

CANCER MORTALITY IN A BELORUSSIAN TANNERY

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Abstract

Background Occupational environment makes an important contribution to the Public health of workers and people who live near the enterprise. Therefore the aim of this study was to evaluate cancer mortality among workers employed in the largest tannery of Belarus.

Methods A total of 768 died workers who were actively employed with a minimum of 6 months employment were followed from 6 July 1953 to 31 December 2000. There were 328 women and 440 men observed. Proportionate mortality ratios (PMRs) were calculated using the population of Minsk to generate expected numbers.

Results Among women employed in the tannery, there was a significant excess of pancreatic cancer, based on eight deaths (expected=2,56, PMR=3,13, 95%CI=1.35-6.17). Six of the eight pancreatic cancer deaths occurred among women occupied in dyeing-stuffing workshop (expected=1.64, PMR=3.67, 95%CI=1.34-7.97), all among workers hired between 1962 and 1984 (expected=1.06, PMR=6.54, 95%CI=2.6-13.4). Insignificant excess, has been found in males buccal cavity-pharynx cancers (PMR=1.61, 95%CI=0.52-3.7); in males pancreatic cancer (PMR=1.95, 95%CI=0.63-4.25); in melanoma and skin cancers both males (PMR=3.0, 95%CI=0.6-8.8) and females (PMR=3.2, 95%CI=0.86-8.1). Among females it was found the insignificant increase in cancers of uteri (PMR=1.7, 95%CI=0.9-2.9) and in urothelial cancers (PMR=1.69, 95%CI=0.54-3.9), but no cases of bladder cancer were found.

Introduction

The tanning industry involves many occupational exposures, including formaldehyde, chromates and bichromates salts, aniline, benzene-based dyes, different organic solvents, such as butyl acetate; inorganic acids, ammonia, hydrogen sulphide and other. It is necessary to note, that the basic strategy of leather production is in using the most hydrophobic substances for optimally deep skin impregnation by them. That also could facilitate their penetration into human organism. In 1987 IARC classified occupational exposures in tannery processes as "not classifiable as to carcinogenicity to humans" (1) Data about cancer mortality among tannery workers in the world are very contradictory. In spite of wide distribution of leather production in the Republic of Belarus the problem of it possible carcinogenicity has been never investigated at all. Thus the question of cancer mortality of tannery workers is very actual in Belarus. Under these circumstances the retrospective cohort study to evaluate mortality among workers at one of the biggest tanneries in the Republic of Belarus, the Minsk Leather Tannery, which has been in operation since the beginning of the last century, was initiated.

Methods

All employees of the Minsk Leather Tannery were identified from personnel records of those hired from 1953 to 1995. Workers with a minimum of 6 months of employment were included in the study. For each subject information was abstracted on year of birth, date hired, employment termination date, and process for all jobs held. The jobs were classified by occupation into three groups: tanning–liming operations, dyeing–stuffing and other, which included jobs thought generally to be without hazardous exposures, such as tannery administration.

The registration of cohort members' deaths was started from January 1, 1953, and finished in December 31, 2000. Death certificates with indicated case of death for all deceased workers were

obtained from the Minsk-City Archive of Civilian Registrars. Underlying cause of death was coded according to the 9th revision of the International Classification of Diseases (ICD-9) (2). Expected deaths were calculated based on gender, age (5-year age groups), and calendar time (5-year groups). Mortality data of the general Minsk population for 1953–1976 were taken from Minsk-City Archive of Civilian Registrar and for 1976–2000 from Minsk Vital Statistics Department. Using Microsoft Excel software based on methods developed by Monson (3, 4, 5) indirectly standardized by age and calendar time proportionate mortality ratios (PMRs) were calculated by comparing the observed number of deaths to the expected number. The summation was going on by j – 5-years age (since 20) and calendar (1953-2000) time intervals. The 95% confidence intervals (95% CI), based on the Poisson distribution were calculated (6). Analyses by primary job, time hired and latency were conducted. The regression linear trend and Pearson correlation analysis of relation between cancer mortality and the duration of employment were provided.

