Mortality study of fertiliser manufacturers in Iceland

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Abstract

A retrospective cohort study was carried out on workers in a fertiliser plant to assess the risk of stomach and lung cancer. The cohort comprised 603 subjects and their death rates were compared with those of the general male population in Iceland. The study period was 1954 to 1985. The results do not provide evidence of an excess of deaths from stomach or lung cancer. Total mortality was lower than expected and even lower when the analysis was restricted to those who had worked at the plant for more than one year. Shiftwork operators had the highest SMRs for all cancers, however, with a reverse dose response according to duration of employment, indicating that this might be due to factors unrelated to manufacture of fertilisers. As examples of these factors life style and social class may be implicated, as well as possible selection of weaker subjects to do this assumed easy work.

Bacterial action in saliva reduces nitrate to nitrite. Under acidic conditions in vivo nitrites nitrosate amines and amides to form N-nitrosamines, which have been shown to cause cancer in laboratory animals.[1] It has not been demonstrated that these compounds are carcinogenic in humans, but if they are, it is suggested that the stomach is the target organ.[2,3] The use of nitrate fertiliser has increased greatly in the last decades. More nitrate in the soil has led to increased concentrations of nitrate in drinking water and vegetables world wide. At the same time, mortality from stomach cancer has declined in many locations, including Iceland.[4,5] Vitamins C and E and certain phenols inhibit the formation of N-nitrosamines, whereas other phenols, thiocyanate, and iodide ion catalyse nitrosation.[1,6,7] Other factors, such as diet and social class, have also been considered in connection with gastric cancer.[4,8]

Investigators have tried to establish whether there is a link between nitrate ingestion and stomach cancer, but have not reached a consensus of opinion; some have found a connection between the two,[9–15] but others have not.[16–18] In a cohort study of fertiliser manufacturers Fraser *et al* found a non-significant excess of cancers of the lung and digestive tract in one of two cohorts,[19,20] but concluded that this was probably not related to exposure to nitrate. The conclusion was based on the failure to find an excess mortality from gastric cancer, and contradictory dose response relations for all cancers and cancer of digestive organs. Al-Dabbagh *et al* conducted a cohort study of fertiliser workers from northern England.[21] Their results also weighed against the idea that exposure to nitrates leads to cancer. Studies of workers in phosphate fertiliser production and in the phosphate industry in the United States showed no special health risk. The number of deaths from lung cancer was somewhat higher than expected, but the authors found more likely explanations for this than exposure to phosphates.[22–24]

In the light of this information, it was thought worthwhile to examine whether or not employees of a plant producing nitrogen fertiliser and compound fertiliser were more likely to die of cancer, especially of the stomach and lung, than other Icelandic men.

Material and methods

The fertiliser plant studied produces ammonia and nitric acid from nitrogen and hydrogen. The product is used to make damp ammonium nitrate granules that are then dried and coated, making a special kind of fertiliser. A compound fertiliser (nitrogen, potassium, phosphate) is also produced by combining phosphate and potassium salts with the ammonium nitrate solution during production of the granules. The fertiliser granules were coated with diatome until 1978, when this was replaced with shell lime.

Dust concentrations were measured in the factory in 1978. The results of measurements of respirable dust ranged between 0·29–35·09 mg/m^3 with a mean value of 1·81 mg/m^3 in 29 personal samples for unskilled workers. For shiftwork operators the range was 0·09–3·59 mg/m^3 (mean 0·69 mg/m^3) in 30 personal samples.[25] Total dust concentrations for unskilled workers were 2·16–520·80 mg/m^3 (mean 96·17 mg/m^3) in 12 personal samples. At the same time, ammonia in the air where the shiftwork operators were employed measured 0–5 ppm and nitrogen dioxide 0–4 ppm.[25] In 1985 the respirable dust concentrations were 0·08–2·73 mg/m^3 (mean

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0·63 mg/m^3) in 29 personal samples for unskilled workers and 0·07–0·59 mg/m^3 (mean 0·26 mg/m^3) in nine samples for shiftwork operators.[26] Total dust concentrations for unskilled workers ranged between 1·56–492·90 mg/m^3 (mean 65·89 mg/m^3) in 17 personal samples.

The dust measurements were not done for the purpose of this mortality study. On both occasions they were performed to evaluate the most dusty tasks in the plant and not to describe the total exposure of the employees. The composition of the dust was not differentiated. According to an estimate of the product manager the dust concentrations in the period 1972–8 were similar to those in 1978 but before 1972 were lower than those in 1985.

The cohort comprised 603 men who were hired during 1954–85 (production started in 1954). The payroll for the years 1954 and 1955 contained no details of employees who had worked less than a year, which may mean that some men are missing. The cumulated employment years were calculated so that any employment on a calendar year counted as one year. Few women were employed and they were omitted. Seventy members of the cohort had died, and information on cause of death was obtained in all cases from the Statistical Bureau of Iceland. From the payroll it was possible to divide the cohort by the jobs on which they were employed into three categories: shiftwork operators, unskilled workers, and others. Shiftwork operators work indoors in three shifts, day and night. Their work is monotonous, mostly operating machinery and their tasks are similar all year round. Unskilled workers perform general labour, mainly out of doors. Their work varies according to season and assignment. The group "others" includes craftsmen and office workers.

