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A Pilot Study on Using Urinary 1-Hydroxypyrene Biomarker for Exposure to PAHs in Beijing

Wenjie Zhang · Dongqun Xu · Guoshun Zhuang · Changming Ding · Guifang Wang · Junrui Chang · Gaiying Ren

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Abstract To study whether the urinary 1-hydroxypyrene (1-OHP) could be the biomarker of atmospheric PAHs, a small-scale pilot study was carried out on the relation of 1-OHP vs PAHs with the traffic policemen in Beijing of smokers and nonsmokers to be subgroups in both the exposure and control groups. Both the PAHs and 1-OHP were analyzed with high performance liquid chromatography (HPLC). The ambient concentrations of PAHs were different at the different sites (the average sum of PAHs (TPAH) were 12.36, 16.27, 18.37 ng/m^3 at the suburban residential, police station and high traffic area, respectively.), but considerably lower than the personal-exposure concentrations (the average TPAH were 65.84 and 47.28 ng/m^3 for patrol cars and inspection station, respectively). Pyrene was correlated well with BaP and the summed PAHs (TPAH), with the correlation coefficients (R) of 0.79, 0.87 for ambient level and 0.92, 0.96 for personal exposure, respectively. The average of 1-hydroxypyrene of smokers and nonsmokers were 0.39, 0.15 μmol/mol creatinine in control group and 0.57, 0.33 μmol/mol creatinine in exposure group, respectively. The better correlation of pyrene to BaP and TPAH especially for personal exposure samples indicated that the probability of urinary 1-hydroxypyrene, the metabolite of pyrene, to be the biomarker of total PAH. Nonsmokers in the exposure and control groups had indistinguishable levels of 1-OHP, presumably because the ambient levels of pyrene were so similar (the average were 3.25, 3.20 ng/m^3 at the police station and high traffic area, respectively.). Smokers in the control group had significantly higher 1-OHP than that of the nonsmokers, but showed indistinguishable differences in the exposure group. These results suggested that urinary 1-OHP could be a biomarker of PAHs only when the level of PAHs was at a relatively higher level. Smoking as an important influencing factor need to be controlled carefully.

Keywords Personal exposure · PAH · BaP · Pyrene · 1-OHP

W. Zhang · G. Zhuang
Center for Atmospheric Environmental Study,
Chemistry Department, Beijing Normal University,
Beijing 100875, China

W. Zhang · D. Xu (✉) · C. Ding · G. Wang · J. Chang · G. Ren
Institute for Environmental Health and Related Products
Safety, China CDC, Beijing 100021, China
e-mail: dongqunxu@yahoo.com.cn

G. Zhuang
Center for Atmospheric Chemistry Study,
Department of Environmental Science & Engineering
Fudan University, Shanghai 200433, China

1 Introduction

Urinary 1-hydroxypyrene (1-OHP, a main metabolite of PAH pyrene) has frequently been used as a biomarker for human exposure to PAHs, especially for workers at high concentrations of PAHs in those places, such as coke plants, oil refineries, tar plants,

aluminum plants, asphalting, coal-burning (Bentsen, Halgard, Notø, Daae, & Øvrebø, 1998; Boogaard & Van Sittert, 1995; Jongeneelen et al., 1990; Pan et al., 1998; Van Schooten, Jongenleen, & Hillebrand, 1995; Zhao, Quan, & Tian, 1990). Because the elevated levels of 1-OHP in such environments correlate well with their high PAHs, it has been suggested that urinary 1-OHP could be the best biomarker for high PAHs (Dor, Dab, Empereur-Bissonnet, & Zmirou, 1999).

The response of 1-OHP to lower levels of PAHs, such as in ambient atmospheres, is less clear, however. The level of urinary 1-OHP of the urban residents of Poland and the policemen in Bangkok differed significantly between the high-polluted and the low-polluted areas (Motykiewicz et al., 1998; Mathuros et al., 2002, respectively), but it did not for the residents of Copenhagen or the policemen in Genoa (Merlo et al., 1998; Sorensen et al., 2003). Given that the first two cities were more polluted than the second two, 1-OHP might be an effective biomarker only for higher levels of PAHs, perhaps the level >3 ng/m^3 for BaP or the level >30 ng/m^3 for the sum of eight PAHs, as they were suggested by Perico et al. (2001).