Results

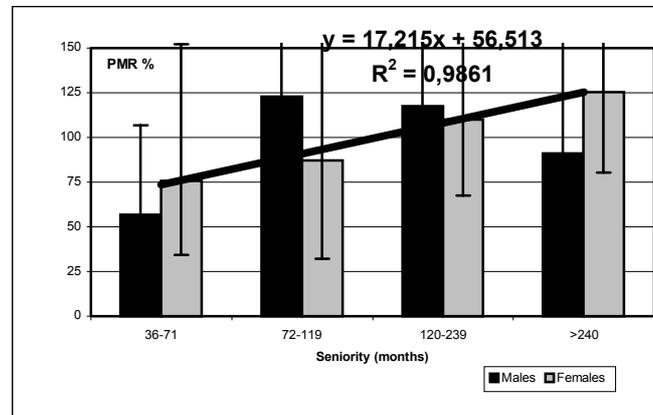
The primary cohort consisted of all employees of a Minsk Leather Tannery (1953–1995) and constituted of 3,500 workers. Seven hundred sixty eight persons (440 males and 328 females) had died by December 31, 2000. The first rank place by causes of deaths was occupied by cardiovascular diseases both men and women workers (46,6% & 52,2% correspondingly); at the second position for men were external and unknown causes of death (accidents, suicides and other – 21,4%), but for women there were malignant neoplasms (26,2%). The third place remained for malignant neoplasms (20,2%) for males and external and unknown causes of deaths (9,5%) for females. This proportion distribution corresponded to the general population. Among the total cohort 175 deaths of all malignant neoplasms were found (89 males and 86 females), that was close to expected numbers. The significant excess in total cohort was shown for female pancreatic cancer. The number of observed and expected deaths, PMR, and 95% Confidence Intervals for workers employed in Minsk tannery by place of employment are presented in Table I.

Table I. Number of Observed and Expected Deaths, PMR^a, and 95% CI for workers^b employed in Minsk Tannery.

Cause of death (ICD-9)		All tannery employees			
		Obs	Exp	PMR	95% CI
All malignant neoplasms (140-208)	M	89	99,4	0,9	0,72-1,1
	F	86	83,6	1,03	0,83-1.3
Buccal cavity, pharynx (140-149)	M	5	3.11	1.61	0.5-3.7
Esophagus (150)	M	1	2.1		
Stomach (151)	M	14	20.3	0.7	0.4-1.2
	F	12	14.2	0.8	0.4-1.5
Colon (153)	M	1	5.6		
	F	5	7.2	0.7	0.2-1.6
Rectum (154)	M	5	5.0	1.0	0.3-2.4
	F	4	5.2	0.8	0.2-2.0
Pancreas (157)	M	5	2.6	1.95	0.6-4.3
	F	8	2.6	3.13	1.35-6.2
Larynx (161)	M	2	3.4	0.6	0.07-2.1
Lung (162)	M	32	26.2	1.22	0.8-1.7
	F	5	4.32	1.16	0.4-2.7
Melanoma, skin (172-173)	M	3	1.0	3.0	0.6-8.1
	F	4	1.26	3.2	0.86-8.1
Breast (174)	F	13	13.3	1.0	0.5-1.7
Corpus, cervix uteri (180-182)	F	13	7.5	1.7	0.9-3.0
Ovary (183)	F	6	6.8	0.87	0.3-1.9
Prostate (185)	M	2	3.9	0.5	0.06-1.8
Testis (186)	M	1	0.48		
Kidney and bladder (188-189)	M	3	6.7	0.45	0.09-1.3
	F	5	2.96	1.7	0.5-3.9
Lymphatic and haematopoeitic tissue (200-208)	M	4	6.4	0.6	0.16-1.6
	F	3	5.6	0.53	0.1-1.55

With regression analysis we have shown the positive association between the increase in PMR of all cancers sites and the duration of female occupation in dyeing–stuffing production with the seniority more than 3 years. Pearson correlation coefficient was $R_{\text{Pearson}}=0,99$; $p<0,05$. For men no linear relation was found. See illustration 1.

Illustration 1: Proportionate Mortality Ratios (PMRs) for tannery workers with different seniority.



