Mixed solvent exposure and hearing impairment: an epidemiological study of 3284 men. The Copenhagen male study

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Animal experiments and human studies have indicated an effect on auditory functions from exposure to organic solvents. In this study the relationship between self-assessed hearing problems and occupational exposure to solvents was investigated in a cross-sectional design with 3284 participating men aged 53–74 years. Exposure to solvents for five years or more resulted in an adjusted relative risk (RR) for hearing impairment of 1.4 (95 per cent CI: 1.1–1.9) in men without occupational exposure to noise. Factors adjusted for were age, noise traumas, chronic middle ear infection and family history of hearing impairment. The prevalence of hearing impairment in men not exposed to organic solvents was 24 per cent and the attributable risk from solvent exposure was 9.6 per cent. Exposure for less than five years had no effect on hearing capacity. Occupational exposure to noise for five years or more had an effect twice that of solvents, RR: 1.9 (95 per cent CI: 1.7–2.1). In men exposed to both solvents and noise the effect of the latter dominated and no additional effect from solvents was found. A subsample of 51 men was examined with pure tone audiometry and 20 of 21 men who reported abnormal hearing also fulfilled an audiometric criterion for hearing impairment. In conclusion a damaging effect on hearing ability from long-term solvent exposure was found in the present study. The relative effect was moderate but with a high background frequency of hearing problems in the unexposed sample the absolute effect, i.e. attributable risk, was considerable and of both clinical and preventive importance.

INTRODUCTION

Animal studies have demonstrated that a few weeks of high level exposure to toluene, styrene and xylenes may cause permanent decrease in auditory sensitivity to high frequency tones. Other solvents may give rise to similar effects. Several exposure regimes for the ototoxicity of toluene have been examined: a threshold for sub-acute exposure is indicated at 700–1000 p.p.m., both continuous and intermittent dosing has been harmful and interaction between toluene and noise has been demonstrated. Histopathological studies and auditory brainstem response have indicated a major effect on the cochlea for toluene, while exposure to n-hexane seems to affect the central auditory pathways.

There are only a few controlled studies of hearing impairment in humans exposed to solvents. Morata found a higher frequency of hearing loss in workers exposed to carbon disulfide and noise than in workers exposed to noise alone. However the finding is uncertain since results for the group exposed to noise only derived from a different study and only restricted information from this study was reported. Muijser et al. found a dose-dependent difference in high frequency hearing thresholds between groups of styrene-exposed workers in a glass fibre factory but no difference was found in comparison to an external control group. In single case reports and case series both cochlear and central effects on auditory functions have been described following occupational exposure or abuse of solvents, and an interaction with the effect of noise has been suggested.

In the Copenhagen male study, we have previously...
found a strong association between self-assessed long-term exposure to mixed solvents and cognitive impairment\textsuperscript{14}. In order to investigate the association between solvent exposure and hearing impairment in humans, the present study was performed.

MATERIAL AND METHODS

In 1971 a closed cohort of 5249 men aged 40–59 years employed in 14 private or public companies in Copenhagen was established in order to study cardiovascular risk factors. The cohort has been described in detail elsewhere\textsuperscript{15,16}. In 1985/1986 all survivors except 36 emigrants (\(n=4520\) men) were invited to a re-examination. Of these, 3387 (75 per cent) agreed to participate. The 3284 men (aged 53–75 years, mean 63 years) who gave valid answers to questions on exposure to noise and solvents and hearing problems were eligible for the present study. The group exposed to solvents consisted mainly of painters, mechanics, repairmen and a large group of unskilled workers who degreased metal parts. The control group consisted of repairmen, unskilled workers without exposure to solvents and white collar workers.

The study design was cross-sectional for health data and retrospective with regard to exposure. Data for the present analysis were collected in a medical interview based on a questionnaire comprising approximately 400 questions on medical history, present health, work, age 

\begin{itemize}
  \item Have you at your present or previous place of work often, ie several times a week or more, been exposed to evaporations from paints or lacquers? 
    \hspace*{1cm} \text{yes no years}
  \item Have you at your present or previous place of work often, ie several times a week or more, been exposed to noise that necessitates raised voices in conversation? 
    \hspace*{1cm} \text{yes no years}
  \item Have you during leisure time or military service been exposed to sudden noise, ie shooting or fireworks? 
    \hspace*{1cm} \text{yes no}
  \item Is there in your family (grandparents, parents, brothers, sisters or children) hereditary deafness or hardness of hearing? 
    \hspace*{1cm} \text{yes no}
  \item Have you at present or have you previously had long periods with middle ear infection or chronic discharge? 
    \hspace*{1cm} \text{yes no}
  \item Do you consider your hearing normal? 
    \hspace*{1cm} \text{yes no}
\end{itemize}

\begin{table}
\caption{Questions and options for answering on exposure to noise and solvents and on health problems considered relevant for analysis of hearing problems.}
\end{table}

\textit{Figures 1.} Questions and options for answering on exposure to noise and solvents and on health problems considered relevant for analysis of hearing problems.