Urinary 1-OHP is also affected by the factors, such as diet and smoking (IARC, 1986). Consequently, these two factors should be considered when evaluating the correlation of 1-OHP vs atmospheric PAHs. For example, participants should be asked not to eat barbecued meat or fish for three days before giving urine samples (Perico, Bavazzano, Gottardi, Lanciotti, & Boddi, 2001), and data for smokers and non-smokers should be considered individually.

Beijing might be an appropriate place to further study the relations between 1-OHP and exposure to atmospheric PAHs, given that it is a city with a typical mix of the coal burning and the vehicular exhausts. Here we report a small-scale pilot study on the relation of 1-OHP vs PAHs with the traffic policemen of smokers and nonsmokers to be subgroups in both the exposed and control groups. The results would provide valuable guidance for future studies.

2 Methods

2.1 Sampling

Ambient $PM_{2.5}$ samples were collected at three sites in Beijing: a suburban residential site (Xin Town, Fangshan District), a police station (Liangxiang Town, Fangshan District), and a site in a high-traffic area (vehicle exhaust inspection station on the road to the "South Gate" of Beijing, mainly for checking heavy-duty diesels). The samplers were placed on the roof of a residential building (12 m high) in the center of Fangshan District, about 30 m from the street, on a platform 1.5 m high in the yard of the police-station, 10 m from the no. 107 National Highway, and on a platform 1.5 m high in the inspection-station, alongside the no. 107 National Highway. Personal-exposure samples were collected with policemen working inside the vehicle-monitoring station and with policemen riding in patrol cars coming from the main police station in Fangshan. The ambient and exposure samples were collected from Oct. 31 to Nov. 3, 2004, except for the ambient samples at the suburban residential site, which were taken from Oct. 10 to Nov. 3, 2004. The ambient samples were taken with medium-volume samplers (Beijing Geological Instrument-Dickel; model: TSP/PM_{10}/$PM_{2.5}$-2; flow rate: 77.6 l/min) on 90-mm glass-fiber filters (Beijing Geological Instrument-Dickel). The personal-exposure samples were collected with a portable multi-pollutant sampler (Universal Sample Pump, Catalog no. 224-PCXR8, SKC, flow rate 1.8 l/min) on 37-mm glass-fiber filters carried by the policemen. All filters were preconditioned at 550°C in a muffle oven (model SX2-4-10, Tianjin Scientific Instrument), and weighed before and after sampling on an analytical balance (Mettler AT261 Delta Range, reading precision 10 μg), after being stabilized in a desiccator for more than 24 h at constant temperature (20°C±1°C) and humidity (40±1%). All procedures were strictly quality-controlled to avoid contaminating the samples.

The population for the personal exposure study was 51 traffic policemen in the exposure group (50 male and 1 female), among which 48 indoor on-duty policemen in the control group (47 male and 1 female). Each of the 99 officers provided a urine sample on Nov. 1 and Nov. 2, 2004. Diet was controlled during the experimental period following the suggestion of Perico et al. (2001). The samples were stored in polyethylene bottles at 0°C and away from light before being analyzed.

2.2 Chemical analysis

PAHs PAHs were extracted and analyzed with HPLC (Water® 2690 Separations Module, Water® 474

Scanning Fluorescence Detector and Symmetry® C_{18} 3.9 mm×150 mm, Φ5 μm column) with the method of the US EPA (US EPA, 1998) and nine PAHs were measured. {Anthracene (Ant), Fluoranthene (FluA), Pyrene (Pyr), Benzo[*a*]anthracene (BaA), Benzo[*b*] fluoranthene (BbF), Benzo[*k*]fluoranthracene (BkF), Benzo[*a*]pyrene (BaP), Dibenzo[*a,h*]anthracene (DBA), and Benzo[*ghi*]perylene (BghiP)}.

