

Effects of 500-Year Mercury Mining and Milling on Cancer Incidence in the Region of Idrija, Slovenia

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ABSTRACT

The aim of the study was to determine whether the 500-year of mercury mining and milling in the Idrija region in Slovenia and the resulting environmental pollution with mercury and smelting wastes containing radon, has caused an increased cancer risk of the inhabitants. The polluted and the non-polluted parts of the region were defined. Cancer incidence from the two regions was compared. Cancer incidence among miners was investigated separately. In the polluted area male and female cancer incidence was higher than in the non-polluted area. Miners had an excess of incidence of total cancer, of oral and pharyngeal cancers and of lung cancer. As indicated by multivariate analysis the increased risk of miners could be assigned to their smoking and alcohol drinking habits. Higher estimated cumulative exposure to inorganic mercury seems to contribute to their risk as well. Most of the excess cancer incidence of the population from the polluted area could be explained by an unhealthy life style. In the case of lung cancer radon exposure contributes to the increased risk as well. Therefore, a well planned health promotion program and further sanitation of old houses is proposed.

Key words: mercury, mining, exposure, pollution, cancer incidence, Idrija

Introduction

A mercury mine with a mill in the town of Idrija (IMM) in the middle of the Idrija region (Figure 1) was in operation for 500 years. Since 1987, the mine was being gradually closed and in 1994 the mercury production ceased. There is a resulting environment pollution in the town of Idrija with mercury (mercury concentrations in the air range from 50 to 290 ng/m³) and with smelting wastes containing ²³⁸U, ²²⁶Ra, ²³²Th, and ⁴⁰K. Several houses have been built on smelting wastes, and elevated radon concentrations have been found in the cellars^{1,2}.

Previous geographical analyses on cancer incidence in the Republic of Slovenia revealed that the age-adjusted total cancer incidence rates in the whole region of Idrija were significantly higher than they were at the national level. Male rates were significantly higher for lung, mouth and pharynx, oesophagus, pancreas and bladder cancers, while female rates were higher for gallbladder and breast cancers³⁻⁷.

There is inadequate evidence for the carcinogenicity of mercury and mercury compounds in humans⁸. The last multicentric study about cancer occurrence among European mercury miners did not clearly support the hy-

pothesis of a carcinogenic effect of inorganic mercury on human lungs, although the results were compatible with a weak effect. It did not find any excess of renal cancer and brain tumors⁹. Radon (²²²Rn) and its short-lived progeny have a proven carcinogenic effect on lung. Their possible carcinogenic effect on gall bladder and bile ducts, multiple myeloma and leukaemia is still under investigation¹⁰.

For the purpose of this study the Idrija region was divided into the polluted area (the town of Idrija) and the non-polluted area (the rest of the region). Our aim was to compare cancer incidence in the two areas to see whether any cancer cluster appears. Furthermore, we wanted to quantify the possible contribution of cancer incidence among miners to the high incidence of lung, mouth and pharynx, oesophagus, pancreas and bladder cancers among male population in the region.

Material

The data source of cancer incidence from the Idrija region (Administrative Unit Idrija) was the population

incidence ratios (SIR) in the polluted and the non-polluted area were calculated according to the following equation¹¹:

$$SIR = \frac{O}{E}$$

O is the observed number of cases in a given area and E is the expected number of cases related to what would have been if the age-specific incidence rate in the investigated area had been the same as in a standard population. As standard population we used the population of AU Idrija. 95% confidence intervals were based on the Poisson distribution of observed cases.

SIRs for male non-miners from the polluted and non-polluted area were compared. The person-years at risk approach was applied. With this approach each subject contributed to the population at risk only as many years of observation as he/she was at risk of becoming a case¹¹. In our analysis the total risk in the particular area thus depended on the miners and non-miners time at risk. In the polluted miners contributed 56,133 person-years while 35,297 in the non-polluted area. Non-miners contributed 62,491 person years and 158,331 person years in the polluted and non-polluted area respectively.

In the second part of our analysis, the possible influence of miners' cumulative mercury exposure on the cancer incidence was identified: We also examined the role of co-exposure to smoking and alcohol consumption as confounders. In addition, the information on silicosis was included into certain analysed datasets.

