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S-Benzylmercapturic Acid (S-BMA) Levels in Urine as an Indicator of Exposure to Toluene in the Kinshasa Population

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Abstract

Background and objectives: Toluene, one of the various volatile organic compounds frequently observed in am-bient air, is an environmental toxicant associated with several adverse effects on the central nervous and reproduc-tive systems. In DR Congo, data on environmental toluene exposure are scarce. The present study aims to assess the toluene exposure in the Kinshasa population through the measurement of S-BMA in urinary samples.

Methods: During January - December 2008, 220 subjects aged 6 to 70 years living in the urban area of Kinshasa (50.5% women) provided urine samples. 50 other participants from the sub-rural area were added as a control. S-BMA levels were measured by LC–MS/MS. Data were expressed as arithmetic means, geometric means, median levels, percentile 95th and range.

Results: The levels of S-BMA in Kinshasa [median (min - max) levels = 18.1 µg/L (0.3 - 97.1, 25.3)] were similar to those reported in the general population. Whereas the median S-BMA levels in this study were in accordance with those found in the literature, the urban area of Kinshasa had a high risk of the toluene exposure as compared to the sub-rural area of the region [median (min - max) levels were 4.3 µg/L (0.3 - 51.9) for sub-rural area and 10.5 µg/L (0.3 - 97.1) for urban area, $p<0.01$].

Conclusions: The present study findings highlight the environmental toluene exposure in the Kinshasa population. The determination of toluene concentrations in airborne of Kinshasa and its limit values are needed for the protec-tion of human health.

Keywords: S-benzylmercapturic acid; Toluene; Biomonitoring; Environmental Exposure; Kinshasa population

Introduction

Toluene is one of the various volatile organic compounds frequently observed in ambient air [1]. Toluene exposure by inhalation is associated with several adverse effects on the central nervous and reproductive systems [2,3,4]. The main sources of toluene exposure include the burning of fossil fuels, toluene-based solvents, thinners and motor vehicle exhaust [5,6]. Others identified sources include cigarette smoke, emissions from volcanoes, forest fires and crude oil [7, 8]. The vapor of toluene in ambient air has been identified as an important source of toluene exposure in the general population [9,10]. The biomarkers of toluene exposure highlighted in the literature include toluene in blood, urine and exhaled air, as well as its urinary metabolites: Hippuric acid, Orto-cresol, S-p-toluylmercapturic acid and S-benzylmercapturic acid (S-BMA) [11]. Among these biomarkers, S-BMA has been proposed as a reliable biomarker of toluene exposure [12,13,14,15]. The present study aims to assess the toluene exposure in the Kinshasa population through the measurement of S-BMA in urinary samples.

Methods

Study Design

During January - December 2008, 220 subjects aged 6 to 70 years, not occupationally exposed to toluene, were selected using a two-stage systematic sampling approach according to [16,17]. After providing some information about this study, subjects were asked to complete a questionnaire, consent in the survey and provide a urine sample. This study was approved by the congolese committee of medical ethics.

Laboratory Method

Spot urine samples were collected in polystyrene containers and stored at −20 ◦ C until analysis in the Louvain Center for Toxicology and Applied Pharmacology (Brussels, Belgium). After thawing and mixing all frozen urine samples, 1 mL of urine aliquot was spiked with 25 µL of an internal standard solution (1 mg/L of D3-SBMA). The sample was diluted with nanopure water (1:1) and centrifuged using Isolute SAX 500 mg 3 mL SPE columns according to the previous procedure used by [18]. Samples were analyzed by using LC–MS/MS system, equipped with Waters Alliance 2795 LC Column: C18 Supersples 100 (125 mm x 4 mm). Solvent-A was 0.5% (v/v) aqueous acetic acid and solvent-B was methanol with 0.5% (v/v) acetic acid. The solvent elution program used a flow rate of 0.40 mL/min at 50 ◦ C. The mass spectrometer was operated in negative ion electrospray mode. Mass spectral data on ions were obtained in multiple reaction monitoring. The limit of detection (LOD) was 0.70 µg/L. The analytical methods used in this study are in accordance with the literature [19, 20, 21]. Additionally, urinary cotinine was determined by HPLC according to the methods previously described by Benowitz (1996).