Urinary 1-OHP Urinary 1-OHP was measured with HPLC (Water® 2690 Separations Module, Water® 474 Scanning Fluorescence Detector and Symmetry® C_{18} 3.9 mm×150 mm, φ5 μm column) by using a modified method of Perico et al. (2001) and Hara et al. (Hara, Hanaoka, Yamano, & Itani, 1997). Ten-milliliter aliquots of the urinary samples and 40 μl of 100,000 β-glucuronidase (Type H-2, Sigma-Aldrich Chemie GmbH, Germany) units were added to a buffer solution at pH 5, and followed by incubation at 37±0.5°C in a water bath for 16 h overnight (free of light). 1-OHP was extracted from the urine sample with 500 mg C_{18}-type solid-phase extraction columns, which had been preconditioned with 3 ml of methanol and 3 ml of water, and eluted with 3 ml methanol. Ten microliters of the leached solution was injected into HPLC (Water® 2690 Separations Module, Water® 474 Scanning Fluorescence Detector and Symmetry® C_{18} 3.9 mm×150 mm, φ5 μm column, $\lambda_{ex}/\lambda_{em}$= 242/388 nm) at a flow rate of 0.8 ml/min, with an 80:20 mixture of methanol and water as the mobile phase. The detection limit for 1-OHP was 0.05 ng/ml.

Urinary creatinine Urinary creatinine was used to normalize the concentrations of 1-OHP. It was measured by spectrophotometry (722 Spectrophotometer, model no. 3 from Shanghai Analytical Instruments), with Jaffe's Method (WS/T97, 1996).

2.3 Statistical analysis

Time-weighted average concentrations of PAHs in the personal and ambient samples, the PAHs and 1-OHP for the total population, the smokers, and the non-smokers between the control and exposure groups were compared by using the *t* test in *SPSS10.0* and the Wilcox two sample test in *SAS 8.0*.

3 Results and Discussion

3.1 Ambient concentrations vs personal exposures

The ambient concentrations of the nine PAHs and their sum (TPAH) followed the expected pattern, being highest at the high-traffic site (seven of the nine PAHs and TPAH being highest there), intermediate at the suburban police station on the same highway, and lowest at the residential site (Table I). The concentrations of the nine PAHs and TPAH were typically 50% higher at the high traffic site than those at the low-concentration site.

The personal exposure to all of the PAHs and TPAH in the patrol cars was higher than the personal exposures in the inspection station (Table II). The high concentrations might have come from tobacco smoke in the cars. Furthermore, it was also shown in Figure 1 of the higher average value, which was due

Table I Ambient concentrations of PAHs and their sum (TPAH) at the three sites (unit: ng/m^3)

	Suburban residential				Police station				High traffic area			
	Number	Range	Mean	BaP_{eq}	*Number*	Range	Mean	BaP_{eq}	*Number*	Range	Mean	BaP_{eq}
AnT	13	0.09–0.85	0.21	0.02	5	0.17–0.58	0.29	0.03	5	0.15–0.58	0.31	0.03
FluA	13	0.09–3.62	1.47	0.001	5	0.33–4.38	1.28	0.001	5	0.31–2.08	0.86	0.001
Pyr	13	0.74–3.86	2.22	0.002	5	1.38–5.24	3.25	0.003	5	1.38–5.84	3.20	0.003
BaA	13	0.42–3.69	2.03	0.20	5	0.69–4.03	2.39	0.24	5	1.24–5.62	3.30	0.33
BbF	13	0.75–4.01	1.92	0.19	5	0.63–4.03	2.57	0.26	5	1.15–4.57	2.62	0.26
BkF	11	0.07–1.74	0.59	0.06	4	0.003–1.02	0.46	0.05	5	0.01–2.33	0.64	0.06
BaP	13	0.15–2.54	1.08	1.08	5	0.45–3.55	1.87	1.87	5	1.09–3.69	2.01	2.01
DbA	13	0.39–2.11	1.22	1.22	5	0.40–2.70	1.65	1.65	5	0.85–2.72	1.84	1.84
BghiP	13	0.64–2.95	1.73	0.02	5	0.87–4.12	2.60	0.03	5	1.87–6.56	3.60	0.04
TPAH	13	3.68–21.6	12.36	2.78	5	5.44–24.8	16.27	4.11	5	9.26–28.9	18.37	4.57

Table II Personal exposure of the individual PAH compound and the sum of measured PAHs (TPAH) in the patrol cars and the inspection station (unit: ng/m^3)

