Waste anaesthetic gases induce sister chromatid exchanges in lymphocytes of operating room personnel


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Genotoxicity related to waste anaesthetic gas exposure is controversial. We have investigated the frequency of sister chromatid exchanges in peripheral lymphocytes of operating room personnel exposed to trace concentrations of isoflurane and nitrous oxide. Occupational exposure was recorded using a direct reading instrument. Frequencies of sister chromatid exchanges were measured in lymphocyte cultures of 27 non-smokers working in the operating room and 27 non-smoking controls. Personnel were exposed to an 8-h time-weighted average of nitrous oxide 11.8 ppm and isoflurane 0.5 ppm. After exposure, sister chromatid exchange frequency was increased significantly (mean 9.0 (SD 1.3) vs 8.0 (1.4) in exposed and control personnel, respectively) (P<0.05). We conclude that exposure to even trace concentrations of waste anaesthetic gases may cause genetic damage comparable with smoking 11–20 cigarettes per day.

Br J Anaesth 1999; 82: 764–6

Keywords: anaesthetics volatile, trace concentrations; anaesthetics gases, trace concentrations; genetic factors; operating rooms, contamination; anaesthetist, risks

Accepted for publication: December 8, 1998

Whether or not chronic exposure to waste anaesthetic gases is hazardous to the health of anaesthetic room personnel is still controversial. It was suggested that chronic exposure to trace concentrations may cause mutations in DNA.1

A sensitive method of evaluating genotoxicity is to count the number of exchanges between the two chromatids of a chromosome of cultured human lymphocytes. An increased number of such sister chromatid exchanges (SCE) reflects the influence of mutagens. In the past, this assay was used to detect increased SCE rates in operating room personnel exposed to high concentrations of halothane and nitrous oxide in a poorly equipped working environment.2,3 Today, two major points should be taken into consideration when evaluating the current situation of occupational risks of inhalation anaesthetics. First, following the recommendations of the epidemiological data to reduce health risks by minimizing occupational exposure, the working environment has been improved technically, resulting in probably low concentrations of waste anaesthetic gases, and second, halothane is classified as a potential embryotoxic substance in the work place by the German Health Regulation Authorities, whereas isoflurane has yet to be classified. Therefore, in our hospital, halothane has generally been substituted with isoflurane.

Because there are few data on the possible association between genotoxicity and low-level exposure to isoflurane and nitrous oxide, we have measured occupational exposure to waste anaesthetic gases and compared these values with the currently valid European exposure limits, and determined their effect on the amount of genetic damage using the SCE test in human lymphocytes.

Methods and results

The study was conducted after IRB approval at the University Hospital of Regensburg. Twenty-seven exposed anaesthetists were compared with 27 non-exposed physicians, working in other non-surgical departments of the hospital (Table 1). Each subject was interviewed using a standardized questionnaire with questions on drug intake, contraception, diseases during the previous 3 months, alcohol intake, and diagnostic and therapeutic x-rays.

Environmental measurements were obtained according to previous published work.4 Briefly, samples were obtained in the breathing zone of the anaesthetist using a direct reading instrument (Bruel & Kjaer 1302, Naerum, Denmark). Time-weighted averages were also calculated according to previous studies and currently valid health
authority regulations. Detailed analysis was performed with an Apple computer system using SPSS 6.1 for Macintosh software.

Venous blood samples (lithium heparin 15 u. ml⁻¹, Sarstedt, Numbrecht, Germany) were obtained from each subject at the end of the working day and at the end of the working week. Whole blood (0.5 ml) cultures were established in 5 ml of chromosome medium 1A (Gibco, Vienna, Austria), containing 5-bromo-2'-deoxyuridine 50 μmol litre⁻¹ (BrdUrd, Sigma, Deisenhofen, Germany) for 72 h. Two hours before harvest, demecolcine (Sigma, Deisenhofen, Germany) was added to each culture at a final concentration of 0.1 µg ml⁻¹. Later the cells were washed, fixed, stained and slides were coded for blinded scoring. Metaphases with few or no overlaps were selected from the coded slides. The frequency of SCE was measured by examining 30 complete second metaphases, one SCE being counted each time two adjacent segments of one of the chromatids in a chromosome were stained differently. The value of SCE for each specimen was taken as the mean rate of SCE per metaphase.

