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Urinary metabolites of polycyclic aromatic hydrocarbons in Saudi Arabian schoolchildren in relation to sources of exposure

Mansour A. Alghamdi [a], Mohammed S. Alam [b], Christopher Stark [b], Nuredin Mohammed [c], Roy M. Harrison [a,b,*,1], Magdy Shamy [a], Mamdouh I. Khoder [a,1], Ibrahim I. Shabbaj [a], Thomas Göen [d]

[a] Department of Environmental Sciences, Faculty of Meteorology Environment and Arid Land Agriculture, King Abdulaziz University, Jeddah, Saudi Arabia
[b] Division of Environmental Health and Risk Management School of Geography, Earth & Environmental Sciences University of Birmingham, Edgbaston, Birmingham B15 2TT, United Kingdom
[c] Institute of Occupational and Environmental Medicine University of Birmingham, Edgbaston, Birmingham B15 2TT, United Kingdom
[d] Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

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ABSTRACT

Polycyclic aromatic hydrocarbons contain a number of known carcinogenic compounds, and urinary biomarkers have been widely used as a measure of exposure but quantitative relationships with exposure variables have proved elusive. This study aimed to quantify the relationship between exposures to phenanthrene and pyrene from atmospheric and dietary sources with the excretion of 1-hydroxypyrene and hydroxyphenanthrenes in urine as biomarkers of exposure. The study population consisted of 204 male schoolchildren attending three schools in different parts of Jeddah, Saudi Arabia who provided urine samples on each of three consecutive days. Outdoor air measurements of polycyclic aromatic hydrocarbons were made at the schools and the children provided information on diet, exposure to environmental tobacco smoke and incense, and various lifestyle factors through a questionnaire. Mixed models with random effects for subjects nested within site were fitted in order to examine the relationship between exposure variables and urinary PAH metabolites. A unit increase (1 ng m^{-3}) in ambient pyrene (particulate plus gaseous phase) was associated with a 3.5% (95% CI: 1.01%, 5.13%) increase in urinary 1-hydroxypyrene concentration. A unit increase in ambient phenanthrene was associated with a 1.01% (95% CI: 0.03%, 2.02%) increase in total hydroxyphenanthrene concentrations. Consumption of chargrilled food increased the 1-hydroxypyrene and hydroxyphenanthrene concentrations by 24% (95% CI: 11%, 37%) and 17% (95% CI: 8%, 26%) respectively. We did not find evidence of association for environmental tobacco smoke exposure or incense burning. It is concluded that both respiratory exposure and consumption of chargrilled food are considerable sources of PAH exposure in this population as reflected by concentrations of urinary biomarkers.

1. Introduction

A number of polycyclic aromatic hydrocarbons (PAH) are known genotoxic carcinogens. The compounds arise mainly from combustion sources and evaporation of petroleum-derived fuels. They are hence widespread in the environment, and exposure occurs by inhalation (Mari et al., 2010), ingestion (Martorell et al., 2012; Perello et al., 2009), and potentially by dermal absorption. PAH occur in the environment as a complex mixture of individual compounds, referred to as congeners. Exposure to polluted air through inhalation poses a risk of lung cancer (Hamra et al., 2014), and PAH exposure appears to make an appreciable contribution to that risk (Harrison et al., 2004). The European Union has set a target value of 1 ng m^{-3} of benzo(a)pyrene (B(a)P), taken as representative of the PAH mixture,

* Corresponding author at: Division of Environmental Health and Risk Management School of Geography, Earth and Environmental Sciences University of Birmingham, Edgbaston, Birmingham B15 2TT, United Kingdom. Fax: +44 121 414 3709.
E-mail addresses: mans99@gmail.com (M.A. Alghamdi), m.s.alam@bham.ac.uk (M.S. Alam), c.p.stark@bham.ac.uk (C. Stark), NIM007@student.bham.ac.uk (N. Mohammed), r.m.harrison@bham.ac.uk (R.M. Harrison), mshamy@kau.edu.sa (M. Shamy), khoder_55@yahoo.com (M.I. Khoder), ishabbaj@yahoo.com (I.I. Shabbaj), thomas.goeen@ipasum.med.uni-erlangen.de (T. Göen).
[1] Also at: Center of Excellence in Environmental Studies, King Abdulaziz University, Jeddah 21589, Saudi Arabia.

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and in the United Kingdom, an air quality objective of 0.25 ng m^{-3} of B(a)P has been adopted. PAH are also carcinogenic in animal models as a result of ingestion in the diet or drinking water. Consequently the European Food Safety Authority has made a detailed assessment of human exposure from dietary sources (EFSA, 2008). In addition to the cancer risk, PAH exposure has been linked to the onset of diabetes mellitus (Yang et al. 2014; Alshaarawy, et al. 2014), metabolic syndrome (Brocato et al. 2014; Hu et al. 2015), and cardiovascular conditions (Xu et al. 2010; Feng et al. 2014). Since all exposure sources can contribute to the body burden of PAH, quantitative evaluation of exposure pathways is important if health risk is to be minimised.

While exposure can be evaluated by separate chemical analysis of PAH in exposure media such as food, water and air, such monitoring is highly resource intensive. The use of urinary biomarkers of exposure is a more practicable means of exposure estimation, although without additional information, it cannot quantify the contribution of different exposure pathways. PAHs are oxidised in the body by P450 enzymes ultimately to form hydroxylated metabolites. Of these, urinary 1-hydroxypyrene (1-OHPyr) has been used most extensively as an exposure biomarker in both occupational cohorts and the general population. It has the advantages of strong correlation with metabolites of other PAH (Li et al. 2008) and of having a relatively short biological half life, and hence being representative of recent exposure. Half-lives from inhalation exposure are reported as between 6 and 35 h (Brzeznicki et al. 1997; Jongeneelen et al. 1990), 4.4 h and 12 h after oral ingestion (Buckley and Lioy, 1992; Viau et al. 1995) and 3.5–5.1 h for the first phase (Li et al., 2012).

