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Health risk evaluation in a population exposed to chemical releases from a petrochemical complex in Thailand

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ABSTRACT

Emissions from petrochemical industries may contain toxic and carcinogenic compounds that can pose health risk to human populations. The scenario may be worse in developing countries where management of such exposure-health problems is typically not well-implemented and the public may not be well-informed about such health risk. In Thailand, increasing incidences of respiratory diseases and cancers have been reported for the population around a major petrochemical complex, the Map Ta Phut Industrial Estate (MTPIE). This study aimed to systematically investigate an exposure-health risk among these populations. One-hundred and twelve healthy residents living nearby MTPIE and 50 controls located approximately 40 km from MTPIE were recruited. Both external and internal exposure doses to benzene and 1,3-butadiene, known to be associated with the types of cancer that are of concern, were measured because they represent exposure to industrial and/or traffic-related emissions. Health risk was assessed using the biomarkers of early biological effects for cancer and inflammatory responses, as well as biomarkers of exposure for benzene and 1,3-butadiene. The exposure levels of benzene and 1,3-butadiene were similar for both the exposed and control groups. This was confirmed by a non-significant difference in the levels of specific urinary metabolites for benzene (*trans,trans*-muconic acid, *t,t*-MA) and 1,3-butadiene (monohydroxy-butyl mercapturic acid, MHBMA). Levels of 8-hydroxydeoxyguanosine (8-OHdG) and DNA strand breaks between the two groups were not statistically significantly different. However, functional biomarkers, *interleukin-8* (*IL-8*) expression was significantly higher ($p < 0.01$) and DNA repair capacity was lower ($p < 0.05$) in the exposed residents compared to the control subjects. This suggests that the exposed residents may have a higher risk for development of diseases such as cancer compared to controls. However, the increased expression of *IL-8* and lower DNA repair capacity were not associated with recent and excessive exposure to benzene and 1,3-butadiene, which were at the similar levels as those in the controls. The data would indicate that previous exposure to the two chemicals together with exposure to other toxic chemicals from the MTPIE may be responsible for the elevated functional biomarkers and health risk. Further studies are required to determine which other pollutants from the industrial complex could be causing these functional abnormalities.

1. Introduction

Emissions from petrochemical industry and oil refineries usually contain a mixture of toxic chemicals, including volatile organic compounds (e.g. benzene and 1,3-butadiene) (Chang et al., 2016), heavy metals, polycyclic aromatic hydrocarbons (Dominguez-Morueco et al., 2015) and polychlorinated biphenyls (Aydin et al., 2014). Excessive exposure to these toxic substances, singly and in combinations, can cause adverse health effects, e.g. respiratory diseases (Rovira et al., 2014), cancers (Koh et al., 2014; Micheli et al., 2014) and preterm deliveries (Yang et al., 2004). However, due to scientific, political and social issues, it is very difficult to address health risk from such emission-exposure conditions. Furthermore, such scenarios may be more serious in developing countries because they typically have inadequate pollution control and management, and the public is not well-informed about such health risk. Consequently, public concerns

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for such risk can be misdirected.

In Thailand, the Map Ta Phut Industrial Estate (MTPIE), which is located in Rayong province, approximately 200 km east of Bangkok, has been in operation since 1989. The MTPIE consists of 32 petrochemical companies, 2 oil refineries, 8 steel companies, 12 chemical and fertilizer companies and 17 public utility companies (Langkulsen et al., 2011). Since it started to operate, the surrounding environment (including soil, water and air) has been reported to be contaminated with hazardous pollutants (PCD, 2014). In addition, air quality monitoring, which was conducted by the Thai Pollution Control Department (PCD) from 2007 to 2013, showed that benzene, 1,3-butadiene, and 1,2-dichloroethane exceeded the national ambient standards (PCD, 2015). Furthermore, health surveys in the entire Rayong province suggested increased incidences of some respiratory diseases and cancer over the national average (Khuhaprema et al., 2012; Kongtip et al., 2013). There have also been incidental reports indicating that residents near the MTPIE had increased levels of bulky DNA adducts (Peluso et al., 2008), reduced visual-motor coordination (Aungudornpukdee and Vichit-Vadakan, 2009) and increased respiratory symptoms (Tanyanont and Vichit-Vadakan, 2012). Consequently, residents in communities around the MTPIE became highly vocal about concerns of health risk from exposure to the aforementioned air pollutants. Due to this increased public concern, the government declared the MTPIE as a pollution-controlled zone in 2009, requiring the Industrial Estate Authority of Thailand (IEAT) and entrepreneurs to seek proper measures to limit and control emissions to the environment. However, whether there was real reduction of emission and/or health risk is unknown.

From previous studies, DNA damage (8-OHdG and DNA strand breaks) was significantly associated with exposure to benzene (Buthbumrung et al., 2008; Navasumrit et al., 2008) and 1,3-butadiene (Arayasiri et al., 2010) and suggestive of increased health risk. Chronic exposure to industrial and environmental pollutants, such as benzene, 1,3-butadiene, arsenic and uranium, has been associated with induction of functional DNA repair deficiencies in human populations (Banerjee et al., 2008; Ruchirawat et al., 2010). Decreased DNA repair capacity is indicative of increased cancer risk which was based on population investigations (Au et al., 2010).