	Patrol cars				Inspection station			
	Number	Range	Mean	BaP_{eq}	*Number*	Range	Mean	BaP_{eq}
AnT	8	1.08–12.7	3.95	0.395	4	0.63–4.78	2.48	0.248
FluA	9	1.54–63	11.06	0.011	4	3.76–7.54	5.55	0.006
Pyr	9	4.76–39.9	14.09	0.014	4	6.56–18.2	11.19	0.011
BaA	8	2.09–47.5	10.57	1.057	4	3.62–8.69	5.95	0.595
BbF	9	2.30–32.7	7.78	0.778	4	3.65–7.96	5.77	0.577
BkF	1	ND–15.67	15.67	1.567	1	ND–1.7	1.70	0.170
BaP	9	1.01–24.6	5.40	5.398	4	2.63–5.37	3.97	3.975
DbA	8	1.66–13.4	5.03	5.035	4	2.03–6.50	4.08	4.080
BghiP	9	3.32–21.1	8.39	0.084	4	4.36–12.6	7.86	0.079
TPAH	9	17.0–270	65.84	12.225	4	28.6–71.5	47.28	9.613

to the tobacco smoking in the patrol car that day and implied why smoking contributed so much to urinary 1-OHP, especially to the exposed group.

Both sets of all of the PAHs and TPAH of personal exposures in the patrol cars and the inspection station were higher than the ambient levels as well. A *t* test in Table III confirmed that the personal exposure were significantly higher than those ambient level ($p < 0.05$), too. For example, the average personal-exposure concentrations for pyrene (14.1 ng/m^3 in the patrol cars and 11.2 ng/m^3 in the inspection station) were several times higher than the ambient concentration at the three sites (2.22–3.25 ng/m^3). For anthracene, the concentrations were 3.95 and 2.48 ng/m^3 of the personal exposures, and 0.21–0.31 ng/m^3 at the ambient sites. For TPAH, the concentrations were 66 and 47 ng/m^3 for the personal exposures and 12–18 ng/m^3 for the ambient sites. The personal exposures here were similar to that in the low-traffic area of Florence, Italy (Perico et al., 2001) and lower than in Bangkok, Thailand (Mathuros et al., 2002).

3.2 Carcinogenicity of PAHs by BaP_{eq}

PAHs have been classified as probable or possible human carcinogens, 2A and 2B, respectively, by the International Agency for Research on Cancer (1987). The carcinogenic potency of a PAH can be expressed as its BaP-equivalent concentration (BaP_{eq}), which is calculated from the toxic equivalent factor (TEF) of the PAH relative to the carcinogenic potency of BaP. TEFs can be estimated in several ways (Chu & Chen, 1984; Dor et al., 1999; Krewski, Thorslund, & Withey, 1989; Larsen & Larsen, 1998; McClure & Schoeny, 1995; Thorslund & Farrer, 1991; Tsai, Shieh, Lee, & Lai, 2001), which have been reviewed by Nisbet and LaGoy (1992). From

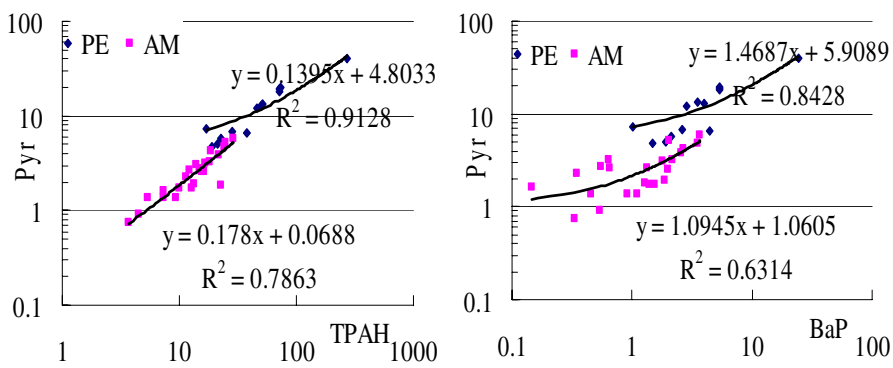

Figure 1 Correlation of pyrene with BaP and TPAH in ambient (*AM*) and personal-exposure (*PE*) samples.