After data acquisition, the arithmetic mean (SD) was calculated for each group. After testing for normal distribution, the Student’s t test was applied to determine statistically significant differences between cell groups, with \( P \leq 0.05 \). The post hoc calculated power of this study was 82% using G-Power for Macintosh software.

All subjects were exposed to isoflurane and nitrous oxide for at least 3 months without interruption (excluding weekends). Furthermore, all were non-smokers, and any other exposure to possible genotoxic factors other than waste anaesthetic gases could not be detected.

Measurements obtained over several months resulted in exposure of operating room personnel to nitrous oxide 11.8 ppm and isoflurane 0.5 ppm, expressed as an 8-h time-weighted average. Although it was not possible to maintain identical workplace pollution, values did not exceed nitrous oxide 25 ppm and isoflurane 2 ppm. Both values were clearly below the proposed European occupational standards.

SCE rates differed significantly between the control and exposed individuals (mean 8.0 (SD 1.4) and 9.0 (1.3)) \((P=0.012, t \text{ test})\). Dividing the groups on the basis of sex, differences between males exposed \((n=13)\) and male controls \((n=18)\) were still statistically significant, whereas for the female comparison (14 exposed, nine controls) there were no significant differences (Table 1). Age did not correlate with SCE rate for the exposed \((r=0.02)\) or control \((r=0.03)\) group.

Comment

To date, there are few epidemiological studies on waste anaesthetic gases and potential adverse effects in healthcare workers.\(^1\) The SCE test measures the number of exchanges between the two chromatids of a chromosome and is used widely to screen chemicals for possible mutagenicity. Therefore, in several studies, Husum compared operating room staff with non-exposed personnel and found no influence of the anaesthetics halothane or nitrous oxide.\(^2\) In contrast, Sardas and colleagues found an increased frequency of SCE in 67 individuals from the operating room exposed to unknown amounts of halothane and nitrous compared with 50 controls.\(^3\) Although occupational exposure data were not available, a potential genetic risk when exposed to waste anaesthetic gases was indicated.

As halothane was not used in our study, we cannot make direct comparisons between previous studies and our present investigation. In contrast with previous work, our study population was large enough to establish a sufficient statistical power of more than 80%, and subjects were within a small age range, were matched for age and most were matched for sex. The major limitation of our study was that in common with previous investigations, we were unable to perform an exact match for sex. This may be the reason for the non-significant difference in the female population. Whether sex should still be seen as a confounding factor is also controversial. However, a recent report did not find sex a confounding factor for SCE frequency,\(^5\) but the most important confounding factor (smoking) was excluded. Further, we were unable to distinguish between the potential genotoxic effects of nitrous oxide and isoflurane, because all subjects were exposed to isoflurane and nitrous oxide simultaneously. However, these data are in accordance with recent in vitro data, demonstrating an increase in SCE rate when human lymphocytes were exposed to isoflurane and nitrous oxide.\(^6\)

We conclude that exposure to even low concentrations of waste anaesthetic gases may result in an increased risk of genetic damage. Whether the observed genetic damage may lead to increased morbidity remains unclear. All efforts should be undertaken to maintain environmental concentrations of anaesthetics as low as possible.

References

1 Boivin J. Risk of spontaneous abortion in women occupationally exposed to anaesthetic gases: a meta-analysis. Occup Environ Med 1997; 54: 541–8
2 Husum B. Mutagenicity of inhalation anaesthetics studied by the sister chromatid exchange test in lymphocytes of patients and operating room personnel. Dan Med Bull 1987; 34: 159–70

Table 1 Morphometric data and sister chromatid exchanges (SCE) of the subgroups (mean (SD) or range)

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Age (yr)</th>
<th>SCE (n/cell)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males exposed</td>
<td>13</td>
<td>33.5 (27–49)</td>
<td>9.0 (1.1)</td>
<td>0.03</td>
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<td>Male controls</td>
<td>18</td>
<td>33.3 (28–40)</td>
<td>7.9 (1.4)</td>
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<tr>
<td>Females exposed</td>
<td>14</td>
<td>33.5 (27–42)</td>
<td>9.0 (1.4)</td>
<td>0.20</td>
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<tr>
<td>Female controls</td>
<td>9</td>
<td>33.0 (30–40)</td>
<td>8.2 (1.5)</td>
<td>0.20</td>
</tr>
</tbody>
</table>
