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1-Hydroxypyrene in children urine after exposure to benzo(a)pyrene at school

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Abstract— Benzo(a)pyrene (BaP) is classified as a carcinogenic compound on humans and animals. The presence of metabolite 1-hydroxypyrene (1-OHP) in the urine is commonly used as biomarker to BaP. We measured the BaP concentration from schools using sorbent tubes with charcoal filter and analyze it using High Performance Liquid Chromatography (HPLC) with a fluorescence detector. To evaluate and measure the exposure risk of benzo(a)pyrene to primary school children in West Jakarta, Indonesia. We used a cross-sectional study design with two different methods of Public Health Assessment, i.e., environmental health risk assessment and environmental health epidemiology. We used 84 students as our sample, which were determined using probability proportional to size; and selected using the purposive sampling method. The risk of carcinogenic exposure of BaP in three study locations was considered under the safety limit (i.e., real-time RQ < 1). The mean BaP concentration was the highest at school number 2 with a value of 0.0092 mg/m3. The mean 1-OHP concentration extracted from urine samples was also the highest at school number 2 with the majority being fourth-grade students. The BaP exposure inside the classroom was positively related to the 1-OHP concentration in the students' urine (p=0.001).

Keywords— Benzo(a)pyrene, indoor, 1-hydroxypirene, primary school students.

1. Introduction

Indonesia is one of the countries with the highest demography, with an annual population growth rate of 1.36%. The increase in a country's population growth is followed by the increase in economic growth, industry, and demand in transportation. Based on the data from the Indonesian Police Traffic Corps (Korlantas Polri) which was released by the Statistics Indonesia (Central Bureau of Statistics, 2017), the number of motor vehicle in Indonesia has increased 1-3% from 2015-2017, while the year-on-year growth production in manufacturing industry (medium to big scale) had increased 5.01% (Central Bureau of Statistics, 2018).

As the capital city of Indonesia, Jakarta has a high population density which impacted its air quality. The measurements of Air Pollution Standard Index (ISPU) in DKI Jakarta province showed that in year 2018 there was 200 days with poor air quality; with West Jakarta being the most vulnerable area (i.e., 160 days with poor air quality and 39 days with really poor air quality) (Government of Jakarta, 2019). The increase in the number of motor vehicle and industrial activity has resulted in the increase of pollutants' emissions which are toxic for humans, plants, and animals [4] and failure to control or treat the polluted air can cause harmful health symptoms in human [5].

Compared with adults, children are a part of the human population which is being more vulnerable to diseases caused by environmental air pollutant exposure. This due to several reasons, i.e., their immature immune system; higher food intake in their growing period; underdeveloped systems: lung, reproductive, nerve, and digestive; and a high inhaled breath per unit mass which allowed higher concentration of air pollutants to enter their body [6]. The World Health Organization has released the results of their study which mentioned that air pollution has caused death of one out of four children. Both ambient air pollution (AAP) and household air pollution (HAP) has been the risk factors of respiratory tract infection which caused death to 543,000 children [8].

School is the second most important environment for children after house since children spend almost a third of their time doing school activities. The duration of a school day in Indonesian primary and secondary school is 8 hours per day or 40 hours per 5 days a week, not to include the extracurricular activities (Ministry of Education and Culture, 2017). This means that children may experience more than 8 hours per day of any air pollutant exposure during school time and through their commuting to school. Therefore, the air quality in school is considered as one of the most important factors affecting the children's health [10].

Polycyclic Aromatic Hydrocarbon (PAH) is one of the most commonly found air pollutant sources in the environment, which originated from vehicle fuel (Ferrari et al, 2002). The percentage of PAH in the air is higher in the developing countries (6.22%) compared with the developed countries (5.73%) since their differences in energy consumptions and technological advances (Shen et al, 2013). There were more than 100 compounds which categorized as PAH and 17 being identified as the main cause of health symptoms in human [14]. Benzo(a)pyrene (BaP) is one of the members of PAH group which considered as probably carcinogenic compounds in humans and animals [15, 16].

