Mercury Impact on the Health of Miners in the Idrija Mercury Mine after the Second World War

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Mercury (Hg) was discovered in Idrija around the year 1490. Dr. J.A. Scopoli was the first physician, appointed in Idrija in 1754, who described in great detail the symptoms and signs of mercurialism among pit and smeltery workers. Despite technical measures introduced after the Second World War in workplaces where native Hg was mined, the air Hg vapour (Hg°) concentration still remained high (0.5-0.8 mg/m³). The number of intoxications exceeded 10% of all employed miners up to 1967. The symptoms and signs of mercurialism among miners from this period had been referred to (Hribernik, 1950; Hunter, 1957; Kobal, 1964, 1975, 1991), but the long-term health effects of occupational exposure were not well elucidated until 1998 (IARC multicentric study; Kobal, Osredkar, Horvat: start of the ex-miners study), in contrast to well-documented studies of long-term effects on the central nervous system and kidney function in chloralkali plant workers (Albers et al., 1993; Ellings et al., 1993). The result obtained from autoptic and mortality studies (Kosta et al., 1975; Byrne et al., 1995; Falnoga et al., 2000; Boffetta et al., 1998) indicate that the long-term health effects of Hg exposure could be associated with the known property of Hg to promote lipid peroxidation (Lund et al., 1993; Salonen 1995) and counteract the antioxidative effects of selenium (Se) (Lourdes, Cuvin-Aralar, Furnes, 1991; Rana and Bora, 1992; WHO, 2003).

AIM: The objective of this presentation is: (1) to evaluate the influence of biological monitoring (BM) on the incidence of Hg° intoxication among miners, and (2) to elucidate possible long-term health risks and biological effects associated with lipid peroxidation and radical-induced DNA damage observed in studies of ex-miners exposed to Hg° in the Idrija Mercury Mine.

METHOD: *The incidence of Hg° intoxication* in miners and smelters was recorded from 1946 onward. The diagnoses were based on clinical signs, symptoms and on urinary Hg (U-Hg) determination. In 1968, we started to conduct regular BM of exposure to Hgº (U-Hg was determined in spot urine samples before, during and after exposure) and studied the relationship between inhaled, blood, urine and breath Hg concentrations, as well as certain potential biological effects (catalase activity, blood and urinary protein) on groups of miners (Kobal, 1975; Kobal and Bohinjec, 1983; Kobal, 1991; Kobal et al., 2000).

Long-term health risk studies. Hg° accumulation in ex-miners was evaluated in human autopsy studies (Kosta et al., 1975; Falnoga et al., 1995). *Mortality from cancer* among European mercury miners was evaluated in an IARC study (Boffetta et al., 1998, 2001). The cohort from the Idrija Mercury Mine comprised 1,589 workers (49,056 person-years).

Sequelae health and biological effects of past Hg° exposures were studied in a group of ex-miners (n-54) in comparison to a control group (n-58). We evaluated the putative appearance of non-specific symptoms and signs of micromercurialism and the potential biological effects associated with antioxidative capacity, lipid peroxidation and radical-induced DNA damage (Prezelj et al., 2000; Falnoga et al., 2002; Kobal et al., 2004a, 2004b; Osredkar et al., 2004;

Kobal-Grum et al., 2006). In the ex-miners we determined: basal level of thyrotropin (TSH) and thyroid hormones (free T3 and T4); urinary proteins (IgG, albumin and α1-μglobulin); Se level in plasma and urine; antioxidative enzymes in erythrocytes (catalase – Cat, seleno enzyme glutathion peroxidase – GSH Px and Cu/Zn superoxide dismutase – SOD); pineal hormone melatonin in blood and urine; malondialdehyde (MDA), a lipid peroxidation product; and 8-Hydroxy-2-Deoxyguanosine (8 -OHdG), a radical-induced DNA damage product in urine. The methodologies of the medical and psychological examinations and biological analyses are presented in the cited publication.

Analyses of Hg: Air Hg° was generally determined by UV photometry using portable instruments (Kobal et al., 1991). Before 1970, Hg in biological material was determined by the dithizone method (Kavčič, 1975), by NAA (Kosta and Byrne, 1969), and later by CV AAS (Horvat et al., 1986).

RESULTS:

Incidence of Hg° intoxication: After 1964, a decrease in the incidence of Hg° intoxication was observed, and by 1976 there were no new cases of intoxication reported, due to the intensive BM implemented after 1967 in the working areas where native Hg was mined. The clinical picture of intoxication was dominated by tremor, oropharyngeal syndrome, erethismus mercurialis and proteinuria, with U-Hg ranging from 300 to 1000 μg/24^{h}.