Discussion

However IARC classified occupational exposures in tannery processes as "not classifiable as to carcinogenicity to humans" (1), but any compounds of tanning process considered as "probably carcinogenic to humans" (formaldehyde and some benzene-based dyes (1)). Moreover, some investigations have demonstrated the mutagenic effect in K-ras oncogenes of leather dust (7) and also of 20 azo-dyes used in leather dyeing in the Salmonella/microsome test (8). Stupar et al. (9) showed the strong ability of proteins in leather dust to bind inorganic chromium III compounds and facilitate their entrance into human in this way.

The main finding in our study was the significantly increased proportionate mortality ratio shown for the pancreatic women cancer based on eight deaths (expected 2.6, PMR 3.13, 95% CI 1.35–6.2). and insignificantly high for men. Six of eight pancreatic cancers in women occurred among those, who worked in dyeing–stuffing workshops (expected 1.6, PMR 3.66, 95% CI 1.34–8.0) and who were engaged between 1961 and 1976 and hired between 1962 and 1984 (expected 1.06, PMR 6.54, 95% CI 2.6–13.4) with an average seniority of about 10 years (PMR=8.58; 95% CI = 2.78-20.0). The average latency period was 20 years. Also insignificantly high mortality was shown for male pancreatic cancer (PMR 1.95, 95% CI 0.6–4.3). There are a few reports linking tannery occupation to pancreatic cancer (10, 11, 12), but the evidence is limited, with most tannery cohorts not showing a pancreatic cancer excess. The risk factors for pancreatic cancer are smoking habits, diet, benign diseases such as pancreatitis, confounded with alcohol consumption, diabetes mellitus, inherited genetic susceptibility and acquired mutations in the oncogenes K-ras and HER2/neu, and in the tumor suppressor genes p16, p53, SMAD4, BRCA2 (13, 14, 15). Although it is not known if the cohort had different patterns of alcohol and tobacco consumption than the Minsk general population, but both as cancers of the liver, esophagus and lung, sites associated with these exposures as deaths with pancreatitis (one case was observed) were not elevated among nor women neither men employees in the tanning plant. It is one important thing to note, in our research men and women were distributed in workshops unequally. There was the prevalence of men 77% over 23% of women worked at tanning processes and 90% women over 10% of men in dyeing-stuffing workshops. Thus males were mainly occupied in processes with chemical exposures of bichromates, inorganic acids, formaldehyde and leather dust, in contrast to females, who were worked with aniline, benzene dyes, leather dust and organic solvents. Under these circumstances the relatively high mortality of pancreatic cancer both men and women points to the presence of any common factors, like leather dust and chromium compounds. Moreover Stupar (9) reported about ability of chromium compounds to change the tolerance to glucose in older people, the effect was demonstrated in the cohort of tannery workers. Thus, the changing of intolerance to glucose due to chromium compounds exposure could be supposed as one of mechanism of pancreatic cancer developing in tannery workers.

It was found the significantly elevated mortality from melanoma and skin cancers for women-workers of dyeing–stuffing workshops (PMR =4.54; 95%CI = 1.3-11.3), with the seniority more then 10 years

(PMR=8.0; 95% CI = 1.0-28.46), that could be associated with aniline dyes and synthetic stuffing mixes used in leather dyeing.

A non-significant growth was found in buccal cavity–pharynx cancers for males but no cases of nasal cancer, for males engaged for 1971 - 1980 significantly (PMR=5.1; 95% CI = 1.05-14.97). The significant excess in cancers of corpus and cervix uteri was shown for females engaged before 1950 (PMR=2.9; 95%CI=1.06-6.33) and hired before 1960 (PMR=3.39; 95% CI = 1.36-7.0) with the seniority more than 10 years (PMR=2.87; 95% CI = 1.05-6.25). Surprisingly, we did not find any excess of bladder cancer, with only one case in a male who was occupied in the tanning–liming workshops. A non-significant increase in bladder-kidney cancers was shown for women – workers of painting and finishing processes. A total of five kidney cancers were noted for female workers with a mean of 15 years seniority in dyeing–stuffing workshops. Low PMR was shown for male’s colon cancer: one observed case against five expected. The average latency period counted out the central point of the period of the occupation was 20 years.

