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The occupational environment and its impact on occurrence of cancer cases among workers in nickel refinery

Środowisko pracy i jego wpływ na występowanie przypadków raka wśród pracowników rafinerii niklu

Abstract:
***Objective**: To demonstrate an occupation exposure impact on incidence of cancer diseases among nickel smelter workers in Sereď, Slovakia. To analyze the occurrence of cancer diseases among smelter workers. To make a risk assessment and survival analyses in selected group of workers.*
***Methods**: Retrospective cohort study is based on data about outcomes of work-related exposures in the present and also on the date about known nickel exposure in the past among smelter workers. Observed historical cohort group were 4622 workers in the nickel smelter in Sereď (Galanta district) who were employed during the years 1963 – 1993. Odds ratio (OR), logistic regression and survival analyses were calculate.*
***Results**: There were 1348 non-exposed employees (29%) and 3274 exposed employees (71%). There were 4222 employees without recorded cancer (91%) and 400 employees had recorded cancer disease (9%). Among cancer cases we can assess that they mostly work on manufacture department (52% of cases). The most cases were employed in nickel smelter over the 20 years (42%). The 36% of cases were first time employed in nickel smelter at the age of 31 – 40 years old. With increasing age to start work is increasing chance to be sick (OR = 1,48, $CI_{95\%}$ = 1,30 – 1,69, P ≤ 0,001). Furthermore, with increasing duration of employment is also higher chance to have cancer (OR = 2,23, $CI_{95\%}$ = 2,05 – 2,41, P ≤ 0,001). Also the higher risk exposure has impact on higher chance to have cancer (OR = 1,46, $CI_{95\%}$ = 1,22 – 1,75, P ≤ 0,001).*
***Conclusions**: Presented study was the first study, which discussed aspects of the possible occupational exposure in the nickel refinery in Sereď in the Slovak Republic.*

Streszczenie:
***Cel:** Zaprezentowanie wpływu narażenia zawodowego na występowanie chorób nowotworowych u pracowników huty niklu w Sereď, Słowacja. Analiza występowania przypadków zachorowań na raka wśród pracowników huty. Ocena ryzyka zawodowego i analiza przeżycia wybranej grupy pracowników.*
***Metodyka:** Retrospektywne badanie kohortowe w oparciu o dane na temat wyników narażeń związanych z obecnym wykonywaniem pracy zawodowej jak i na podstawie rozpoznanych przypadków narażenia zawodowego pracowników huty w przeszłości. Historyczne badania kohortowe obejmowały grupę 4622 pracowników huty niklu w Sereď (okręg Galanta), zatrudnionych w latach 1963 – 1993. Obliczono iloraz szans, regresję logistyczną oraz wykonano analizę przeżycia.*
***Wyniki:** Badana grupa obejmowała 1348 (29%) pracowników nie narażonych oraz 3274 narażonych (71%). U 4222 (91%) pracowników nie rozpoznano choroby nowotworowej, raka stwierdzono natomiast u 400 pracowników (9%). Pośród pracowników z wykrytą chorobą nowotworową większość (52% przypadków) była zatrudniona w dziale wytwórczym, przy czym 42% przypadków to osoby o stażu zatrudnienia w hucie niklu przekraczającym 20 lat. 36% zatrudnionych ze stwierdzoną chorobą nowotworową rozpoczęło pracę w hucie w wieku 31 – 40 lat. Wraz ze wzrastającym wiekiem zatrudnienia w hucie wzrasta ryzyko zachorowania na raka (OR = 1,48, $CI_{95\%}$ = 1,30 – 1,69, P ≤ 0,001). Ponadto, im dłuższy staż pracy tym większe ryzyko raka (OR = 2,23, $CI_{95\%}$ = 2,05 – 2,41, P ≤ 0,001). Ryzyko to wzrasta też wraz z wydłużeniem okresu narażenia (OR = 1,46, $CI_{95\%}$ = 1,22 – 1,75, P ≤ 0,001).*
***Wnioski:** Zaprezentowane badania stanowią pierwszą próbę omówienia aspektów potencjalnego narażenia zawodowego występującego w hucie niklu w Sereď, Słowacja.*

***Keywords**: nickel, occupational exposure, cancer*
***Słowa kluczowe**: nikiel, narażenie zawodowe, choroby nowotworowe*

Nickel, in the form of various alloys and compounds, has been in widespread commercial use for over 100 years. Exposures by inhalation, ingestion or skin contact occur in nickel and nickel alloy production plants as well as in welding, electroplating, grinding and cutting operations. Chronic exposure to nickel and nickel compounds can have adverse effects on human health because of their toxic and carcinogenic activity [1,2].

