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GENOTOXIC EFFECTS IN WORKERS EXPOSED TO FUMES OF BITUMEN. COMPARISON WITH AMBIENT AND BIOLOGICAL MONITORING.

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INTRODUCTION

BACKGROUND

- Bitumen is a complex mixture of hydrocarbons consisting of both aliphatic and aromatic compounds, e.g. polycyclic aromatic hydrocarbons (PAH).
- There is inadequate evidence of carcinogenicity of bitumen in humans. Previous studies cannot be interpreted due to major qualitative or quantitative limitations.
- Overall, bitumen is labelled as „high priority substance“ for future evaluation by the International Agency for Research on Cancer.

OBJECTIVE

- To determine genotoxic properties of exposure to fumes of bitumen in humans.
- To generate dose-response relationships which can help to establish health-based threshold limit values for exposed workers.

METHODS

STUDY DESIGN

- Cross-sectional and cross-shift study design.

STUDY SUBJECTS

- 202 bitumen exposed-mastic asphalt workers and 55 construction workers without exposure to bitumen were examined (Table 1).

RESULTS

The urinary concentrations of 1-OHP and OHPH of exposed and non-exposed workers were similar before shift (P = 0.68, and P = 0.21, respectively) but different after shift (P = 0.003, and P = 0.002, respectively, Fig. 1). Concentrations of fumes of bitumen were moderately associated with 1-OHP and OHPhe after work shift (r = 0.25, P < 0.001 and r = 0.36, P < 0.001, respectively, Table 1). Significantly more 8-oxo-dGuo adducts and DNA strand breaks were found in bitumen-exposed workers pre- and post-shift compared with the reference group (Fig. 1). Significantly increased 8-oxo-dGuo adduct levels were observed post shift in both groups (P < 0.0001; Fig. 1). Paradoxically, decreased DNA strand break frequencies were observed after shift in both groups (P < 0.05; Fig. 1). No dose-dependent association was observed between exposure to fumes of bitumen and genotoxic effects (Table 1). However, post-shift values in DNA strand break frequency were associated with 1-OHP (r = 0.19, P = 0.01; Table 2).

Table 2: Spearman rank correlations between exposure to fumes of bitumen, urinary metabolites, 8-oxo-dGuo and Olive tail moment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Independent variable</th>
<th>Pre shift</th>
<th>Post shift</th>
<th>Shift difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-OHP (ng/L)</td>
<td></td>
<td>1.00</td>
<td>0.99</td>
<td>0.01</td>
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<tr>
<td>OHPhe (ng/L)</td>
<td></td>
<td>0.99</td>
<td>0.99</td>
<td>0.00</td>
</tr>
<tr>
<td>8-oxo-dGuo</td>
<td></td>
<td>0.99</td>
<td>0.99</td>
<td>0.00</td>
</tr>
<tr>
<td>Olive tail moment (median)</td>
<td></td>
<td>0.99</td>
<td>0.99</td>
<td>0.00</td>
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</tbody>
</table>

Fig. 1: Biomarker levels before and after shift presented as adjusted geometric means and 95% confidence intervals.

CONCLUSIONS

- Exposure to fumes of bitumen results in excretion of 1-OHP and five isomers of OHPH in urine after the shift.
- The excetration of urine metabolites was dependent on bitumen fume concentrations. Therefore, 1-OHP and sum of OHPH are suitable biomarkers to assess exposure to fumes of bitumen.
- Exposed workers had higher levels of oxidative DNA damage (8-oxo-dGuo) and higher frequencies of DNA strand breaks in both pre-and postshift blood samples compared to non-exposed individuals. Consequently, these workers showed increased biomarkers of genotoxicity.
- Increases in oxidative DNA damage during the shift were of statistical significance but did not depend on external exposure. Therefore, 8-oxo-dGuo is capable to assess oxidative DNA damage but is not specific to exposure to fumes of bitumen.
- Decreases of DNA strand breaks (significant) were observed after shift in both study groups. A good correlation was found between DNA strand break frequencies and 1-OHP concentrations after shift.
- Due to only weak association between 1-OHP and DNA strand breaks the reasons for increased DNA damage in workers exposed to fumes of bitumen remains unclear.

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