Table III Independent *t* test of the ambient concentration and personal exposure in the patrol cars and the inspection station (0.05 level)

		AnT	FluA	Pyr	BaA	BbF	BkF	BaP	DbA	BghiP	tPAHs
Patrol cars	*t*	−3.57	−1.77	−3.82	−2.06	−2.2	−23.95	−2.12	−3.48	−4.09	−2.43
	p	0.00	0.09	0.00	0.05	0.04	0.00	0.05	0.00	0.00	0.02
Inspection station	*t*	−2.78	−5.19	−3.04	−2.01	−2.78	−1.01	−2.55	−2.47	−2.29	−3.16
	p	0.03	0.00	0.02	0.08	0.03	0.37	0.04	0.04	0.06	0.02

TEFs and the listings in the latter two references, the BaP equivalent concentration (BaP_{eq}) of each PAH and TPAH were calculated for the ambient sites (Table I) and the personal exposures (Table II). These results indicated that although the ambient concentration and the personal exposure of the individual BaP did not reach the national limit of 10 ng/m^3, the personal exposure to the true TPAH might have considerably exceeded it, as the sum of the personal exposure to BaP_{eq} for only nine PAHs exceeded the limit. BaP is one of the most important PAHs in the carcinogenic group. In the ambient samples BaP accounted for 40% of the total BaP_{eq} with only 10% of the total concentration (Table I). The concentrations of BaP were similar in those personal-exposure samples (Table II).

3.3 Correlation of pyrene with BaP and TPAH

To clarify whether 1-OHP can be used as a biomarker for PAHs in general, the relations of its precursor, pyrene, to TPAH and to BaP need to be addressed (the latter for purposes of toxicity). Scatter-plots of pyrene against TPAH and BaP showed that it was better related to TPAH than to BaP, and better in the personal-exposure samples than in the ambient samples. The latter effect may be because the two sets of personal-exposure samples were geographically closer than the three sets of ambient samples. On balance, these results indicated that pyrene was linked closely enough with TPAH and BaP to serve as a reasonable surrogate for them. This meant that if 1-OHP was related closely enough with atmospheric pyrene (which it turned out only partly to be), it could be a biomarker for atmospheric PAHs.

3.4 Urinary 1-OHP in the policemen

If urinary 1-OHP could serve as a bio-indicator of exposure to atmospheric PAHs, it must show statistically significant relation with the atmospheric pyrene after the effects of diet and smoking were removed. Since diet was removed by the experimental design, only smoking remained to be removed. For this purpose, the traffic policemen were divided into an exposure group (those in the patrol cars) and a control group (those working indoors). Each of these groups was divided into smokers and nonsmokers. The gender, age, health, living habits, diet, smoking, the working years of the exposure, and those control groups were considered and listed in Table IV. There was no statistically significant difference of the properties of the groups ($p>0.05$ for a *t* test).

As urine samples were taken only once, the average of 1-OHP for the subgroups was compared with other properties of interest in average, such as smoking and exposure to pyrene. A simple display of the values of 1-OHP/creatinine for the four

Table IV Information on the control group and the exposure group

		Age			Working years	
		Number	Mean	Range	Mean	Range
Control	Total	48	36.3	26–50	11.7	0.1–24
	Smokers	32	36.5	26–48	11.6	1–24
	Non-smokers	16	35.9	26–50	11.9	0.1–20
Exposure	Total	51	36.3	25–50	11.1	1–25
	Smokers	36	35.7	25–50	11.0	3–25
	Non-smokers	15	37.8	27–44	11.3	1–21

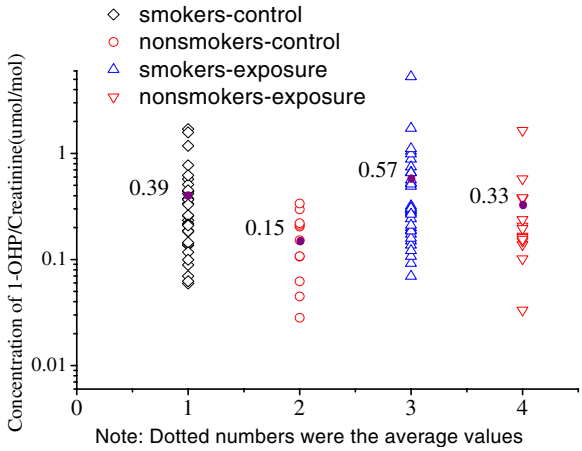

Figure 2 Urinary 1-OHP concentrations for smokers and nonsmokers in the control group and the exposure group.