This is a retrospective cohort study with a design similar to that used in other mortality studies.[27 28] Through the personal number and date of birth, it was possible to identify and trace all the living subjects in the national register and those who had died were found through the register of deceased; both of these registers are kept at the Statistical Bureau of Iceland. In this way the vital state of the study population was ascertained for all subjects. Death certificates were obtained and thereby the officially classified underlying cause of death. Different revisions of the International Classification of Diseases (ICD) have been in use during the period of study. The certificated cause of death has been reclassified according to the seventh revision[29] as the Cancer Register in Iceland uses this revision.[5]

The expected number of deaths was calculated on the basis of person-years of observation within five year age categories during respective single calendar years of the study period, multiplied by the cause and calendar year specific death rates for Icelandic men. The ratio between observed and expected numbers, the standardised mortality ratio (SMR), was calculated with 95% confidence intervals (95% CI) assuming a Poisson distribution.

Separate analyses were done on subcohorts according to year when hired and job categories. The calculation of the SMR, when the subcohort of shift work operators was divided according to cumulated years of employment, was done with and without a requirement of a latent period of 15 years. By requiring 15 years latency the effect of the selection of subjects into different exposure groups has been eliminated.[30] Table 1 shows the number of subjects, person-years, and deaths among the workers in the total cohort and the subcohorts.

Permission was obtained from The Data Protection Commission to compare the datafiles in this study.

Table 1 Number of workers, person-years, and deaths in total cohort and in different subcohorts

Groups	*Study period*	*No of subjects*	*No of person-years*	*No of deaths*
Total cohort:	1954–85	603	8804·5	70
Hired before 1963	1954–85	206	5121·5	51
Hired 1964–73	1964–85	145	2459·5	18
Hired after 1974	1974–85	252	1223·5	1
Worked more than one year:				
Total cohort	1954–85	421	6893·5	54
Shiftwork operators	1954–85	160	3306·0	34
Unskilled workers	1954–85	191	2385·0	15
Others	1954–85	70	1202·5	5
Shiftwork operators (all)	1954–85	211	4376·0	43
Employed ≤1 y	1956–85	51	1070·0	9
Employed 2–5 y	1956–85	47	876·5	8
Employed 6–15 y	1954–85	46	760·5	11
Employed ≥16 y	1954–85	67	1669·0	15
Latency of 15 years:				
Shiftwork operators (all)	1967–85	169	1517·5	25
Employed ≤1 y	1971–85	45	345·0	5
Employed 2–5 y	1971–85	32	280·0	2
Employed 6–15 y	1967–85	25	193·5	3
Employed ≥16 y	1967–85	67	699·0	15

Results

There were fewer deaths than expected in the cohort as a whole (table 2). The SMR for stomach cancer was 93 but there was an excess of observed deaths recorded for lung cancer and cancer of the colon, rectum, and pancreas. An excess of observed deaths was recorded for ischaemic heart disease (SMR 103) and accidents (SMR 130). The SMR for all other causes of death was 33 (95% CI 9–85).

Table 3 shows the SMR for all causes of death, all cancers, and ischaemic heart disease when the cohort was subdivided according to the year when hired. The observed number of deaths was higher than expected in the first group for cancers and ischaemic heart disease and in the second group for ischaemic heart disease.

Table 4 shows the results when the cohort was subdivided according to job categories and restricted to those who had worked for more than one year. The observed deaths were higher than expected for cancer and heart diseases among shiftwork operators. There was a significant deficit for all causes of death among unskilled workers (SMR 60) and the total cohort (SMR 73).

Table 5 shows duration of employment and mortality for shiftwork operators. The SMR for all causes of death and cancer was highest among those who had worked the shortest time, declining with the number of years of employment completed. The SMR for all cancers in the group which had shortest duration of employment was 412. There were inverse gradients for increasing duration of exposure and mortality both with regard to all cancers and all causes. The SMR for heart disease varied independently of duration of employment.

Table 5 also shows duration of employment and mortality for shiftwork operators, with a requirement of 15 years of latency. For all cancers the inverse gradients in risk were clearer than in the analysis without a requirement of latency, and the SMR for those with the shortest duration of employment rose to 789.

