Cancer morbidity in workers exposed to cutting fluids containing nitrites and amines

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In the mid-1970s it was recognised that cutting fluids containing nitrites and amines may also contain N-nitrosoamines in concentrations between 200 and 30 000 ppm before dilution.1 2 Since many N-nitrosoamines are carcinogenic to animals3 cutting fluids containing these substances were withdrawn from the market in the late 1970s and the nitrites replaced with other substances. Even if there is overwhelming experimental evidence indicating the carcinogenicity of many N-nitrosoamines, there is, to our knowledge, no study conclusively showing such effects in man. Cutting fluids with nitrites and amines have been used only since the 1950s and since the latency for many chemically induced tumours is at least 15 to 20 years, we would have expected to see an increased incidence in tumours due to these cutting fluids develop only recently.

The object of the present study was to evaluate the cancer morbidity and mortality in machine workers exposed to cutting fluids containing nitrites and amines.

Material and methods

The investigation was designed as a cohort study in which cancer morbidity and mortality in men exposed to cutting fluids with nitrites and amines was compared with that of the general population in the city of Gothenburg, population 440 000. The study was carried out at a firm in Gothenburg that produces bearing rings. It was founded in 1907 and employs about 4000 workers.

There are complete personnel files from the foundation of the firm to date. The files contain information about where and when every man has worked. From these files we selected every man who was employed at any time between 1950 and 1966 and who had worked in certain grinding departments for at least five years. A total of 556 grinders were selected. A study of the mortality in this group between 1958 and 1976 has been published.4

Of these 556 men, we selected the 219 who had worked for at least one year on a machine where cutting fluids with amines and nitrites had been used (table 1). Cutting fluids containing these components have been used since at least 1956. As we wanted to study the long term effects we allowed for a latent period of at least ten years, setting the first year of observation at 1966. The mortality of the 219 men was collected from the death register and the underlying causes of death have been used in the analysis. The cancer register provided their cancer morbidity by linkage of the men's national identity number with files in the cancer register. Every man was followed up until 31 December 1983. Seven men had emigrated but there was no other loss to follow up.

The expected numbers of deaths or cases of cancer were calculated by multiplying the number of person-years of observation by the corresponding incidence rates, stratifying for calendar year, age class, exposure time, latency, and sex and summarising the fractional contributions over the whole cohort.5 Cause specific mortality and morbidity rates for the general population of Gothenburg were obtained from the death register and the regional tumour register. The rates were stratified for calendar year (1966–82 (death register); 1966–80 (tumour register)), age class (five year age classes), and sex. When calendar year rates were not available they were approximated by taking the average of the two most recent years.

The difference between observed and expected incidences and confidence intervals of the rate ratio were calculated according to a Poisson distribution.6 Only p values below 0·05 are indicated (two tailed test).

Exposure

We have information about which cutting fluids have been used in the selected grinding departments since about 1940. From the beginning, a mixture of sodium carbonate (0·5–1·0%) and sodium nitrite (0·2–0·6%) was used. In the mid 1950s more complex cutting fluids with emulsifiers, corrosion inhibitors, and anti-foaming agents came into use. Through the chemical department of the firm and the suppliers we learnt...
about the composition of most of the fluids. Between 1956 and 1978 both sodium nitrite and amines, mostly alkanolamines such as triethanolamine and diethanolamine or monoethanolamine, occurred simultaneously in some products in varying concentrations. No measurements of the concentration of N-nitrosoamines in the fluids in question were made. In 1978 the concentration of sodium nitrite in the air close to some machines using fluids with 0.1–0.3% sodium nitrite was between 0.02 and 0.26 mg/m³.

There has always been oil mist in the atmosphere of these departments; in 1978 the average concentration was about 3 mg/m³ but before 1965 it is estimated to have been 5 mg/m³ or more.

Results

Mortality for the grinders was similar to that of the reference group (table 2). Fewer grinders had developed cancer than the reference group but the difference is not significant (table 3). The number of cancers at each site is few and no site shows an indication of increased risk. The records of the cases of cancer have been reviewed and none seems to be misclassified; all diagnoses were based on histopathological examination.