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The first brief report on occupational respiratory cancer diseases among nickel refinery workers was reported from Clydach, Wales in 1933. Next epidemiological evidence of elevated lung cancer risk in the same cohort was published 25 years later [3,4]. Other Norwegian and Finland studies also indicated an increased risk of lung cancer among workers in the nickel refinery [5-7].

During the years 1963 to 1993 was in Slovakia the production and processing of heavy metals in Sered' (Galanta district) oriented on nickel and nickel compounds. There were more than 5000 employees in nickel smelter during the last 30 years of nickel production.

Since there were not any occupational exposure information and research about one and only nickel refinery in Slovakia published, it was of interest by professionals from Department of Public Health, Trnava University (Slovakia) to collect an available data about employees and other determinants.

Because the nickel is registered as chemical carcinogen, we assumed that occupational exposure, length of work and age of began work could have negative impact on the health among exposed workers, especially of developing malignancies of respiratory, gastrointestinal and skin.

Among workers employed in nickel smelter in Sered' (Slovakia) during 1963 – 1993 an elevated risk of cancer diseases has been demonstrated in retrospective cohort study. The objective of this study was to demonstrate an occupation exposure impact on incidence of cancer diseases among nickel smelter workers in Sered', Slovakia. The first aim was to analyze the occurrence of cancer diseases among smelter workers. Than were made a risk assessment and survival analyses in selected group of workers.

We assume that professional exposure to nickel had a significant impact on the emergence of cancer diseases as well as to survival proportion.

Methods

Presented retrospective cohort study is based on data about outcomes of work-related exposures in the present and also on the date about known nickel exposure in the past among smelter workers. Observed historical cohort group were workers in the nickel smelter in Sered' (Galanta district) who were employed during the years 1963 – 1993. The studied parameter were: gender, date of birth, education, marital status, work position, work start date and end date of employment, nickel level exposure, a type of cancer and date of death due to cancer. Given that nickel is a proven carcinogen, the study was not based only on the type of cancer, but also on survival period from the disease histology confirmation.

Data collection was in the period 2005 – 2007. Data were obtained from work records. Information about health status was focused on occurrence of cancer type. Other source of information related to the occupational environment and work process were occupational records from the Regional Office of Public Health. Additional sources of information were the National Health information Center of the Slovak Republic. There were 5413 registered employees. During the years 2007 – 2008 database was finished and supplemented with missing information such as risk exposure by occupation position. The anonymity of participant was assigned by identification numbers.

From the 5413 total registered employees we exclude students and employees who were not exactly working in the smelter but they were registered as a full-time staff (employees in recreational facilities, vocational school and daily care). Afterward were analyzed a total of 4622 records, which represented 85% of all registered employees from nickel smelter.

The nickel production and processing was done in many different production departments. Overall, nickel smelter had more that 40 section, which were part of the 5 departments (economy management, wet and dry operations of manufacture, metallurgy production and administrative department). In individual departments employees worked at more than 80 various jobs as well as in different exposure to risk factors. After the processing of all available data, the risks in the workplaces were divided into 4 categories and jobs were grouped into 8 main groups (administration, temporary job, chemistry, mechanization, fire guard, maintenance, manufacture, research & development).

Statistical analyses were done by program R project (http://www.r-project.org). The lowest level of significance was $P \leq 0,05$. Confidence interval (CI) was 95% for all results. For statistical analyses were calculate Odds ratio (OR), logistic regression and survival analyses through Kapplan-Meier survival curves. The confounders were smoking and over-occupational exposure.

Results

The results described the proportions according to different type of workplaces and exposures are presented in Table 1. The study group was divided to 2 groups according to nickel exposure. There were 1348 non-exposed employees (29%) and 3274 exposed employees (71%). The most participants had basic and secondary school education. The major proportion of employees worked on manufacture department (33% of non-exposed, 64% of exposed). Occupation duration was in range from 0,1 to 48,6 years. The average work duration was 9,1 ($CI_{95\%}$ = 8,8 – 9,4) years. Median was 5,0 years. The most workers were employed until 5 years (50% of non-exposed, 51% of exposed).