The cumulative mercury exposure level was measured by the following three elements:

- time since the first exposure (less than 9 years, from 10 till 19 years, from 20 till 29 years and more than 30 years),
- the period of the first exposure (before 1950, from 1950 till 1960, from 1960 till 1970 and after 1970),
- the estimated cumulative exposure to the inorganic mercury (ECEIM), expressed as µg/L and classified into four categories: 0–2000 µg/L, 2001–5000 µg/L, 5001–7000 µg/L, 7001 and more µg/L. ECEIM was estimated on the basis of urinary and blood biomonitoring data, industrial hygiene measurements, and reconstruction of technological and hygienic conditions in different periods¹².

SIRs were calculated using the miners' person-years data and the Slovenian men population as standard. The Poisson regression model was applied in the multivariate analysis¹¹. The magnitude of the association between the exposure and disease was presented as relative risk (RR)¹¹:

$$RR = \frac{\text{incidence rate in the exposed group}}{\text{incidence rate in the unexposed group}}$$

A value of 1.0 indicates that the incidence of the disease in the exposed and the unexposed group is identical and thus that there is no observed association between the exposure and the disease. A value greater than 1.0 indicates a positive association and RR less than 1.0 means

that there is an inverse association. The significance level of $p < 0.05$ was considered as statistically significant. All the calculations were made by using Stata software (Intercooled Stata 7.0 for Windows).

Results

Cancer incidence in the administrative unit idrija

During the period 1961–2000, 2227 new cancer cases were registered in the AU Idrija. Among them, 1139 were male cases (568 from the polluted area and 571 from the non-polluted area) and 1088 female (598 from the polluted area and 490 from the non-polluted area). SIRs together with their 95% confidence intervals for the most common cancer sites for man and woman from the exposed and unexposed group are shown in Tables 1 and 2. In addition SIRs for miners and non-miners by the area are shown separately in Table 1.

In the forty-year target period SIRs for all men (miners and non-miners) from the polluted area were significantly higher for total cancer, lung and bladder cancers. For most other cancer sites the incidence was higher as well, but not significantly. In the group of non-miners a significantly higher SIR for oral and pharyngeal cancers was observed in the polluted area. In the group of miners SIR differences between the polluted and the non-polluted area were smaller. In the first twenty-year period (1961–1980) SIRs for the male population of the polluted area were smaller. SIR was significantly higher only for the total cancer incidence. In the second twenty-year period (1981–2000) SIRs were significantly higher also for lung and bladder cancer. Mouth and pharynx cancers were close to a significant excess (data not shown).

In the forty-year target period SIRs for women from the polluted area were significantly higher for total cancer, for breast and gallbladder cancers. Insignificantly higher SIRs were observed for some other cancer sites as well (Table 2). In the first twenty-year period (1961–1980) SIRs for the female population were higher than they were in the second twenty-year period (1981–2000). In the second period, SIR was significantly higher only for total cancer. SIRs for breast and gallbladder cancers decreased, while SIRs for lung and pancreas cancers increased (data not shown).

Cancer incidence among Idrija mercury mine miners

During the period 1961–2000, 1589 IMM miners contributed 92,060 person-years (56,133 in the polluted area, and 35,297 in the non-polluted area). During this period 233 miners contracted cancer. 84 miners got lung cancer, 24 mouth and pharyngeal cancers, 6 oesophageal cancer, 6 bladder cancer, 6 kidney cancer and 5 pancreas cancer. When comparing IMM miners with the total Slovenian male population, SIRs were higher for total cancers, lung cancer, mouth and pharyngeal cancers. The influence of time since the first exposure and the esti-

TABLE 1
NUMBER OF CANCER CASES AND STANDARDIZED INCIDENCE RATIOS (SIR) IN MEN IN THE ADMINISTRATIVE UNIT (AU) IDRİJA
IN THE PERIOD 1961–2000 SHOWN SEPARATELY FOR POLLUTED AREA AND NON-POLLUTED AREA AND FOR MINERS AND
THE REMAINING NON-MINERS INHABITANTS (OTHER)