The analysis by time of work showed the highest PMR for all cancers for workers who started their operation before 1971 and were hired before 1990. At that time “Direct Black 3” and “Basic Black 3” aniline dyes, with benzidine solvents and formaldehyde were broadly used. The level of Chromium exposure was stable for the all time under investigation. So we could indirectly suspect that tannery reconstruction carried out in 1988 contributed to reduction of cancer risk. But some further investigations are needed because it is not enough time elapsed to realize the cancer risk in new recruited workers.

The strong positive seniority-cancer mortality relation for women suggested that occupation in leather tannery raise the level of cancers in workers. But the absence of this relation for men was the evidence that men were less liable to carcinogenic occupational factors and more often died with non-cancer causes induced by pernicious habits.

Conclusions

Women - workers are more the subjects of occupational exposition impact than men. This could be provoked by different level of smoking and alcohol consumption and more permanent seniority. Leather tannery production could influence the mean age of death but the distribution of workers death causes correspond to general population.

The pancreatic, melanoma & skin cancers could be associated with tannery occupation.

The analysis of exposure and conditions of work suggests that cancer could be initiated by exposure of aniline, benzidine based dyes and formaldehyde, which were broadly used before 1988 year. But pancreatic cancer could be promoted by Chromium III compounds, after mutagenic alterations by noted above exposures. Further investigations of possible Chromium affect the pancreas and dose-respond relations are the primary goals of our further researches.

Thus further follow-up of this cohort, which would allow more in-depth analysis of rare cancer sites, confounders and adjust for different risk factors, are warranted. Sites of interest include melanoma, pancreas. The large number in this cohort provides an opportunity for further trials.

References

- 1 IARC monographs on the evaluation of carcinogenic risks to humans, Leather and tanning processing, Vol. 25, Supp. 7, IARC, Lyon, (1987)
- 2 WHO (World Health Organization). International classification of diseases, vol. 1, tabular list, ninth revision, World Health Organization, Geneva, (1992)
- 3 Monson R.R. Analysis of relative survival and proportional mortality, *Comp. Biomed. Res.*, **7/3**, 325 (1974)
- 4 Monson R.R. Occupational Epidemiology, CRC Press, Boca Raton Florida, (1990)
- 5 Breslow N. E., Day N. E. Statistical methods in cancer research. The design and analysis of cohort studies, Vol. 2, IARC, Lyon, (1987)
- 6 Silva I. Cancer Epidemiology: Principles and Methods, IARC, Lyon,(1999)
- 7 Saber AT, Nielsen LR, Dictor M, Hagmar L, Mikoczy Z, Wallin H. K-ras mutations in sinonasal adenocarcinomas in patients occupationally exposed to wood or leather dust, *Cancer Lett* **126/1**, 59, (1998)
- 8 Clonfero E, Venier P, Granella M, Levis AG. Leather azo dyes: mutagenic and carcinogenic risks, *Med. Lav.* **81/3**, 222, (1990)
- 9 Stupar J, Vrtovec M, Kocijancic A, Gantar A. Chromium status of tannery workers in relation to metabolic disorders, *J Appl Toxicol*, **19/6**, 437, (1999)
- 10 Edling C, Kling H, Flodin U, Axelson O. Cancer mortality among leather tanners, *Br J Ind Med*, **43/7**, 494, (1986)
- 11 Pietri F, Clavel F, Auquier A, Flamant R. Occupational risk factors for cancer of the pancreas: a case-control study, *Br J Ind Med*, **47/6**, 425, (1990)
- 12 Mikoczy Z, Schutz A, Stromberg U, Hagmar L. Cancer incidence and specific occupational exposures in the Swedish leather tanning industry: a cohort based case-control study, *Occup Environ Med*, **53/7**, 463, (1996)
- 13 Lowenfels AB, Maisonneuve P. Epidemiologic and etiologic factors of pancreatic cancer, *Hematol Oncol Clin North Am*, **16/1**, 1, (2002)
- 14 Stolzenberg-Solomon RZ, Pietinen P, Taylor PR, Virtamo J, Albanes D. Prospective study of diet and pancreatic cancer in male smokers, *Am J Epidemiol*, **155/9**, 783, (2002)
- 15 Konner J, O'Reilly E. Pancreatic cancer: epidemiology, genetics, and approaches to screening, *Oncology (Huntingt)*, **16/12**, 1615, (2002)