Tab. 1. Description by Ni exposure in an occupational environment

	Exposure				
Parameter			Exposed to Ni		
	Non-exposed to Ni	%	n = 3274	%	P value
Gender	n = 1348				
Female		34 %	423	13 %	P ≤ 0,001
Male	464	66 %	2851	87 %	
Total	884	100%		100%	
Education					
Basic		33 %	1241	38 %	P ≤ 0,001
Secondary without Graduation	446	26 %	1084	33 %	
Secondary with Graduation	349	35 %	838	26 %	
University	474	6 %	111	3 %	
Total	79	100%		100%	
Position					
Administration		16 %	49	2 %	P ≤ 0,001
Temporary job	214	8 %	130	4 %	
Chemistry	111	7 %	189	6 %	
Mechanization	97	3 %	74	2 %	
Fire guard	44	3 %	26	1 %	
Maintenance	33	25 %	626	19 %	
Manufacture	341	33 %	2100	64 %	
Research & Development	444	5 %	80	2 %	
Total	64	100%		100%	
Work duration (years)					
0 - 5		50 %	1656	51 %	P ≤ 0,05
6 - 10	663	16 %	448	14 %	
11 - 15	218	10 %	307	9 %	
16 - 20	140	8 %	232	7 %	
> 20	109	16 %	631	19 %	
Total	218	100%		100%	

Tab. 2. Health status and occupational exposure among nickel smelter workers

	Health status				
Parameter	no Ca		with Ca		
	n = 4222	%	n = 400	%	P value
Gender					
Female	814	19 %	73	18 %	n.s.
Male	3408	81 %	327	82 %	
Total		100%		100%	
Exposure to Ni					
Non-exposed (I.+II. cat.)	1265	30 %	83	21 %	P ≤ 0,001
Exposed (III. + IV. cat)	2957	70 %	317	79 %	
Total		100%		100%	
Position					
Administration	235	6 %	28	7 %	P ≤ 0,001
Temporary job	231	6 %	10	2 %	
Chemistry	272	6 %	14	4 %	
Mechanization	113	3 %	5	1 %	
Fire guard	49	1 %	10	2 %	
Maintenance	853	20 %	114	29 %	
Manufacture	2336	55 %	208	52 %	
Research & Development	133	3 %	11	3 %	
Total		100%		100%	
Age of first employment					
≤ 20	1124	27 %	54	14 %	P ≤ 0,001
21- 30	1825	43 %	131	33 %	
31- 40	716	17 %	146	36 %	
> 40	557	13 %	69	17 %	
Total		100%		100%	

Work duration (years)					
0 - 5	2307	55 %	12	3 %	
6 - 10	651	15 %	15	4 %	
11 - 15	352	8 %	95	24 %	P ≤ 0,001
16 - 20	252	6 %	89	22 %	
> 20	660	16 %	189	47 %	
Total		100%		100%	

Table 2 displays the health status by various type and length of occupational exposure. There were 4222 employees without recorded cancer (91%) and 400 employees had recorded cancer disease (9%). Among cancer cases we can assess that they mostly work on manufacture department (52% of cases). The most cases were employed in nickel smelter over the 20 years (42%). The 36% of cases were first time employed in nickel smelter at the age of 31 – 40 years old.

Among the all cases, there were respiratory cancers (24%), digestive cancers (24%), melanoma (15%), lip and oral cavity cancers (9%), reproductive organ cancers (9%), urinary cancers (6%), breast cancer (4%) and other cancer types (9%).

The results from the regression analyses describe the interaction of various selected parameters (gender, education, marital status, age of the first employment, duration of work and level of risk in the workplace) between sick and healthy workers. Depended variable (effector) was a health status (sick = 1, healthy = 0). We did not detected a statistically significance difference in the variable of gender. We found that with the higher education is less chance to be sick (OR = 0,79, $CI_{95\%}$ = 0,69 – 0,91, P ≤ 0,01). Furthermore, we found that marriage reduces the chance to have cancer disease (OR = 0,73, $CI_{95\%}$ = 0,56 – 0,96, P ≤ 0,05). From the perspective of age of the first employment, we found that with increasing age to start work is increasing chance to be sick (OR = 1,48, $CI_{95\%}$ = 1,30 – 1,69, P ≤ 0,001). Furthermore, with increasing duration of employment is also higher chance to have cancer (OR = 2,23, $CI_{95\%}$ = 2,05 – 2,41, P ≤ 0,001). Also the higher risk exposure has impact on higher chance to have cancer (OR = 1,46, $CI_{95\%}$ = 1,22 – 1,75, P ≤ 0,001) (Table 3).