Cancer site	Number of cases							SIR (95% confidence interval)					
	AU Idrija	Polluted area			Non-polluted area			Polluted area			Non-polluted area		
		All	Miners	Other	All	Miners	Other	All	Miners	Other	All	Miners	Other
All cancers	1139	568	161	407	571	86	485	1.29 (1.18–1.40)	1.05 (0.90–1.23)	1.40 (1.27–1.54)	0.82 (0.75–0.89)	0.95 (0.76–1.17)	0.80 (0.73–0.87)
Mouth and pharynx	94	49	15	34	45	9	36	1.29 (0.95–1.70)	1.00 (0.56–1.66)	1.47 (1.02–2.05)	0.81 (0.59–1.08)	0.98 (0.45–1.86)	0.77 (0.54–1.07)
Oesophagus	22	15	7	8	7	0	7	1.69 (0.44–1.31)	2.13 (0.86–4.40)	1.43 (0.62–2.82)	0.53 (0.21–1.10)	0.00 (0.00–1.87)	0.63 (0.25–1.29)
Pancreas	33	17	4	13	16	1	15	1.34 (0.78–2.15)	0.98 (0.27–2.50)	1.52 (0.81–2.60)	0.79 (0.45–1.28)	0.42 (0.01–2.32)	0.84 (0.47–1.38)
Lung	306	154	55	99	152	31	121	1.29 (1.10–1.52)	1.36 (1.03–1.77)	1.26 (1.02–1.53)	0.81 (0.70–0.95)	1.31 (0.89–1.86)	0.74 (0.61–0.88)
Bladder	52	30	3	27	22	3	19	1.50 (1.01–2.14)	0.47 (0.10–1.38)	1.98 (1.31–2.88)	0.69 (0.43–1.04)	0.81 (0.17–2.37)	0.67 (0.40–1.05)
Kidney	19	5	0	5	14	6	8	0.64 (0.21–1.50)	0.00 (0.00–1.21)	1.06 (0.34–2.37)	1.25 (0.68–2.10)	3.23 (1.18–7.02)	0.86 (0.37–1.69)
Brain	17	8	2	6	9	1	8	1.19 (0.51–2.34)	0.65 (0.08–2.35)	1.64 (0.60–3.56)	0.88 (0.40–1.67)	0.51 (0.01–2.84)	0.96 (0.42–1.90)
Non-Hodgkin lymphoma	22	9	3	6	13	0	13	1.06 (0.48–2.01)	0.89 (0.18–2.61)	1.16 (0.43–2.53)	0.96 (0.51–1.65)	0.00 (0.00–1.77)	1.14 (0.61–1.95)
Hodgkin disease	10	3	1	2	7	1	6	0.76 (0.17–2.38)	0.64 (0.02–3.57)	0.83 (0.10–3.01)	1.16 (0.47–2.39)	1.02 (0.03–5.69)	1.19 (0.43–2.58)
Multiple myeloma	10	6	2	4	4	1	3	1.67 (0.61–3.64)	2.43 (0.29–8.81)	1.44 (0.39–3.70)	0.62 (0.17–1.60)	2.31 (0.06–13.0)	0.50 (0.10–1.34)

All cancers – International Classification of Diseases codes: C00–C96, Mouth and pharynx – International Classification of Diseases codes: C00–C14

TABLE 2
NUMBER OF CANCER CASES AND STANDARDIZED INCIDENCE RATIOS (SIR) IN WOMEN IN THE ADMINISTRATIVE UNIT (AU) IDRİJA
IN THE PERIOD 1961–2000 SHOWN SEPARATELY FOR POLLUTED AREA AND NON-POLLUTED AREA