The statistical data analysis was performed using NCSS version 2004 [22]. We expressed the results as AM (Arithmetic means), GM (Geometric means), median, P95th (percentile 95th) and range. Dealing with laboratory results below the LOD (limit of detection), we used LOD/2. All parametric tests and stepwise multiple linear regression analyses were used according to the statistical procedure described by [22].

Results and Discussion

In the present work, we assessed the environmental exposure to toluene in the Kinshasa population using a urinary S-BMA as a biomarker. The characteristics of the participants from urban area as well as rural area are reported in. The average of age was 31 years (min = 6 and max= 70), with 50.5% of female, 36% of current smokers and 77.3% of adults.

One absorbed through the lungs, toluene is biotransformed and secreted rapidly in the urine (IARC, 1999; ATSDR, 2015). Several toluene exposure studies have been conducted among population in environmental and occupational settings using urinary metabolites as the indicator of toluene exposure [22, 23, 24, 25]. Some of these studies reported also that the urinary metabolites are GST-dependent [26, 27, 28]. Considering that GSTs are dimeric enzymes with two polymorphic genes in the general population [29], this information should be considered when interpreting urinary levels of S-BMA [27].

Median (range, P95th) urinary S-BMA was 18.1 µg/L (0.3 - 97.1, 25.3). Women had high levels of S-BMA as compared to men (0 for female, GM: 7.9 µg/L vs 1 for male, GM: 5.8 µg/L, $p<0.01$). This can be explained by cooking activities mostly found in women in DR Congo (Tuakuila et al., 2013).

Comparing non-smokers and current smokers, higher levels of S-BMA were found in current smokers (0 for non-smokers, GM: 2.1 µg/L vs 1 for current smokers, GM: 11.8 µg/L, $p<0.01$). This is in accordance with the results of other studies in the literature (IARC, 2004; Polzin et al., 2007; Schettgen et al., 2008; B'Humer, 2011; ATSDR, 2015). For example, Schettgen et al. (2008) reported median (min-max) levels for S-BMA in non-smokers and smokers of 8.2 µg/L (1.6 - 77.4) and 11.5 µg/L (0.9 - 51.2), respectively. B'Humer (2011) found median (min-max) levels for S-BMA in non-smokers and smokers of 6.9 µg/L (0.3 - 23.3) and 7.4 µg/L (1.3 - 28.3), respectively.

The Levels of S-BMA were lower in children as compared to adults (0 for 6-14 years, GM: 2.7 µg/L vs 1 for >14 years, GM: 11.2 µg/L, $p<0.01$). This is because no child was a smoker.

Levels of S-BMA found in the present study were in accordance with those previously reported in the general population. The median (min - max, n) levels reported were 9.8 µg/L (0.9 - 77.4, n = 30) [28, 29].

The stepwise multivariable analyses were performed to compare urban area to sub-rural area (0 for sub-rural area/1 for urban area). The potential confounders were age (continuous variable), sex (qualitative variable) and smoking habits (urinary cotinine levels, continuous variable). The partial R2 was 0.016 for age, 0.013 for sex, 0.126 for smoking habits and 0.019 for area. The variables used in this model explained approximately 17% (Total R2 was 0.174) of the variance of the S-BMA levels : median (min - max) levels were 4.3 µg/L (0.3 - 51.9) for sub-rural area and 10.5 µg/L (0.3 - 97.1) for urban area. About 2-fold higher levels of S-BMA were found in the urban area of Kinshasa as compare to the sub-rural area of the same region.

This study had two major limitations. First, the participants were not randomly selected because of the absence population registers in Kinshasa. Second, passive smoking, an other source of toluene exposure in the general population, did not evaluate [30].

Despite these limitations, the levels of S-BMA in Kinshasa were similar to those reported in the general population. Whereas the median S-BMA levels in our study were in accordance with those found in the literature, the highest risk of exposure was observed in the urban area of Kinshasa. The present study findings highlight the environmental toluene exposure in the Kinshasa population. The determination of toluene concentrations in airborne of Kinshasa and its limit values are needed for the protection of human health [31].

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