Hansen et al. (2008) have reviewed 132 studies addressing the use of 1-hydroxypyrene as a biomarker of both occupational and environmental exposure to PAH. Of these, 25 studies addressed environmental exposure, and only nine included children. Studies of children not included in that review include those of Vyskocil et al. (2000) and Freire et al. (2009). It is notable that rather few environmental studies have made measurements of exposure, either through chemical analysis of air or diet, or by questionnaire in relation to diet. Several have used a cross-sectional design in which subjects from areas deemed to be more polluted are compared to groups from less polluted areas (Vyskocil et al. 2000; Wilhelm et al. 2007; Lee et al. 2007; Hansen et al. 2005). This can provide useful insights into relative exposures, but does not quantify the contribution of different pathways to intake. Some studies of adults have used benzo(a)pyrene or a sum of PAH in air concentrations as an indication of airborne PAH exposure (Fiala et al. 2001; Merlo et al. 1998), but since the relative amounts of PAH congeners in mixtures vary from place-to-place, this does not provide direct information on the relationship between exposure to pyrene and urinary 1-hydroxypyrene concentrations. Very few studies have used measurements of pyrene in exposure media (Vyskocil et al. 2000; Cavanagh et al. 2007), and not all have fully recognised the importance of measuring both the vapour and particulate components of airborne pyrene (Suzuki and Yoshinaga, 2007), as unlike benzo(a)pyrene, it is the vapour phase component which is typically dominant. Other studies have used nitrogen dioxide or NO_x as a marker of road traffic exposure (Freire et al. 2009; Kanoh et al. 1993), but this is not necessarily reflective of total atmospheric PAH exposure, as PAH have other important sources (Jang et al., 2013; Alghamdi et al., 2015).

In this study, the PAH exposure of children of median age 11 years attending three schools in Jeddah, Saudi Arabia has been evaluated through analysis of hydroxylated metabolites of phenanthrene and pyrene in urine. Urinary metabolite concentrations have been related to sources of exposure through a questionnaire on diet, passive smoking and other lifestyle factors, and chemical analysis of airborne concentrations.

2. Materials and methods

2.1. Data collection

A total of 204 school boys in Jeddah city were recruited for the study. A questionnaire was used to obtain data on baseline characteristics including age, gender, passive smoking, socio-economic indicators, housing conditions and current health status. The questionnaire was validated through trials on adult subjects and children with additional questions to gauge comprehension. The children were enrolled in three different schools located in differing environments; the first school was located near to an oil refinery (Site A), the second to a major highway (Site B) and the last to the Red Sea (Site C). Daily ambient atmospheric PAH concentrations were measured in both particle-associated and vapour phases for each site on consecutive days. A summary of covariates appears in Table 1. Full details of the sampling and analytical methods, and measured concentrations have been reported elsewhere (Alghamdi et al. 2015). For sites A and B air sampling data for 23, 24 and 25 February 2013 was used in conjunction with the corresponding urine samples collected on 24, 25 and 26 February 2013 respectively. For site C the air and urine samples used in the data analysis were collected on 20, 21 and 22 April and 21, 22 and 23 April 2013 respectively. The questionnaire was updated on each urine sampling occasion by asking additional information about the previous day's dietary and cooking patterns as well as use of incense. Urine samples were provided from the first morning micturition event, and were rapidly frozen and stored at –80 °C before being transported in dry ice to the analytical laboratory. They were analysed for hydroxyphenanthrenes and 1-hydroxypyrene by HPLC according to a recommended method of the German Research Foundation (DFG, 1999) as described by Hemat et al. (2012). For values which fell below the limit of detection, a value of LOD$\div\sqrt{2}$ was adopted, following the recommendation of Hornung and Reed (1990). Creatinine in urine was determined photometrically as picrate according to the Jaffé method (Taussky, 1954). A total of five biomarkers, both raw and after creatinine correction, were available. These included 1-OH-phenanthrene, sum of 2-/9-OH-phenanthrene, 3-OH-phenanthrene, 4-OH-phenanthrene and 1-OH-pyrene. From the 204 students enrolled, 170 presented three urine samples (58 from School A; 66 from School B and 46 from School C). The statistical analysis was based upon these 510 (i.e. 170 $\times$ 3) samples.

Table 1
Summary[a] of covariates by site.

Variable		Site		
		A (Refinery)	B (Highway)	C (Red sea)
Consumed chargrilled food	*No*	102 (61.08)	117 (62.57)	87 (65.91)
	Yes	65 (38.92)	70 (37.43)	45 (34.09)
Consumed fried food	*No*	60 (35.71)	33 (17.19)	54 (40.6)
	Yes	108 (64.29)	159 (82.81)	79 (59.4)
Use of incense	*No*	89 (53.29)	99 (52.11)	98 (74.81)
	Yes	78 (46.71)	91 (47.89)	33 (25.19)
Smokers in the house	*None*	118 (64.13)	119 (60.41)	103 (66.88)
	1	48 (26.09)	66 (33.5)	38 (24.68)
	2	9 (4.89)	9 (4.57)	10 (6.49)
	≥ 3	9 (4.89)	3 (1.52)	3 (1.95)
Age, Median (IQR)		11 (2)	11 (1)	11 (2)
BMI, Median (IQR)		16.64 (6.16)	16.64 (4.47)	19.29 (6.9)

[a] *N* (%)