Table 1  Year of birth of the 219 grinders

<table>
<thead>
<tr>
<th>Year of birth</th>
<th>No</th>
</tr>
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<tbody>
<tr>
<td>&lt;1899</td>
<td>2</td>
</tr>
<tr>
<td>1900–9</td>
<td>14</td>
</tr>
<tr>
<td>1910–9</td>
<td>50</td>
</tr>
<tr>
<td>1920–9</td>
<td>73</td>
</tr>
<tr>
<td>1930–9</td>
<td>64</td>
</tr>
<tr>
<td>1940–7</td>
<td>16</td>
</tr>
</tbody>
</table>

Discussion and conclusions

The most common N-nitrosoamine occurring in cutting fluids is N-nitrosodiethanolamine (NDELA). It is usually formed by a reaction between sodium nitrite and diethanolamine but a reaction with other alkanolamines is also possible. The reaction is favoured by a low pH. The pH of cutting fluids in the diluted form is usually between 8 and 10. The highest reported concentration of NDELA, 3%, was found in an undiluted fluid. The fluids are almost always diluted to 2–5% before use. Limited measurements of diluted fluids have shown lower concentrations of NDELA, with a maximum of 3 ppm. NDELA may be absorbed through inhalation of an aerosol or through the skin.

The carcinogenicity of NDELA was previously considered to be weak, but more recent animal experiments have shown it to be a rather potent carcinogen. Lijinsky et al fed mice with drinking water containing 3900 to 31 250 ppm NDELA for about six months. When the animals were killed after 34 weeks all had hepatocellular carcinomas. In our study no cases of primary liver cancer were found.

Our findings are essentially negative but because of the small numbers we cannot exclude an increased risk for cancer of a specific site. The results indicate, however, that use in this industry has not resulted in an increased risk of cancer. Unfortunately we have no analysis of the NDELA in the fluids during the study years but we assume that the composition and handling of the fluids were similar to that in other industries in Sweden and probably also in Europe.

Table 2  Mortality of 219 men exposed to cutting fluids containing both amines and nitrites

<table>
<thead>
<tr>
<th>Cause</th>
<th>Exposure</th>
<th>±1 year</th>
<th>±5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SMR†</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>29</td>
<td>0.6–1.4</td>
<td>23.7</td>
</tr>
<tr>
<td>Tumours (140–209)*</td>
<td>4</td>
<td>0.1–1.3</td>
<td>3</td>
</tr>
<tr>
<td>Cardiovascular diseases (390–458)</td>
<td>15</td>
<td>0.6–1.8</td>
<td>11</td>
</tr>
<tr>
<td>Lung diseases (460–519)</td>
<td>2</td>
<td>0.2–5.6</td>
<td>2</td>
</tr>
<tr>
<td>No of person-years</td>
<td>2577</td>
<td></td>
<td>2028</td>
</tr>
</tbody>
</table>

Table 3  Number of cases of cancer in 219 men exposed to cutting fluids containing both amines and nitrites

<table>
<thead>
<tr>
<th>Cause</th>
<th>Exposure</th>
<th>±1 year</th>
<th>±5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SMR†</td>
<td></td>
</tr>
<tr>
<td>All (140–209)*</td>
<td>7</td>
<td>0.2–1.1</td>
<td>5</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>4‡</td>
<td>0.3–2.9</td>
<td>2</td>
</tr>
<tr>
<td>Lung (162)</td>
<td>1‡</td>
<td>0.0–2.9</td>
<td>1</td>
</tr>
<tr>
<td>Urinary bladder (188)</td>
<td>1</td>
<td>0.0–6.2</td>
<td>1</td>
</tr>
<tr>
<td>Prostate (185)</td>
<td>1</td>
<td>0.0–2.9</td>
<td>1</td>
</tr>
</tbody>
</table>

*International Classification of Diseases, 8th revision.
†95% Confidence interval.
‡Including one case of stomach cancer (151), one of colon cancer (153), and two of pancreas cancer (157).
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References


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