Cancer site	Number of cases			SIR (95% confidence interval)	
	AU Idrija	Polluted area	Non-polluted area	Polluted area	Non-polluted area
All cancers	1088	598	490	1.34 (1.24–1.45)	0.76 (0.70–0.83)
Mouth and pharynx	12	5	7	1.03 (0.33–2.40)	0.98 (0.39–2.02)
Oesophagus	10	4	6	1.00 (0.27–2.57)	1.00 (0.37–2.17)
Gallbladder	26	18	8	1.74 (1.03–2.75)	0.51 (0.22–1.01)
Pancreas	31	19	12	1.53 (0.92–2.39)	0.64 (0.33–1.13)
Lung	48	25	23	1.29 (0.83–1.90)	0.81 (0.51–1.21)
Ovary	48	24	24	1.23 (0.79–1.83)	0.84 (0.54–1.26)
Bladder	17	9	8	1.33 (0.61–2.52)	0.78 (0.34–1.54)
Brain	13	6	7	1.12 (0.41–2.41)	0.91 (0.37–1.88)
Non-Hodgkin lymphoma	18	6	12	0.81 (0.30–1.76)	1.13 (0.58–1.98)
Multiple myeloma	11	6	5	1.40 (0.51–3.04)	0.75 (0.24–1.74)
Breast	232	123	109	1.27 (1.06–1.25)	0.81 (0.66–0.97)

All cancers – International Classification of Diseases codes: C00–C96, Mouth and pharynx – International Classification of Diseases codes: C00–C14

mated cumulative exposure to the inorganic mercury on the incidence of total cancer and lung cancer is shown in Table 3. The analysis of the influence of the period of the first exposure was not added to Table 3 because this variable did not turn out to have any significant influence on SIR.

For total cancer SIR was the highest during the first twenty-year of exposure. The Poisson regression was used for the estimation of the relative risk of the miners exposed for 10 to 19 years. As reference the group of less exposed miners was used. The RR of 1.16 decreased when the adjustment for the cumulative number of smoked cigarettes (RR=0.89) or alcohol consumed (RR=0.99) was done. The decrease of RR was significant, when in addition to the smoked cigarettes and consumed alco-

hol, the period of the first exposure and ECEIM were included into the model (RR=0.19). The ECEIM level alone did not influence SIR. The adjustment for the cumulative number of smoked cigarettes, alcohol consumption, the time since the first exposure and the period of the first exposure did not show any significant influence of the ECEIM level on the incidence of total cancer. However, a trend of higher RR with higher ECEIM levels was indicated when applying all four confounding variables into the model (RR4 and RR5, Table 3).

For lung cancer, SIR was 18.5 in the group who was exposed up to ten years. SIR decreased when the time since the first exposure increased. All SIRs were significant. The RR was the highest in the group 0–9 years since the first exposure. After the adjustment to the cu-

TABLE 3
EFFECTS OF THE CUMULATIVE TIME SINCE FIRST EXPOSURE AND THE LEVEL OF THE ESTIMATED EXPOSURE TO THE INORGANIC MERCURY ON THE INCIDENCE OF ALL CANCERS AND LUNG CANCER AMONG MINERS OF THE IDRİJA MERCURY MINE IN 1961–2000