Epidemiological studies showed that BaP has been linked to several health symptoms, i.e., lung and bladder cancer [17], asthma, eyes and skin irritations [18,19,20], DNA and chromosome damage in embryonic liver, bronchial epithelium, and peripheral lymphocytes [21]. After entering the human body and being biotransformed, BaP is then being excreted as a hydroxylated form into urine or feces [22]. The metabolite 1-hydroxypirene (1-OHP) is commonly used as a biomarker exposure of BaP compound (Jongeneelen et al, 1994; Jacob and Seidel, 2002; Gunier et al, 2006; Guo et al, 2013) due to its good dosage-response relation [27].

Research from a school surrounded by a busy traffic area in Bangkok, Thailand showed a high concentration of BaP (4.13 ± 0.21 ng/m3), which was 3.5 times higher than the BaP concentration in schools surrounded by medium traffic activity in Chonburi province, Thailand (1,18 ± 0,09 ng/m3) (Tuntawiroon et al, 2007). Another research from the school area in Bandung, Indonesia showed the BaP concentration from 10 sampling points of less than 0.02 mg/m3 (Kurnia et al, 2017). Research on schoolchildren aged 6-10 years from school area nearby an industrial area of Mexico showed that 59% of children had a higher 1-OHP concentration (0.37 µmol/mol creatinine) compared with adults (0.024 µmol/mol kreatinin) (Guerra et al, 2012). Similar result was also shown by a study in China with urinary 1-OHP concentration in children aged 6-11 years being 30% higher than the adults in similar conditions (Fan et al, 2012). This proved that children were being more vulnerable to BaP exposure than adults and has a higher risk potential. Therefore, a study on health risk analysis on benzo(a)pyrene and concentration of 1-hydroxypirene in primary school children in West Jakarta, as one of the most air-polluted areas in Indonesia, is needed.

2. Materials and Methods

This study was done in three public primary schools in West Jakarta. The three primary schools studied were not using air conditioner inside the classroom and differed in the location characteristics, i.e., (1) Public primary school 03 West Cengkareng (SDN 03 Cengkareng Barat Pagi) which located in the school areas and more than 400 m from highway (from herewith will be called school 1), (2) Public primary school 05 East Cengkareng (SDN 05 Cengkareng Timur Pagi) which located nearby the controlled-access highway and fuel station (from herewith will be called school 2), and (3) Public primary school 06 Pinangsia (SDN 06 Pinangsia Pagi) which located nearby the busy highway and next to the train station (from herewith will be called school 3). We studied the population of students from those three primary schools with a total number of 1,055 students between April to May 2019.

We used the two complementary studies of Public Health Assessment (PHA), i.e., Environmental Health Risk Analysis (EHRA) and epidemiology with a cross-sectional design. Through EHRA, we aimed to estimate the intake value of BaP from the 1-OHP concentration in the students' urine samples. We calculated the daily intake milligrams BaP on students per kilogram weight using the following equation:

$$I = \frac{C \ x \ R \ x \ tE \ x \ fE \ x \ Dt}{Wb \ x \ tavg} \quad \text{...... (Equation 1)}$$

with:

I = daily intake (mg/kg/day)
C = risk agent concentration (mg/m^3)
R = inhalation rate (m^3/hour) = 0,5
tE = exposure time (hour/day) = 6
fE = frequency of exposure (day/year) = 209
Dt = duration of exposure (year) = 6
Wb = weight (kg)
tavg = average daily period = 1254

We then compared the BaP intake value with the reference dose (RfD), which resulted in the Risk Quotient (RQ) value (RQ = BaP intake / RfD). The reference dose toxicity for BaP inhalation exposure was 2 x 10^{-6} mg/m^3. The Cancer Slope Factor (CSF) or the estimate of cancer risk was derived from the Inhalation Unit Risk (IUR) of 6E-4 (6 x 10^{-4}) per mg/m^3. If the value of RQ > 1, then the BaP exposure has a risk of causing health symptoms; on contrary, if RQ $\leq$ 1, then the BaP exposure has a low or no risk of causing health symptoms [37, 34].

