAN, 1992).

RESULTS AND DISCUSSION

Present mercury exposure was low in both groups, while the U-Hg level was slightly higher in miners (2.29±1.4 μg/g creatinine) than in the controls ($p=0.006$) due to higher U-Hg excretion in ex-mercury miners with a shorter interval since their last exposure. However, no correlation (evaluated by Pearson's correlation coefficient) between present urine mercury and past occupational exposure was established. The mean miners' U-Hg levels obtained during past exposure

varied from 21 to 85 μg/L (geometrical mean of all cycles U-Hg concentrations). The cumulative U-Hg level (sum of all cycles U-Hg levels) varied from 1286 to 21390 μg/L. The occupational exposure in this range could lead to reversible renal tubular or glomerular impairment (ROELS ET ALL., 1985; WHO 1991), cytotoxicity and biochemical alternations (BARREGÅRD ET ALL., 1988; WOODS ET ALL., 1993). 75 % (N=37) of observed miners were co-exposed to silica dust during their work in the mine, which varied from 7–31 years. No pulmonal silicosis was established among these miners due to their reduced exposure to silica dust following the application of stricter health safety measures after 1967 (KAVČIČ, 1972). The application of these preventive measures resulted in a lower incidence of pulmonal silicosis among Idrija mercury miners in the period after 1975 (KOBAL, 1990). No differences in background exposure to Cd and Pb were observed between the two groups. Slight increases in urinary albumin (p=0.041) and α1-μglobulin (p=0.025) were observed in ex-miners. No differences in the urinary total NAG enzyme and percentage of NAG izoenzyme B activity were observed between the controls and ex-mercury miners.

The model tree predicting the albumin level in urine shows the following: (1) in 73 subjects with lower blood Pb levels (<57.8 μg/L), age is a dominant independent variable, but (2) in 22 ex-miners with blood Pb levels over 57.8 mg/L, the albumin level in urine increased with alcohol consumption and the mean cycles U-Hg level. The model tree predicting the α1-μglobulin level in urine shows the following: (1) in 62 subjects with blood Cd levels < 2.1 μg/L and years of exposure to silica dust < 9.5, the level of

Table 1. Characteristics of ex-miners and controls

	Ex-mercury miners (N=49)			Controls (N=56)			P value
	Mean	SD	Range	Mean	SD	Range	
Years of exposure to silica dust	14.7	5.6	7 –31	-	-	-	-
Number of Hg° exposure cycles	39.9	21.4	13 – 119	-	-	-	-
Geometrical mean of U-Hg cycles (μg/L)	53.4	16.3	21 – 85	-	-	-	-
Cumulative U-Hg (μg/L)	6584	4444	1286 -21390	-	-	-	-
Present U-Hg (μg/g creatinine)	2.2	1.4	0.2 – 7.5	1.5	1.2	0.1 – 5.7	0.006
B-Cd	1.8	1.5	0.2 – 9.5	1.4	1.5	0.3 – 7.3	0.164
B-Pb	50.8	19.7	15 – 91	46.7	13.6	21 – 83	0.236
U-albumin	1.2	1.8	0.4 – 12.9	0.7	0.4	0.3 – 2.6	0.041
U-α1-μglobulin	1.4	2.8	0.2 – 15.6	0.5	2.8	0.2 – 1.9	0.025
U-NAG total	4.8	5.9	1.3 – 42.7	5.6	3.1	1.4 – 13.6	0.401
U-NAG %B	49.5	33.0	0 – 100	37.3	25.5	0 – 100	0.038
U-Ph value	5.9	0.6	5 - 8	5.9	0.7	5 - 8	0.867

α1-μglobulin was low, (2) in 18 ex-miners with years of exposure to silica dust over 9.5, and partly (in 13 ex-miners) with blood Pb levels exceeding 27.5 μg/L, the level of a1-mglobulin in urine depends on the number of exposure cycles to Hg^o, and (3) in 22 miners with blood Cd levels >2.1 μg/L, the dominant independent variable capable of increasing the a1-mglobulin level in urine was the cumulative U-Hg level.

Moderate past occupational exposure to Hg^o and lower co-exposure to silica dust in observed ex-miners seem to be associated with slight subclinical functional kidney changes. Our results partly agree with the results of studies of observed workers previously substantially exposed to silica dust (NG ET AL., 1992) as well as with the results of studies of workers previously exposed to Hg^o (ELLINGSEN ET AL., 1993). The association of glomerular and tubular functional changes with past exposure to Hg^o and co-exposure to silica dust in our study was not consistent throughout the entire group of ex-miners, and does not appear to depend solely on the doses received during past exposure, but also on background exposure to Cd, Pb, and miners' alcohol consumption, all of which could modify interindividual susceptibility to exposure response.

CONCLUSIONS

The present study suggests that a slight degree of kidney subclinical functional changes is demonstrable in ex-miners, mostlikely arising from moderate Hg^o exposure and co-exposure to silica dust. The role of background exposure to Pb and Cd and some other confounders can not be ruled out. The magnitude of the observed levels of glomerular and tubular proteins represents no clinically significant alteration of kidney function in ex-miners of the Idrija mercury Mine.

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