In this study, we have conducted a systematic health risk evaluation study of the population. This involves the assessment of exposure (ambient and internal) and early biological effects that can be linked to possible manifestation of disease. Exposure assessment of benzene and 1,3-butadiene was carried out by direct measurement of the ambient levels and individual exposure levels, while the internal exposure assessment was carried out through the use of biomarkers of exposure determined as the concentration of the chemical or a metabolite in blood or urine (van Sittert, 1989). In this study we used blood benzene and a urinary metabolite *trans,trans*-muconic acid (*t,t*-MA) for benzene and a urinary monohydroxy-butyl mercapturic acid (MHBMA) for 1,3-butadiene as biomarkers of internal dose of exposure. The biomarkers of early biological effects related to cancer (8-hydroxydeoxyguanosine, 8-OHdG; and DNA strand breaks), as well as functional biomarkers for long-term effects (inflammatory response measured as *interleukin-8* (*IL-8*) mRNA expression; and DNA repair capacity) were used to evaluate health effects. The collected data were used to assess risk for cancer from acute and chronic exposure to the MTPIE emissions.

2. Methods

2.1. Study location and subject recruitment

The present study was conducted from 2008 to 2010 in Map Ta Phut district, Rayong province, Thailand (Fig. 1). Based on previous ambient air monitoring data from Thai Pollution Department (PCD), three high-exposure locations downwind (within 1.5 km) of the MTPIE were selected as exposed sites. The control site was located 40 km east of the MTPIE and contained no petrochemical industries. The exposed and control subjects were randomly recruited. The purpose of the study was clearly explained to all subjects. Exclusion criteria for both groups of study subjects were recent illness, cigarette smoking, occupational exposure to benzene and 1,3-butadiene and subject ages of < 18 and > 60 years old. Volunteers were asked to sign an informed consent form prior to their enrollment in this study. They also completed a questionnaire to allow assessment of accommodation, work history, and lifestyle (smoking status, alcohol consumption, medication and type of diet). The study protocol was approved by the Institutional Ethical Committee in agreement with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

2.2. Sample collection

Ambient and personal air sampling was carried out in the dry season, between March and May, 2008, to avoid effects from humidity. Ambient air samples were collected at a height of approximately 1.50 m above the ground and approximately 50 m from the main roads. Air samples were collected from various sites in the vicinity of the MTPIE. Personal air samples were collected in the breathing zone of the study subjects. Ambient and individual air samples were collected for 8 h (8 a.m. to 4 p.m.). Blood and urine samples were collected at the end of the air-sampling period. Urine samples were stored at −80 °C until analysis, while whole blood samples were processed immediately upon arrival at the laboratory for analysis of DNA strand breaks and 8-OHdG.

2.3. Determination of benzene and 1,3-butadiene in air samples

Benzene and 1,3-butadiene were collected using thermal desorption tubes (Tenax TA and Carbopack X, respectively; Markes International Ltd., UK) for a duration of 8 h, after which samples were capped, transported to the laboratory, and stored at 4 °C until analysis. For quantification, benzene and 1,3-butadiene were desorbed from the tubes using a thermal desorption unit (UNITY, Markes International Ltd., UK) and analyzed by gas chromatography equipped with mass spectrometry (GC–MS, Agilent 6890, USA) as previously described (Navasumrit et al., 2008). The limits of detection for benzene and 1,3-butadiene were 0.38 and 0.0012 $\mu g/m^3$, respectively.

2.4. Determination of benzene in blood

Venous blood samples were collected in tubes containing EDTA and stored at 4 °C until analysis. Analysis was performed using solid phase micro extraction (SPME) and detection was carried out through GC–MS. Analysis was completed within 24 h of sample collection according to a method previously described (Navasumrit et al., 2005).

2.5. Determination of urinary trans,trans-muconic acid (t,t-MA)

Urinary *t,t*-MA was analyzed using liquid chromatography equipped with a triple quadrupole mass spectrometer (LC-MS/MS). The urine samples were thawed at room temperature for 15 min with frequent stirring and then centrifuged at 3000*g* for 5 min. The supernatant was diluted 1:5 in deionized water. Thirty microliters of diluted samples were resolved by HPLC (Agilent 1100 series) equipped with a reverse-phase column (Phenomenax, 3 μm Luna C18(2) connected to Phenomenax C18 guard cartridges). The MS/MS system (Micromass Quattro micro™) was operated in negative electrospray ionization mode. Transition of the molecular ion for *t,t*-MA was done in the multiple reaction monitoring (MRM) mode at m/z 141→m/z 97 (Melikian et al., 1999). Urinary creatinine was measured using a CREATININE liquicolor kit (Human GmbH, Wiesbaden, Germany). The concentration of *t,t*-MA in urine was normalized to creatinine