We divided our sample size based on the probability proportional to size due to the uneven number of students of each school. We used the purposive sampling method to obtain primary data of indoor BaP concentration. We measured the indoor BaP using sorbent tubes with charcoal filter and minimum sample volume of 200 L (NIOSH 5515) at 7 am (i.e., when students started their school activities). The sorbent tube was placed at 150 cm height or adjusted with the students' inhalation height. The BaP concentration was then measured for 270 minutes on the peak traffic hours during the school hours (filter and sorbent tube was changed 3 times).

The students' urine samples were collected by each student (5-30 ml) using a special container just before the school hours end. The samples were placed in a coolbox with ice pack to maintain the quality of the urine, then transported to the laboratory and kept at the temperature of -20^{o}C before being analyzed. The urine was analyzed with High Performance Liquid Chromatography (HPLC) with fluorescence detector. The other risk factors were identified using the structured interview on the questionnaire. We also measured the Body Mass Index (BMI) with microtoise and digital weighing scale.

3. Results

From overall data, we found the concentration of indoor BaP was between 0.006 – 0.131 mg/m^3. The mean concentration of BaP on school 1 was 0.0006 mg/m^3 (4th grade classroom) and 0.0029 mg/m^3 (5th grade classroom; see Table 1). In school 2, the mean concentration of BaP in fourth-grade classroom was 0.0131 mg/m^3 and in the fifth-grade classroom was 0.0054 mg/m^3. We found the BaP mean concentration on school 3 was 0.0055 mg/m^3 (fourth-grade classroom) and 0.0069 mg/m^3 (fifth-grade classroom).

The calculation of indoor BaP exposure through inhalation on students was done with a real-time scenario. Based on the calculation of carcinogenic BaP intake (c.f. Equation 1), we found the mean daily BaP intake value of 0.000114 mg/kg/day (school 1), 0.000663 mg/kg/day (school 2), and 0.000412 mg/kg/day (school 3). The health risk of BaP exposure on three primary schools showed RQ value lower than one, thus the BaP exposure was considered to be insignificant and not lethal. However, we found that the mean daily BaP inhaled by the students was significantly associated with the production of metabolite 1-OHP in the urine. Our analysis showed a positive relationship (r = 0.4) between the mean daily BaP and urinary 1-OHP concentration (Table 2).

Table 1. The benzo(a)pyrene concentration on three primary schools studied

	Benzo(a)pyrene (mg/m^3)					
	School 1 (SDN Cengkareng Barat)		**School 2 (SDN Cengkareng Timur)**		**School 3 (SDN Pinangsia)**	
Hours	4th-grade	5th-grade	4th-grade	5th-grade	4th-grade	5th-grade
T1	0.0009	0.0035	0.0301	0.0048	0.0063	0.0109
T2	0.0003	0.0004	0.0029	0.0005	0.0052	0.0060
T3	0.0005	0.0048	0.0064	0.0063	0.0050	0.0039
Mean±SD	0.0017±0.0019		0.0092±0.0103		0.0062±0.0024	

*T1 = morning class; T2 = break time; T3= noon class

Table 2. Association of 1-hydroxypyrene levels (µmol/ml creatinine) to benzo(a)pyrene intake and the characteristics of the school children

Variables	**n**	**%**	**Mean±SD**	***p*-value**
Intake	84	100	6.778±6.748	0.001*
Sex				
Female	41	48.8	5.837±6.002	0.214
Male	43	51.2	7.674±7.349	
Grade				
Fifth	32	38	4.641±3.541	0.008*
Fourth	52	62	8.092±7.866	
School				
School 1	42	50	4.034±4.677	0.0005*
School 2	29	34.5	10.959±8.188	
School 3	13	15.6	6.314±3.872	
Body Mass Index				
Abnormal	39	46.4	7.611±7.008	0.295
Normal	45	53.6	6.056±6.507	
Extracurricular				
Yes	41	48.8	8.229±7.688	0.056
No	43	51.2	5.393±5.449	
Cigarette fume exposure				

Variables	n	%	Mean±SD	*p*-value
Yes	56	66.7	7.346±6.965	0.278
No	28	33.3	5.641±6.257	
Grilled food consumption				
Yes	45	53.6	8.426±7.45	0.015*
No	39	46.4	4.876±5.317	

* p-value <0.05 statistically significant

The median values of the urinary 1-OHP from three primary schools were under 10 µmol/mol kreatinin, however, we also found a student with a high 1-OHP concentration of 30 µmol/mol kreatinin (i.e., fourth-grade student from school 2). We also found that the fourth-grader in school 1 and 2 have urinary 1-OHP higher than the fifth-grader from the same school (Table 2).