Table 2 Observed (Obs) and expected (Exp) number of deaths, SMR, and 95% CI among 603 fertiliser workers

Cause of death (ICD, 7th revision)	*Obs*	*Exp*	*SMR (95% CI)*
All causes (001–E985)	70	81·40	86 (67–109)
Malignant neoplasms (140–205)	17	18·59	91 (53–146)
Stomach (151)	4	4·32	93 (25–237)
Large intestine (152, 153)	2	1·25	160 (19–578)
Rectum (154)	1	0·61	164 (4–913)
Pancreas (157)	3	1·31	229 (47–669)
Trachea, bronchus, and lung (162, 163)	4	2·88	139 (38–356)
Other neoplasms	3	8·47	35 (7–104)
Cerebrovascular diseases (330–334)	5	7·08	71 (23–165)
Ischaemic heart disease (420)	29	28·06	103 (69–148)
Respiratory diseases (470–527)	2	5·62	36 (4–129)
Accidents, poisonings, and violence (E800–E985)	13	9·98	130 (69–223)
All other causes	4	12·07	33* (9–85)

*p < 0·05, two tailed.

Table 3 Observed (Obs) and expected (Exp) number of deaths and SMR according to time when hired

	Time when hired (calendar years)								
	1954–63 (n = 206)			*1964–73 (n = 145)*			*1974–85 (n = 252)*		
Cause of death (ICD, 7th revision)	*Obs*	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*
All causes	51	56·26	91	18	21·58	83	1	3·56	28
Malignant neoplasms	14	12·76	110	3	5·07	59	0	0·75	—
Ischaemic heart disease	21	19·26	109	8	7·71	104	0	1·09	—

Table 4 Observed (Obs) and expected (Exp) number of deaths and SMR in the job categories and in the total cohort among those who had worked for more than one year

Cause of death (ICD, 7th revision)	*Shiftwork operators (n = 160)*			*Unskilled workers (n = 191)*			*Others (n = 70)*			*All (n = 421)*		
	Obs	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*
All causes	34	37·78	90	15	25·04	60*	5	11·22	45	54	74·03	73*
Malignant neoplasms	10	9·01	111	2	5·80	34	0	2·28	—	12	17·10	70
Ischaemic heart disease	17	13·57	125	6	8·93	68	3	3·66	82	26	26·06	100

*p < 0·05, two tailed.

Table 5 Observed (Obs) and expected (Exp) numbers of deaths and SMR by duration of employment as a shiftwork operator without and with requirement of 15 years latency

Cause of death (ICD, 7th revision)	Duration of employment (y)														
	≤1 (n = 51)			2–5 (n = 47)			6–15 (n = 46)			≥16 (n = 67)			All (n = 211)		
	Obs	Exp	SMR	Obs	Exp	SMR	Obs	Exp	SMR	Obs	Exp	SMR	Obs	Exp	SMR
Without latency time:															
All causes	9	4·74	190	8	4·53	177	11	12·48	88	15	20·77	72	43	42·51	101
Malignant neoplasms	4	0·97	412*	2	0·99	202	5	2·93	171	3	5·09	59	14	9·98	140
Ischaemic heart disease	1	1·30	77	4	1·47	272	6	4·48	134	7	7·62	92	18	14·87	121
With 15 years latency:															
All causes	5	1·86	269	2	2·24	89	3	5·56	53	15	13·81	109	25	23·46	107
Malignant neoplasms	3	0·38	789*	1	0·54	185	2	1·29	155	3	3·42	88	9	5·64	160
Ischaemic heart disease	0	0·56	—	1	0·86	116	1	1·99	50	7	5·44	129	9	8·84	102

*$p < 0·05$, two tailed.

Discussion

The objective of our study was to see whether men working in fertiliser production had an excess risk of dying of cancer, especially of the stomach and lung. The results do not allow us to give a definite answer.

There are some weaknesses in the study. For instance, the cohort is compared with the entire Icelandic male population and not with other working men, and this comparison invites the "healthy worker effect."[31] The cohort is small, and significant results regarding gastric and lung cancer would only be obtained with a risk of at least three times that of the general population.

The possible relation between consumption of nitrate and stomach cancer has been discussed. It was therefore decided to study the mortality from gastric cancer in the cohort at the outset, even though it was not a question of actual ingestion of nitrates, but rather of exposure to dust that could enter the lungs or mouth. On this basis it was considered appropriate to study lung cancer as well.

The results do not indicate that exposure to nitrate during fertiliser manufacturing leads to excess risk of dying from gastric or lung cancer and are in agreement with the findings of Al-Dabbagh *et al*[21] and Fraser *et al*.[19 20] As in the results of Fraser *et al* the highest risk of cancer was found in a group exposed to the least amount of nitrogen fertiliser. This inverse dose response relation indicates that the explanation is not to be found in the environment of work. The causes are, however, not clear.

A possible explanation may relate to selection. According to information from the plant the task and the work setting for the shiftwork operators were assumed by the workers themselves to be convenient, which might have caused a selection of weaker subjects to that job category.

Studies of fertiliser plant employees have discussed the possible importance of lifestyle and social class;[19] those from England and Wales showed that mortality ratios from cancer vary according to social class.[32] Social divisions in Iceland are said to be primarily based on educational rather than economic grounds.[33] Whether lifestyle and educational factors connected with the social classes play an important part in the explanation of cancer mortality in Iceland is not yet known.

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