URINARY PROFILES OF MONOHYDROXYLATED METABOLITES OF POLYCYCLIC AROMATIC HYDROCARBONS IN DIFFERENT INDUSTRIAL ACTIVITIES

Catherine Nisse,
University Department of Occupational Health, Lille, France
Nadège Lepage, Ariane Leroyer, Michael Hawsan, Patrice Simon, Anne Maitre, Franck Broly, Jean-Paul Bonte, Michel Lhermite

30th International Congress on Occupational Health, Cancun, March 18-23, 2012

MOTIVATIONS AND OBJECTIVES

- PAHs ubiquitous in the environment
- Present in numerous workplaces
- Importance of characterization of exposure for prevention
- Biomonitoring is complementary to monitoring of ambient air
- 1-OH-pyrene, is the metabolite the most used for routinely estimation of internal exposure to PAH,
- But Pyrene is not a carcinogen (underestimation of carcinogenic risk?),
- Other biomarkers have been proposed for biomonitoring

Aim of the study:

- To evaluate the current levels of exposure to PAHs in different industrial activities, using air sampling and simultaneous analysis of several PAHs monohydroxy metabolites in urines
- To compare the profiles of exposure
- To evaluate the influence of individual factors (smoking, genetic polymorphism) on metabolites levels

METHOD

- Cross sectional study
- Study population: 125 male workers
  - aged: 21-57, average: 41
  - 45% of smokers
- Industrial sectors and Activities
  - Coke production (n=45)
  - Aluminium production (n=20)
  - Glass production (n=15)
  - Landscape service activities (two stroke engine utilisation) (n=15)
  - Metal machining industry (mineral oil exposure) (n=30)

RESULTS

EXTERNAL DOSE ASSESSMENT: AIRBORNE PERSONAL SAMPLING

- The highest median airborne level of total PAH → coke production
- The proportion of particulate PAH depends on the sector of activity

EXTERNAL EXPOSURE ASSESSMENT: PROFILE OF 16 EPA-PAH IN DIFFERENT INDUSTRIAL ACTIVITIES

- Very different profiles of PAH
- Gaseous PAH always majoritary: naphtalene, acenaphtene, fluorene

EXPOSURE ASSESSMENT

- External PAH exposure: personal air sampling during the shift: 16 EPA-PAHs (vapours and particulate bound PAHs) collected on biphasic system (filters and XAD-2 sorbent)

- Internal PAH exposure: Urinary spot samples collected at the end of shift (ES) and 16 hours later (ES+16). Monohydroxymetabolites, analysed by LC-MS/MS and HPLC-Fluorescence detection: 2-3,8,1-4,9-hydroxyphenanthrenes (1-OH-phen), 1-hydroxyphenyrene (1-OH-pyr), 3-hydroxybenzo[a]pyrene (3-OH-B(a)P), 1,2-hydroxynaphthalenes (2-OH-naph), 2-hydroxyfluorene (2-OH-fluo), 3-hydroxyfluoranthenes (3-OH-flua), 1,2-hydroxybenzo[a]anthracenes (1,2-OH-B(a)A), 3,6-hydroxychrysenes (3,6-OHchry)

Evaluation of individual factors

- Genetic polymorphism in the genes coding for enzymes involved in the metabolism of PAHs: GSTM1, GSTT1, CYP1A1, EPHX1A, EPHX1T
- Self administered questionnaire (individual protections, smoking habits, food ...)

METHOD
Very different profiles of PAH

Median urinary concentrations are higher at the end of shift, except for 3 OHBaP which is higher at the beginning of the shift.

For all metabolites, the highest median level is observed in coke production workers, followed by aluminium production workers.

In coherence with airborne level, ΣNaph is high in landscape gardeners.

For particulate PAH the highest levels are present in coke production: example for BaP.
### Variation Factors of Urinary OH-PAH Excretion

Multivariate analysis: only factors with significant influence on metabolites excretion are presented (multiplicative factor).

<table>
<thead>
<tr>
<th>Smoking (previous 8 h)</th>
<th>1OHPyr</th>
<th>3OHBaP</th>
<th>2Naph</th>
<th>2OHFluo</th>
<th>2OHPhen</th>
<th>3OHFlua</th>
</tr>
</thead>
<tbody>
<tr>
<td>X 6.23</td>
<td>X 2.17</td>
<td>X 17.00</td>
<td>X 7.94</td>
<td>X 5.22</td>
<td>X 8.81</td>
<td></td>
</tr>
<tr>
<td>Corresponding airborne PAH level</td>
<td>X 7.85</td>
<td>X 4.98</td>
<td>X 3.70</td>
<td>X 8.79</td>
<td>X 5.79</td>
<td>X 1.54</td>
</tr>
<tr>
<td>Grilled/smoked food (previous 12 h)</td>
<td>X 3.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contact with oils</td>
<td>X 2.84</td>
<td>X 1.77</td>
<td>X 3.55</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cutaneous exposure</td>
<td>X 2.80</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No gloves protection</td>
<td>X 8.79</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intense Physical activity</td>
<td>X 4.97</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No significant impact of: genetic polymorphism, use of protective mask.

### Correlations Between OH-PAH Metabolites

- For each metabolite, the best correlation is always observed with 1-OHPyr.
- Good correlation between 1-OHPyr, 3-OH BaP and OH-Phen.
- Worst correlation between naphthols, 3OH-Flua and the other metabolites.

### Conclusion

- Levels and Profiles of PAH and their metabolites are different in various industrial activities.
- Metabolites with 2 and 3 cycles are more often detected (naphthols, OH-Phen, 1OH-Pyr, 2OH-Fluo, 3OH-Flua).
- Influence of smoking even at occupational exposure level:
  - Best parameter is the number of cigarettes smoked during the 8 previous hours.
  - Best time for urinary spot sampling: end of shift for all metabolites except for 3OH BaP.
- Metabolites best correlated together and to atmospheric concentrations.

### Acknowledgements

- The Occupational Physicians and the participants of the different companies.
- The Occupational and Environmental Toxicology Laboratory, GRENOBLE.
- The National Institute of Research and Security, VANDOEUVRE, France.
- The University Center of Measurements and Analyses, Université of Lille 2, LILLE, France.

For Grants from:
- French Agency for Food, Environment and Occupational health and safety, ANSES, France.
- Nord Pas de Calais Region, France.