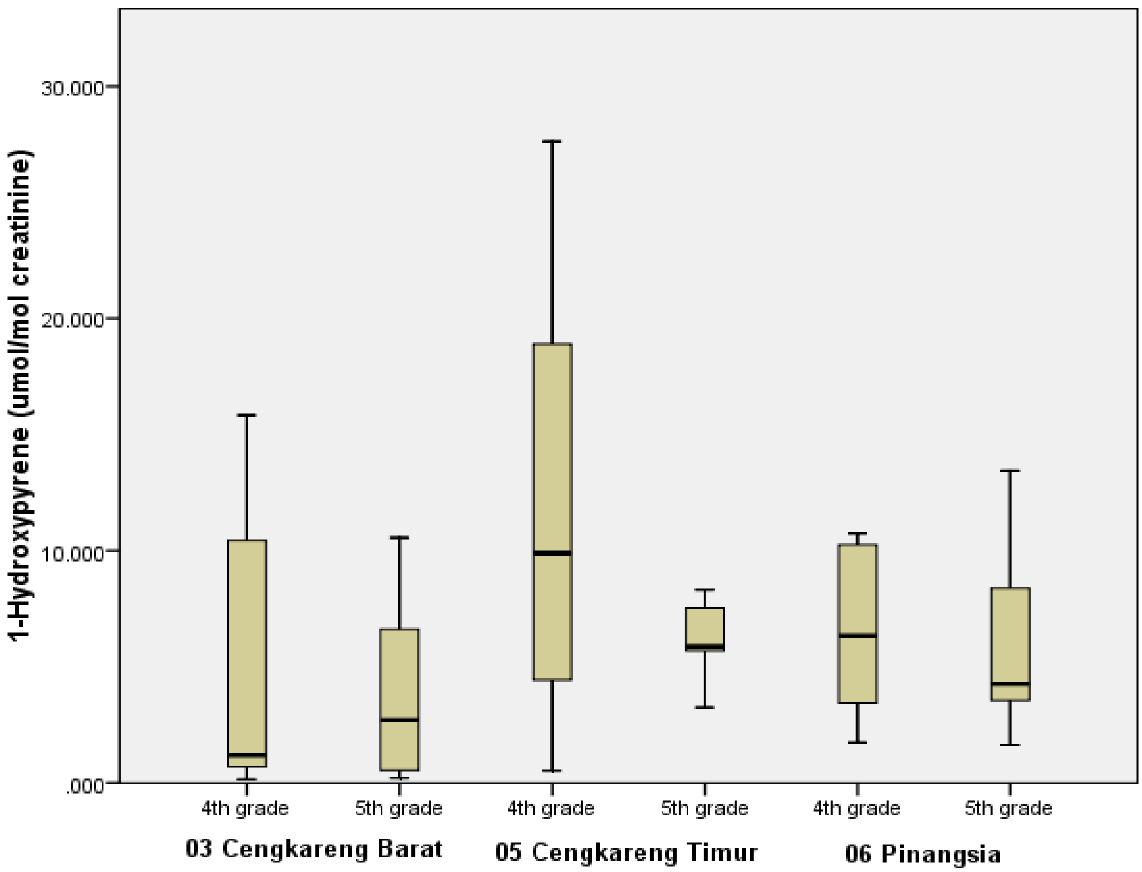

Figure 1. Urinary 1-hydroxypyrene among school children according to the grade and school

From the seven-variable studied, three variables (i.e., grade, school location, habit of eating grilled food) were associated with the urinary 1-OHP concentration on students. In general, students of the fourth grade in school 2 and 3 and have consumed grilled food frequently has a significantly higher urinary 1-OHP concentration than students who did not consume grilled food (Table 2).