Cancer site	Exposure		Number of cases	SIR (95% confidence interval)	RR1 (p)	RR2 (p)	RR3 (p)	RR4 (p)	RR5 (p)	
All cancers	Cumulative time since first exposure	0–9 years	5	12.5 (5.2–29.9)	1	1	1	1	1	
		10–19 years	25	14.5 (9.8–21.5)	1.16 (0.756)	0.89 (0.799)	0.99 (0.987)	0.21 (0.007)	0.19 (0.046)	
		20–29 years	80	2.2 (1.8–2.8)	0.18 (0.000)	0.15 (0.000)	0.17 (0.000)	0.04 (0.000)	0.04 (0.024)	
		30 years and more	123	0.8 (0.6–0.9)	0.06 (0.000)	0.05 (0.000)	0.06 (0.000)	0.01 (0.000)	0.01 (0.002)	
	Estimated exposure to the inorganic mercury (µg/l)	< 2000	61	1.2 (0.9–1.5)	1	1	1	1	1	
		2001–5000	120	1.2 (0.9–1.4)	0.99 (0.932)	0.94 (0.703)	0.98 (0.881)	1.23 (0.397)	1.11 (0.865)	
		5001–7000	39	1.2 (0.9–1.7)	1.02 (0.916)	0.92 (0.667)	1.06 (0.779)	1.64 (0.098)	1.49 (0.688)	
		> 7000	13	1.1 (0.7–2.0)	0.96 (0.894)	0.90 (0.739)	1.02 (0.952)	1.43 (0.341)	1.27 (0.745)	
	Lung cancer	Cumulative time since first exposure	0–9 years	1	18.5 (2.6–130.9)	1	1	1	1	1
			10–19 years	3	10.0 (3.2–31.1)	0.54 (0.597)	0.25 (0.597)	0.38 (0.235)	0.07 (0.399)	0.04 (0.022)
20–29 years			26	3.3 (2.3–4.9)	0.18 (0.094)	0.10 (0.094)	0.16 (0.025)	0.02 (0.072)	0.02 (0.001)	
30 years and more			54	1.5 (1.1–1.9)	0.08 (0.012)	0.04 (0.012)	0.07 (0.002)	0.01 (0.010)	0.01 (0.000)	
Estimated exposure to the inorganic mercury (µg/l)		< 2000	21	1.9 (1.2–2.9)	1	1	1	1	1	
		2001–5000	41	1.8 (1.3–2.4)	0.94 (0.820)	0.81 (0.445)	0.94 (0.815)	1.37 (0.395)	1.17 (0.665)	
		5001–7000	16	2.1 (1.3–3.4)	1.12 (0.728)	0.94 (0.854)	1.19 (0.596)	2.01 (0.140)	1.77 (0.210)	
		> 7000	6	2.3 (1.1–5.1)	1.21 (0.676)	0.98 (0.967)	1.37 (0.499)	2.05 (0.209)	1.76 (0.310)	

SIR – standardized incidence ratio, RR1 – relative risk, RR2 – relative risk adjusted to the cumulative number of the cigarettes smoked, RR3 – relative risk adjusted to the alcohol consumed, RR4 – relative risk adjusted to the variables period of first exposure and the cumulative time since first exposure/estimated exposure to the inorganic mercury, RR5 – relative risk adjusted to all four variables

mulative number of smoked cigarettes, RR decreased approximately two times. Considering the period of the first exposure, SIR was greater than 1 only for the miners who were first exposed before the year 1970. The estimated exposure to the inorganic mercury did not cause any significant change in SIR. Models were built to adjust the RR to the cumulative number of smoked cigarettes, alcohol consumption, and cumulative time since the first exposure to mercury and the period of the first exposure (RR2–RR5, Table 3). Already after the adjustment to the cumulative number of cigarettes smoked, RR dropped below 1. In addition, the information about silicosis was included into the model (data not shown). Of all 1589 miners, 142 contracted silicosis. RR did not change much after adjusting to silicosis. As for total cancer, a trend of a higher RR with higher ECEIM levels was indicated for lung cancers as well.

First cases of oral and pharyngeal cancers emerge only after ten-year of exposure. SIR was the highest after 10–19 years since the first exposure. The level of the estimated exposure to the inorganic mercury did not cause any significant change in SIR. Crude or adjusted RR did not significantly differ between the four ECEIM levels. As for total cancer and lung cancer a trend of a higher ECEIM levels was indicated for oral and pharyngeal cancers too.

Discussion

In the studied forty-year period in the Administrative Unit Idrija male and female cancer incidence was higher in the polluted area than it was in the non-polluted area. Cancer incidence among miners did not affect the total male cancer incidence. Miners' smoking and alcohol drinking habits contributed to the high total, lung, mouth and pharynx cancer incidence. A non-significant trend of higher RR with higher ECEIM levels was indicated.

In the polluted area, the percentage of miners' families is higher (almost 50% of the population) than in the not polluted area (only 15%). According to the data collected for the multicentric study, the prevalence of heavy smokers in miners was high (70% of miners smoked more than 20 cigarettes per day)¹². The life style of the miners' families during the last 40 years was described on a sample of 100 miners by Vanja Mavri¹³. In general in the time of the IMM's full operation families of miners enjoyed a relatively high standard of living. However, the relatively high standard of living was not followed by an appropriate health education. Miners' families used pork fat. A high percentage of miners were overweight and obese. Only 30% had normal weight. Nobody was undernourished. 78% often consumed alcohol, and only 20% considered to stop drinking. Therefore, most of the excess cancer incidence among men from the polluted area could be explained by their unhealthy life style (smoking, alcohol drinking, and obesity)^{14–18}.

