Analysis of cancer mortality risk among workers of a research uranium metallurgy division in France

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Abstract

This cohort study has been undertaken in response to a suspected cluster of cancers mentioned by workers involved in research activities concerning the metallurgy of uranium. The studied population included all persons having worked between 1950 and 1968 at the Metallurgy Division of the French Atomic Energy Commission (CEA). Exposures were registered on an individual annual basis. For analysis, they were grouped in three categories: use of chemicals agents (Benzene, beryllium, alcohols, solvents...), manipulation of radioactive materials (uranium, thorium, fission decay products), and exposure to external radiation.

This relatively small cohort included 356 workers followed up to December 1990. Out of observed deaths, 21 were from cancer. Total mortality from cancer was less than expected from national rates (Standardised Mortality Ratio = 0.73). Cancer mortality did not increase with duration of exposure to external radiation or with duration of manipulation of radioactive materials. Risk of cancer was increasing with the number of years of exposure to chemicals.

The small size of this cohort limits the conclusion of the observed results. The purpose, despite this lack of power, was to answer a worry of the workers, more than to estimate a clear dose-response relationship linked to a specific cancer site. The effect studied here is "all cancers", a distinction of the different sites being uninformative because of the very small number of cases observed. Nevertheless, this study suggests some routes for further research: it highlights the importance of considering concomitant exposures like chemical ones in studies of nuclear workers.

1. INTRODUCTION

This epidemiological follow-up has been undertaken in response to a suspected cluster of several cases of cancer in 1983-1984 among workers from the Metallurgy Division of the French Atomic Energy Commission (CEA). These workers were involved in research activities concerning the metallurgy of uranium. In the framework of their occupational activity, they were manipulating uranium and other radioactive materials, and were also using chemicals.

The aim of this study was to screen for an increased risk of cancer mortality related to occupational exposure.

2. MATERIAL AND METHODS

The studied population included all subjects who had worked at the Metallurgy Division for at least one year between 1950 and 1968. Follow-up was completed up to December 1990. The dates and causes of deaths were obtained from the occupational medicine staff of CEA. Causes of deaths were coded according to the ninth International Codification of Deaths. The observed number of deaths from cancer were compared with the expected ones based on French national rates with adjustment for age, sex and calendar time and expressed by the Standardised Mortality Ratio (SMR).

Information on occupational exposure was obtained by a qualitative approach, from medical files and collective memory. Several meetings were organised with retired workers to discuss and precise individual yearly exposure (collective memory). For each worker, exposure to more than 30 different products was reconstructed per working year in a qualitative way (exposed/not exposed). For the analysis, these exposures were grouped in three categories, reflecting three different types of activity: use of chemicals (Benzene, ketones, beryllium, alcohols, solvents...), manipulation of radioactive materials (uranium, thorium, fission products), and exposure to external radiation (β, γ, X). Quantification of exposure was expressed by the number of years of exposure to each of the main components. Individual dosimetric records were also used to assess quantitatively the cumulative exposure to external radiation. Relationship between risk of cancer and exposure was examined using 3 methods: Poisson trend test, external Poisson regression modelling, using national rates of mortality as external reference, and internal Poisson regression modelling [1]. Only those results showing good agreement between the three methods were considered as significant.

3. RESULTS

3.1. Mortality

The cohort included 356 workers. Mean age at entry into the cohort was 30 years. Mean duration of follow-up was 30.4 years. The total number of person-years was 10,850. 24 subjects (6.7 %) could not be traced up to 1990. The observed number of deaths was 44. Cause of death was obtained for 31 cases.

For all causes of death, the studied population showed a strong « healthy worker » effect. The observed number of deaths from cancer (ICD 140-208) was 21. Total mortality from cancer was less than expected from the national rates of mortality (SMR = 0.73, Confidence Interval

$IC_{95\%}$=[0.49-1.06]). We found no evidence of any excess of cancers in the period 1983-1984. On the whole cohort, a significant excess of death was observed for multiple myeloma (SMR= 8.38, $IC_{95\%}$=[1.44-26.2]), but based on only 2 observed deaths.

3.2. Exposure-Mortality relationship

Of the 356 included workers:

- 191 have been exposed at least one year to chemicals, with a mean duration of exposure of 12 years.
- 255 manipulated radioactive materials at least one year. The mean duration of exposure was 11 years.
- 262 have been exposed at least one year to external radiation. The mean duration of exposure was 11 years. Mean dosimetric cumulative exposure was of 8.7 mSv (from a minimum of 0.4 to a maximum of 85.2 mSv)
- 20 % were never exposed to any of the materials from the three groups. 45 % were exposed in the three groups for at least one year.

When studying relationship between number of years of exposure and risk of cancer mortality, the three methods showed a high degree of agreement (Table I). No increase of cancer mortality was observed with the duration of exposure to external radiation. An increase with the duration of manipulation of radioactive materials was not consistent among the three methods. An increase of the risk of cancer mortality was observed with the number of years of positive exposure to chemicals (Table I).

Table I: Tests of a linear relationship between number of years of exposure and risk of cancer mortality

	Trend tests		**Poisson regression external ***		**Poisson regression internal ****	
	Chi-2	p	ERR	p	ERR	p
Number of years with						
exposure to chemicals	17.7	0.001	0.26	0.005	0.20	0.002
manipulation of radioactive materials	4.69	0.03	0.14	0.043	0.10	0.08
external exposure to radiation	1.51	0.22	0.05	0.276	0.03	0.42

*: using national rates of mortality from cancer as an external reference

**: stratified on sex, age and calendar year

ERR: excess relative risk (per year of exposure)

p: significance probability of the exposure-response relationship

4. DISCUSSION

The study was decided in response to questions coming from the workers of the Metallurgy Division, suspecting an excess of cancers in the period 1983-84. Despite its reduced size, this cohort study answers the following points:

(a) No excess of cancer mortality was observed on the whole follow-up period

(b) No cluster of cancers appeared in the period 1983-1984

(c) No increase of cancer mortality was observed with the duration of exposure to external radiation or with the duration of manipulation of radioactive materials.

On the other hand, two positive results were obtained:
(a) An excess of mortality from multiple myeloma was observed,
(b) The analysis suggested that exposure to chemicals might be a risk factor of cancer in the studied population.

When considering these results, we should remember the very small size of the study, and consequently its lack of power. Due to this reduced size, it was not possible to consider multiple exposures, nor to analyse separately the exposure to different chemicals. Also, we were not able to distinguish between different sites of cancer when analysing the exposure-effect relationship. For example, beryllium was included in the group of chemical exposures. This material has already been proposed as a carcinogen of lung cancer [2,3], but the size of our study was not sufficient to analyse this potential relationship. For multiple myeloma, the observed excess was based on only two cases. This excess is therefore susceptible to be a chance finding, but we have to note that a significant excess of multiple myeloma was also observed in some nuclear workers studies [4].

This study shows also the practical limits of such a precise reconstruction of past multiple exposures: what was possible here in a small population appears unfeasible on a large scale in cohorts of several thousands of nuclear workers. In our opinion, a nested case-control approach should be preferred when taking into account the influence of concomitant exposures on the dose-response relationship linked to external radiation in nuclear workers studies.

5. CONCLUSION

Due to the limited size of the study, conclusions have to be considered very cautiously. But it suggests some results that should be considered in further research on the risk of cancer among nuclear workers: particularly, it highlights the importance to consider exposures to chemicals in subgroups of nuclear workers.

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