Tab. 3. Logistic regression analyses by selected parameters with the health status as a depended variable (sick = 1, healthy = 0)

	Standard Error	z value	P value	**OR** (95% CI)
Gender	0,150	-1,350	n.s.	**0,82** (0,61-1,10)
Education	0,070	-3,269	P ≤ 0,01	**0,79** (0,69-0,91)
Family status	0,139	-2,277	P ≤ 0,05	**0,73** (0,56-0,96)
Starting Age (years)	0,067	5,854	P ≤ 0,001	**1,48** (1,30-1,69)
Work duration (years)	0,041	19,456	P ≤ 0,001	**2,23** (2,05-2,41)
Occup. Risks	0,092	4,132	P ≤ 0,001	**1,46** (1,22-1,75)

Discussion

Other published studies dealing with the emergence of malignances among workers in a nickel refinery also worked with the cohort of employees. The first information about professional respiratory cancers in nickel refinery workers came from Wales in UK in 1993 [8]. The source data are from the period 1902 to 1934. In the observed cohort were 679 men from the refiners, who were than monitored by "follow up in the period 1934 to 1981 [9]. Other refineries, which had been also previously investigated, were in Finland, Norway and Canada. Cohort in Finland consisted of 1385 employees in the period 1953 to 1987. In the Norway there were 5297 refinery worker since 1910 to 1977 and in the Canada were 1659 followed men cohort in nickel refineries since 1954 to 1995 (KARJALAINEN 1992, GRIMSRUD 2003, EGEDAHL 2001) [7,8].

From 1992 to 1996 were published the results of research examining the relationship of the risk of cancer among two high-risk cohorts of South Wales and Norway. The main objective of research in Norway was to find out that the forms and nickel compounds contribute most to the carcinogenic risk (water-soluble, sulphides, oxides or metallic nickel).

It was the first study which used the statistical analysis of cumulative exposure measurement [9-11].

Sorahan (2004, 2005) presents quite similar results from the cohort of nickel refinery workers in Clydach, South Wales. In observed cohort were 812 men employed at the refinery since 1953 to 1992. Similar to our study methods, Sorahan excluded from monitoring those workers who worked in the canteen and other administrative work outside the company. Saharan's results are also oriented on type of work, length of work in the company, the type of cancer and the mortality rate for selected types of tumors. The highest mortality was within lung cancer and bronchi, and stomach tumors and prostate tumors. Again, confirm to our finding that with increasing duration of employment is risk of lung cancer 1,21 times higher. Furthermore, the authors found that higher mortality for lung cancer were among those workers who worked directly in the manufacturing process of nickel processing). Sorahan also followed among workers in a nickel refinery in South Wales, mortality and fatality by different types of cancers [12,13]. His results confirm to our finding that the highest proportion had respiratory and digestive cancers.

The relationship between nickel exposure and cancer of the lung was further examined in the study of cases and controls, which is based on a cohort of Norwegian workers. There was a new matrix used for detection of nickel exposure in respect of smoking and other carcinogenic risks in the workplace as well as in the internal and external environment of refineries. To the analysis were included also other factors that can make the emergence of lung cancer among exposed workers (age, length of employment, working hours, work at different departments, changes in production and the manufacturing process, changes in the occupational environment. The incidence of cancers was compared with national male population with regard to age and smoking habits [8,14].

Other researches investigated further accumulation of nickel in the lung between smokers and nonsmokers in the different professional exposure to nickel. Their results show that cumulative exposure is a cause of lung cancer with high risk. On the other hand, the differences of nickel concentration in plasma and urine among smokers and nonsmokers were not significant [15,16].

In our monitoring and analyzing of cancer occurrence among workers in the nickel refinery in Sered' we relied on the available data (gender, age, length of employment, work at different departments and levels of nickel exposure in the workplace). Since data about smoking and intensity of smoking were not collected, we could only rely that the estimated 65% of all smokers in the cohort will spread evenly between the exposed and non-exposed.

The reason of this bias is that the data collection was not based on interview but only on medical records and employment records. And these sources did not have information about smoking habits because this information was not required for recording the medical records of every employee. For valid and comprehensive analysis about impact of heavy metal exposure on health is necessary to add any missing information. There were also missing information about over-occupational exposure or about previous jobs.

The above biases of the monitoring are reasonable criticism by experts in the field of public health as well as other professionals. For follow-up and statistical processing should be considered another selection criteria of employees. Based on experience with the processing of this database would be useful to exclude all employees who were employed less than 12 months. We should avoid to confounding the results, because there were 20% short-employed workers in the refinery in Sered'.

The nickel production in Sered' is finished sine 1993. At this time exist other fact, that in addition to the separation of pollutants, there were produced solid waste contain 78% iron in the form of ferric oxide. This means that the next step for the analysis of the impact on human health may be by secondary exposure from the environment.

Conclusion

Presented study was the first study, which discussed aspects of the possible occupational exposure in the nickel refinery in Sered' in the Slovak Republic. Available data on Department of Public Health (Trnava University) are unique collection of information about all registered refinery employees during 30 years of production. Thus, despite the systematic errors from confounding smoking to the analysis, is this study challenge for dealing with the impact of nickel refinery on population health in the Slovak Republic in the future. We see the necessary cooperation with experts from the meteorological monitoring, the regional public health authorities but mainly by people from Galanta district in Trnava region.

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