\textit{Results}

The distribution of characteristics in the total study population and in groups with and without self-assessed hearing problems is shown in \textit{Table 1}. Age, exposure to solvents and noise at work, noise traumas and family history of hearing problems were significantly associated with reporting of hearing problems in the bivariate analysis. In multivariate analysis occupational noise exposure was the strongest predictor for hearing problems (\(P<0.0001\)). Exposure to solvents was still
Table 1. Distribution of characteristics of the total population and according to self-assessed hearing problems

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Yes</th>
<th>No</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>3284</td>
<td>1076</td>
<td>2208</td>
<td></td>
</tr>
<tr>
<td>Age (years; mean ± SD)</td>
<td>62.9 ± 5.1</td>
<td>63.5 ± 5.2</td>
<td>62.6 ± 5.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low social class (%)**</td>
<td>51.3</td>
<td>53.0</td>
<td>50.0</td>
<td>n.s.</td>
</tr>
<tr>
<td>Occupational exposure to solvents ≥ 1 year (%)</td>
<td>13.0</td>
<td>16.8</td>
<td>11.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Occupational exposure to noise ≥ 1 year (%)</td>
<td>37.0</td>
<td>52.9</td>
<td>28.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Noise traumas unrelated to work (%)</td>
<td>37.2</td>
<td>44.8</td>
<td>33.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history of hearing problems (%)</td>
<td>7.1</td>
<td>13.4</td>
<td>4.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic middle ear infection (%)</td>
<td>11.2</td>
<td>13.0</td>
<td>10.3</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

**Level of significance in Student's t or χ² tests.
**Social class is dichotomized, ie high social class = 1, 2, 3 and low social class = 4, 5.

Table 2. Rate (%) and adjusted relative risks for self-assessed hearing impairment in long- and short-term solvent-exposed men, stratified by occupational noise exposure

<table>
<thead>
<tr>
<th>Solvent exposure (years)</th>
<th>0 (RR)*</th>
<th>1–4 (RR)*</th>
<th>≥5 (RR)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unexposed to noise</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>1940</td>
<td>33</td>
<td>112</td>
</tr>
<tr>
<td>Hearing problems (%)</td>
<td>24</td>
<td>27</td>
<td>32</td>
</tr>
<tr>
<td>RR* (95% CI)</td>
<td>1</td>
<td>1.1(0.6–1.9)</td>
<td>1.4(1.1–1.9)</td>
</tr>
<tr>
<td>Exposed to noise ≥ 1 year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>917</td>
<td>52</td>
<td>230</td>
</tr>
<tr>
<td>Hearing problems (%)</td>
<td>47</td>
<td>43</td>
<td>50</td>
</tr>
<tr>
<td>RR* (95% CI)</td>
<td>1</td>
<td>0.9(0.5–1.2)</td>
<td>1.1(0.9–1.2)</td>
</tr>
</tbody>
</table>

*Mantel–Haenszel relative risk weighted across strata, adjusting for age, noise traumas, and family history of hearing problems with 95 per cent confidence intervals.

The effect of solvent exposure on self-assessed hearing impairment in men without noise exposure and in men reporting occupational exposure to noise for one year or more is shown in Table 2. The calculated relative risks were adjusted for age, noise traumas and family history of hearing impairment. In the group without exposure to noise the relative risk after exposure to solvents for five years or more was 1.4 (95 per cent CI: 1.1–1.9). Short-term solvent exposure (1–4 years) had no effect on the reporting of hearing problems, ie relative risk was 1.1 (95 per cent CI: 0.6–1.9). In men exposed to noise for more than one year the adjusted relative risk of long-term solvent exposure was reduced to 1.1 (95 per cent CI: 1.1–1.9). The interaction between solvent and noise exposure was further evaluated by calculating relative risks in groups with exposure to either solvents or noise for five years or more and in a group with the two exposures combined, using unexposed individuals as a reference group (Table 3). The effect of solvent exposure alone on hearing impairment was clearly weaker than the well-known effect of noise (RR 1.4 and 1.9). Concomitant long-term exposure to solvents and noise was associated with a relative risk of 1.8 (1.6–2.1) for hearing impairment, the same as the effect of exposure to noise alone.