Smoking and drinking habits of women and men non-miners were not explored. Neither was explored

their working-place. It is also possible that in the 60s, 70s, and the beginning of the 80s some of the non-miners were exposed to the asbestos or some other working hazards that were later recognized as carcinogenic.

An additional effect of radon on the lung cancer incidence in the polluted area should be considered as well. Likewise, in the case of bladder cancer excess among men non-miners from the polluted area, the smoking habits can not be the sole element causing the excess. Most probably there were other hazardous working conditions. Maybe there was an overuse of phenacetin analgesic mixtures. Mercury could have affected the bio-availability of selenium; in a prospective study of 120,852 men and women, an inverse association was found between toenail selenium and bladder cancer risk¹⁹.

The fact that the place of living (polluted versus non-polluted area) did not affect the cancer incidence among miners could be explained by the healthy workers effect¹¹ as well as by a better health-care that the miners enjoyed. The results of the Poisson regression analysis clearly show the high relative risk of smoking and alcohol abuse for total and especially for lung (smoking only), mouth and pharyngeal cancer. The analysis also revealed a trend of an increasing risk following the increasing estimated cumulative mercury exposure of miners. A small additional mercury carcinogenic effect on lung, and mouth and pharyngeal cancer is possible. However, there might be other concomitant risk factors like radon that were not considered in the study. There is a good reason to believe that radon exposure would be a parallel to the years a miner spent in the mine regardless of mercury or silica dust exposure. Most probably, radon did act as an independent additional lung cancer risk factor that would not change the indicated trend of an increasing risk following the increasing estimated cumulative mercury exposure.

We do not have reliable data on the known risk factors²⁰ to understand the excess of female breast cancer incidence from the polluted area. Maybe, there was less population mixture due to a stable miners' population in the town of Idrija and very bad traffic conditions. Therefore the percentage of genetically predisposed women may be higher. Nutrition high in fat and the resulting obesity could also be related to high postmenopausal breast cancer¹⁷ as well as gallbladder cancer¹⁶. Gallstones are a precancerous condition. Most of them are formed from cholesterol. An excess of gallstones prevalence could be connected to the recently described disturbance of the antioxidative capacity and lipid peroxidation²¹. It is possible that gallstones were not detected, and women not surgically treated.

Various studies have been carried out investigating the environmental pollution of the 500-year mercury mining and milling in the town of Idrija. We are aware that, the Idrija town is a natural laboratory and that problems connected with the environmental radon pollution must further be treated. However a well planned health promotion program, respecting the latest European Code Against Cancer, should be introduced²².

Acknowledgements

This analysis was prepared as a part of the research Lipid peroxidation and functional damage in target tissues and organs in citizens of Idrija and mercury miners

exposed to elementary mercury (principal investigator J. Osredkar). The research was financed by the Ministry of Education, Science and Sport of the Republic of Slovenia, grant number J3-3076.

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UTJECAJI 500 GODIŠNJEG RUDARENJA I PRERADE ŽIVE NA INCIDENCIJU KARCINOMA U IDRIJSKOJ REGIJI, SLOVENIJA

SAŽETAK

Cilj studije bio je otkriti utjecaj 500 godišnjeg rudarenja i prerade žive na okolišno zagađenje Iridijske regije te povezanost sa incidencijom karcinoma. Definirani su zagađeni i nezagađeni dijelovi regije te su uspoređivane incidencije karcinoma. U zagađenim dijelovima incidencija karcinoma bila je veća. Rudari su imali povećanu incidenciju svih karcinoma, oralnih, faringealnih i plućnih karcinoma. Povećana incidencija karcinoma kod rudara može se dovesti i u vezu sa njihovim životnim navikama kao što su pušenje i povećana konzumacija alkohola. Veća izloženost živi pridonosi riziku od oboljenja. Većina incidencija karcinoma populacije iz te regije može se pripisati nezdravom životu. U slučaju karcinoma pluća, rizik povećava i radon. Preporučeno je bolji zdravstveni program kao i sanacija starih kuća.