4. Discussion

The mean indoor BaP concentration was the highest at school 2, followed by school 3, and school 1. The indoor BaP concentrations on those schools were still under the national air quality threshold of 0.2 mg/m^3 [37] and the Environmental Protection Agency of the USA threshold of 0.01 mg/m^3 [37]. However, compared with the air quality standard of WHO 0.001 mg/m^3, the indoor BaP concentration from each school studied was higher (i.e., school 1 was 2 times higher, school 2 was 9 times higher, and school 3 was 6 times higher). Our values were also higher compared with the air quality standards in countries such as Germany (0.00001 mg/m^3); Italy, Australia, and India (0.000001 mg/m^3); Belgium and The Netherlands (0.0000005 mg/m^3); Croatia, France, and Sweden (0.0000005 mg/m^3); and United States of America (0.0000084 mg/m^3) [37, 38, 39].

The high concentration of BaP found in school 2 was probably due to its location which was next to the controlled-access highway and fuel station. This condition allows the polluted air from the traffic and the fuel station to infiltrate the classroom and increasing the indoor BaP concentration. The same explanation goes with the high indoor BaP concentration found in school 3; the location of school 3 which was in front of a busy highway and close proximity to a railway station contributed to the polluted air in the school area. Even though school 1 is located in school areas with several schools nearby and quite distant from the main highway (>400 m), at certain hours (before and after the school starts), the BaP concentration was high. This was due to the fume from the motor vehicle drove by the parents commuting their children to the school which contributed to the increase in the indoor BaP concentration.

The mean concentration of 1-OHP in all schools that we studied was higher in the fourth-grade students compared with the fifth-grade students because their classroom was closer to the pollutant source. The significant relationship between BaP intake with urinary 1-OHP concentration in our study was also reported by another study in Thailand (Tuntawiroon et al, 2007). The study in Thailand was comparing between Bangkok (busy traffic area) and Chonburi (less busy traffic area), and the results showed that the ambient air BaP concentration in Bangkok was 3.5 times higher (4.13 ± 0.21 ng/m^3 or equal to 0.0004 ± 0.00002 mg/m^3) than Chonburi ($1.18 \pm 0,09$ ng/m^3 or equal to 0.00012 ± 0.000009 mg/m^3). The urinary 1-OHP concentration was significantly affected by the BaP concentration (p-value < 0.001) with a higher value in Bangkok (0.15 µmol/mol kreatinin) compared with Chonburi (0.09 µmol/mol kreatinin) [28].

Similar research was also done to the bus drivers and limited-access highway officers in Indonesia. The mean urinary 1-OHP concentration of bus drivers in Depok bus station was higher (0.51 µmol/mol kreatinin) than the other non-driver's comparator group (0.29 µmol/mol kreatinin) [40]. The limited-access highway officers in Jabodetabek area also showed a higher urinary 1-OHP concentration (1089.05 ng/gr kreatinin or equal to 56412.79 µmol/mol kreatinin) compared to non-officers' comparator group (700.69 ng/gr kreatinin or equal to 36295.742 µmol/mol kreatinin) [41].

The real-time exposure intake describes the amount of exposure gained by students since they started school until the moment that this study was started. Individual intake was different and influenced by students' weight, frequency of exposure, the individual inhalation rate, and probably the difference in their activities. The biggest intake of real-time exposure was shown by school 2. The real-time and 6-year RQ value were less than 1, which means that students were not subjected to the risk of exposure during the 6 years of the school period. This value can be interpreted as the inhalation exposure of BaP with exposure time of 6 hours, exposure frequency of 1,254 days, and duration of 4 to 6 years was declared safe to carcinogenic risks. The minimum real-time RQ and the 6 years projection was in school 3 and the maximum real-time and 6 years projection was in school 1. This was affected by the school location and the distance to the source of the BaP pollutant.

5. Conclusion

There was a significant association between the benzo(a)pyrene intake with the 1-hydroxypyrene concentration, classroom, schools, and the fuel consumption habit. The carcinogenic health risk of BaP exposure was still considered safe for the students. The exposure of BaP concentration can still be controlled by maintaining classroom cleanliness, good ventilation system, and using air purifiers. We suggest that the government can pay more attention to this issue by creating school areas far from the source of air pollution.

6. Conflict of Interest

There is no conflict of interest.

7. Acknowledgment

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