Table 3. Effect on self-assessed hearing impairment from long-term exposure to noise and solvents calculated as relative risks

<table>
<thead>
<tr>
<th>Years of noise exposure</th>
<th>0 (RR)*</th>
<th>≥5 (RR)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>1.9(1.7–2.1)</td>
</tr>
<tr>
<td>≥5</td>
<td>1.4(1.1–1.9)</td>
<td>1.8(1.6–2.1)</td>
</tr>
</tbody>
</table>

*Mantel–Haenszel relative risk weighted across strata, adjusting for age, noise traumas, and family history of hearing problems with 95 per cent confidence intervals.

Table 4. The relationship between audiometric pure-tone threshold averaged over 0.5, 1, 2, 3 and 4 kHz ≥ 20 dB HL and self-assessed hearing problems

<table>
<thead>
<tr>
<th>Audiometric impairment</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing problems</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>20</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>No</td>
<td>14</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>17</td>
<td>51</td>
</tr>
</tbody>
</table>

The relationship between self-assessed hearing problems and audiometry for a subsample of 51 men is shown in Table 4. Twenty of 21 men who reported hearing problems also fulfilled the audiometric criterion for hearing impairment, ie pure tone auditory thresholds averaged over 0.5, 1, 2, 3 and 4 kHz ≥ 20 dB HL. Of 30 men reporting normal hearing 14 fulfilled the objective
DISCUSSION

Men exposed to organic solvents for five years or more had a significantly higher risk of self-assessed hearing impairment than unexposed men. The relative effect was moderate with a point estimate of 1.4. Since the frequency of hearing impairment in the unexposed sample was as high as 24 per cent, the attributable risk from solvent exposure was 9.6 per cent (8 per cent unadjusted) provided the association was causal. No increase in relative risk was found in the group with solvent exposure for less than five years.

Noise was a strong confounding factor with an isolated effect twice that of solvents. In the present study population a substantial number of men were exposed to both noise and organic solvents. In the group with exposure to both factors the effect of solvents was overshadowed by that of noise, and no indications of an additive effect from the two exposures were found (Table 3). An additive effect from exposure to solvents and noise cannot be ruled out, but it can be stated that the combination of these exposures does not seem to have greater impact on the hearing ability in the present population than exposure to noise only.

Information bias might explain the results if men with hearing problems had under-reported noise exposure or over-reported solvent exposure. The association between noise and hearing problems has been known for years and over-reporting of noise exposure is more likely for a person with hearing problems than the opposite. A bias in this direction would lead to under-estimation of the relative risk, ie the true relative risk would be higher than that estimated. A better recall of solvent exposure in men with hearing problems than in men without should not be expected since the association between hearing problems and solvent exposure at the time of data collection in 1985/1986 was an issue discussed among professionals only.

Information bias resulting in non-differential misclassification of exposure and effect is more likely since the applied measures of exposure and effect are relatively imprecise. Such a bias would result in weaker relative risk estimates.

The response rate to the examination was 75 per cent of the invited men, lowest in the low social groups. Only if the association between solvent exposure and hearing problems in non-responders was different from that of participants, would the results be biased due to selection. Since solvent exposure is associated with low social group the exposure may be more frequent in non-responders than in responders. If non-response was also associated with better health, including better hearing, a true bias might be present. However, such a bias would hardly be strong compared to bias in the opposite direction from over-estimation of noise exposure and from non-differential misclassification of solvent exposure and hearing capability and it is unlikely that this may explain the effect.

A precise audiological characterization of the effect cannot be made in the present study since self-assessment of hearing problems does not permit this. However, the results of pure tone audiometry in a subsample of 51 men show that those who reported hearing problems also fulfilled an objective criterion for hearing impairment. The results are therefore in agreement with a damaging effect on the cochlea, including the frequencies most important for discrimination of speech in quiet and noise (2, 3 and 4 kHz).

The validity of the interview method used for data collection was further supported by a strong correlation between noise exposure and hearing problems. The previous finding of a dose-dependent association between solvent exposure and self-reported cognitive problems in the same study population also supports the validity of the interview method used in this study.

Based on this study it can be concluded that occupational exposure to solvents seems to have a damaging effect on hearing ability. The estimated relative risk was moderate but since the disease frequency in unexposed men was high, the attributable risk from solvent exposure was substantial. If the association between organic solvent exposure and hearing impairment is causal this considerable attributable risk is of both clinical and preventive importance.

ACKNOWLEDGEMENTS

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REFERENCES