subgroups was shown in Figure 2 and proved to be very informative, however. Relative to the levels previously reported (Bentsen et al., 1998; Gilbert & Viau, 1997; Hara et al., 1997; Jongeneelen et al., 1990; Motykiewicz et al., 1998; Perico et al., 2001; Tsai et al., 2004; Van Delft et al., 1997), the results reported here were higher than that of Japanese garbage collectors (Chetiyanukornkul, Toriba, Kizu, & Hayakawa, 2004), and lower than that of Thailand policemen (Mathuros et al., 2002) and other occupationally exposed workers. The 1-OHP for the nonsmokers in the control group (0.15 μmol/mol creatinine) was higher than the 0.08 μmol/mol in Quebec (Viau, Vyskocil, & Martel, 1995) and the 0.06 μmol/mol in Japan (Chetiyanukornkul et al., 2004). This value of 0.15 μmol/mol creatinine could be considered a "background level" at Beijing.

The levels of 1-OHP in the four subgroups of policemen could reveal three major issues. First, the levels for nonsmokers in both groups (exposure and control) were statistically indistinguishable (0.15 and 0.33 μmol/mol creatinine for control and exposure, respectively, $p>0.05$ for a Wilcoxon two-sample test). This suggested that the groups had been exposed to similar levels of pyrene, and the data confirmed that: (a) The personal exposures to pyrene were 11.2 and 14.1 ng/m^3 for control and exposed groups, respectively. (b) Assuming that Fangshan police station reasonably represented the patrol cars driving in Fangshan, as the ambient concentrations of pyrene were 3.20 and 3.25 ng/m^3 for the control and exposure groups. This was why the control and exposed group came out so similarly. Second, the levels of 1-OHP for smokers in the two groups were also indistinguishable (0.39 and 0.57 μmol/mol creatinine for control and exposure, respectively, $p>0.05$ for a Wilcoxon two-sample test). Interestingly, the additional levels of 1-OHP from the smokers in each group were identical (0.24 1-OHP/creatinine). This might mean that the contribution of smoking to the two groups were similar. Further, the personal exposure contributed the same amount to the 1-OHP (0.18 μmol/mol) of both the smoking and the nonsmoking groups. Third, the levels of 1-OHP for smokers were significantly higher than that for nonsmokers in the control group ($p=0.013$ for the Wilcoxon two-sample test), but not in the exposed group.

The three results together implied that when ambient PAHs were low enough, smoking could contribute equal or greater amounts of urinary 1-OHP and mask the smaller differences in contribution from different places. This was why no effect of exposure could be found in Beijing. It has been clear that smoking contributed most to the urinary 1-OHP. This could imply that urinary 1-OHP in Beijing was sensitive enough to be a biomarker of PAHs from smoking.

4 Conclusions

This pilot study of the effect of various ambient exposures to PAHs on the potential biomarker 1-OHP led to three main conclusions. First, 1-OHP might not be a good biomarker for lower differences of exposures, and did not respond detectably to the scale of differences in personal exposures to PAHs between the exposed and control group (30% or so). This means that future studies on the effects of different exposures need to build in bigger differences in exposures. Second, smokers in the control group had significantly higher 1-OHP than the nonsmokers, but showed indistinguishable differences in the exposure group. In the future, studies whose goal is to isolate the effect of differing exposures to ambient aerosol need to control the smoking factor very carefully. Third, it seemed that the numbers of samples in those areas of the similar exposures have to be significantly greater than the numbers used here (<100 samples in total), because the levels of 1-OHP in the groups and

subgroups varied by more than an order of magnitude. To make the small differences in large ranges to become significant, it is likely that several hundred samples are needed. These results suggested that urinary 1-OHP could be a biomarker of PAHs only when the level of PAHs was at a relatively higher level. Smoking as an important influencing factor need to be controlled carefully.

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