BM of Hg exposure: BM of miners exposed to Hgº enabled prevention of the appearance of symptoms and signs of micromercurialism, but not the increased Hg° absorption observed in about 40% of exposed miners (U-Hg ranged from 60–150 μg/L). We defined the ratio between air-blood (1 μg/m^{3} :0.54 μg/L), blood-urine (1 μg/L:2.7 μg/L), and air-urine (1 μg/L:1.0 μg/L) Hg concentrations, which served as a basis for the application of biological action levels.

Human autopsy studies have shown that Hg° accumulated in ex-miners predominantly in the pituitary and thyroid glands, kidneys and brain tissue (dentate nucleus). Selenium was co-accumulated in tissues bound to Hg in a 1:1 ratio.

An increase in mortality from lung cancer (standardised mortality ratio – SMR 1.89, 95% confidence interval – CI 1.45 to 2.41), pneumoconiosis (SMR 13.6, 95% CI 2.81 to 39.9), nephritis-nephrosis (SMR 1.60, 95% CI 0.44 to 4.10), IHD (SMR 1.60, 95% CI 1.35 to 2.02) and suicide (SMR 1.23, 95% CI 0.88 to 1.68) was found in miners from the Idrija Mercury Mine. Increased liver cancer was present among miners from the Idrija Mercury Mine and a mercury mine from Italy, but no excess risk was found in a parallel analysis of cancer incidence among miners from Idrija. Exposure to Hgº in miners does not seem to be strongly associated with cancer risk. The increase in lung cancer may be explained by co-exposure to silica dust and radon. Despite the limitation in assessment of exposure, the study suggests a possible association between Hgº exposure (employment in mercury mining) and risk in some group of cardiovascular diseases .

Sequelae health effects: The results of our recent studies support the assumption that miners' remote long-term occupational exposure to Hgo (miners' integrated average U-Hg varied from 20 to 120 μg/L) was associated: (1) with sub-clinical neurotoxic effects (tremor, $p< 0.01$; vibratory sensation and two-point discrimination, $p< 0.05$); (2) with sub-clinical glomerular ($p< 0.01$) and tubular ($p< 0.05$) kidney dysfunction, where the exposure to silica dust was also a relevant risk factor; (3) with depression and negative self-concept ($p< 0.01$), where the

interaction with moderate alcohol consumption (< 26.6 ml/day) has a presumably decisive influence; (4) but not with thyroid dysfunction (TSH, free T3 and T4). Observed neurotoxic and nephrotoxic sequelae effects were also found in other studies (Albers et al., 1993; Ellingsen et al., 1993; IARC, 1997; Hotz et al., 1999: Mathiesen et al., 1999; Letz et al., 2000), but depression in miners had already been reported in the study of Scopoli in 1754.

Sequelae biological effects: A slightly decreased plasma Se level (p= 0.03) at increasedurinary Se and the redestribution of Se from the selenoprotein P to selenoenzyme GSH Px (after submaximal work stress) seem to be associated with the relative reduction of bioavailable Se, probably due to the interaction with Hg accumulated during past exposure (negative correlation between cumulative U-Hg peak level and Se in plasma, r = - 0.38, p = 0.006), which could affect the antioxidative capacity of ex-miners. The increased catalase and melatonin in blood (as a compensatory mechanism in response to oxidative stress), the increased indices of lipid peroxidation (MDA, p< 0.01) and DNA damage (8-OH dG, p = 0.011) in urine, probably resulting from the interaction with internal doses of Hg, silica dust and radon received and accumulated during past exposure, indicate a moderate increase in free radical production, which could enhance the atherosclerosis and mutagenesis in ex-miners. These results agree with the study of Salonen et al. in 1995 and to an extent with certain other studies (Barregård et al., 1990; Ellingsenetal., 1993; Loft and Pulsen, 1996; Pigler et al., 1999; Chen et al., 2005, 2006).

CONCLUSIONS: BM enabled us to prevent Hgo intoxication, but not the increased absorption of Hg° in exposed miners. Long-term increased Hgo absorption and co-exposure to silica dust and radon, as well as miners' lifestyle-related factors, could be critical risk factors for increased mortality from lung cancer, ischaemic heart diseases, suicide and nephritis-nephrosis among miners at the Idrija Mercury Mine in the last 50 years.

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