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Health hazard assessment of occupationally di-(2-ethylhexyl)-phthalate-exposed workers in China

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HIGHLIGHTS

- Occupational exposure to ambient DEHP presented a potential health risk to workers.
- Comparatively high levels of DEHP were measured in respirable workplace dust samples.
- A correspondence between ambient DEHP level and biochemical markers was indicated.
- Daily intake of DEHP can be calculated by its ambient level.

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ABSTRACT

Di-(2-ethylhexyl)-phthalate (DEHP) is a potential hazard to human health. The effects of occupational high level DEHP exposure on human health were evaluated by measuring the plasma cholinesterase, residues, renal and hepatic biochemical markers. The study was conducted in three representative polyvinyl chloride manufacturing facilities from large size (S1), medium side (S2) to small size (S3). Total 456 adult males including 352 exposed workers (occupational) and 104 control workers (background) were selected. The average DEHP concentrations in respirable particulate matter were 233, 291, and 707 $\mu g\ m^{-3}$ for S1–S3, respectively, compared with 0.26 $\mu g\ m^{-3}$ in the background atmosphere (labeled by S4). The results showed significant decreases in post exposure plasma cholinesterase (PChE) levels (<30%) from the exposed workers as compared to baseline. These exposed workers had been evaluated for plasma DEHP residues. Regression analyses explored that PChE decreased significantly with increasing plasma DEHP residues. Serum aspartate aminotransferase, alanine aminotransferase, creatinine, urea, gamma glutamyltransferase, malondialdehyde, total antioxidant and C-reactive protein were significantly raised as compared to the controls. Of the 352 exposed workers, 116 (33.0%) had a daily DEHP intake 22.7 $\mu g\ kg\ bw^{-1}\ d^{-1}$, which is more than 20 $\mu g\ kg\ bw^{-1}\ d^{-1}$ specified by the US Environmental Protection Agency. The study demonstrated that occupational phthalate exposure produces health hazards.

1. Introduction

Phthalate esters (PAEs) are abundant synthetic chemicals in the environment (Liu et al., 2011). Their health hazards are a major concern especially in developing countries, where PAEs are commonly used as plasticizer in the production of polyvinyl chloride (PVC). PVC plastics may contain up to 50% PAEs by weight (Meeker et al., 2009). As a plasticizer, PAEs are not chemically bound to the product and may leach out to the public environment (Staples et al., 1997). Among commercial PAEs, di(2-ethylhexyl)phthalate (DEHP) is the major phthalate plasticizer for PVC, and the content of DEHP is 50–60% (Grande et al., 2007). More than two million tons of DEHP were used each year worldwide. Its potential environmental and health hazards cannot be ignored due to its low degradability (Vermeulen et al., 2005).

Although PAEs furnish some benefits for plastics, building materials, and personal care products, they entail a number of human health hazards (Wittassek et al., 2009). Multiple sources, including the workspace, diet, personal care products and other activities, can contribute to human phthalate exposure, which

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has led to the potentially serious hazardous effects to human health and environmental quality (Matsumoto et al., 2008). Humans can be exposed to PAEs carried by the airborne dust via ingestion and dermal absorption. The skin and respiratory tract provide efficient surfaces for the absorption of PAEs. The airborne dust ingestion and inhalation rates are 0.11 g d^{-1} and 20 m^3 d^{-1} for adults. The dermal exposure area including face, forearms, hands and lower legs is 3300 cm^2, and the dermal adherence factor is 0.2 mg cm^{-2} (Kang et al., 2012). Common exposure to PAEs is often considered to originate from food packaging materials with PAEs plasticizer (Kolarik et al., 2008). Furthermore, special attention has also been directed towards medical treatment, i.e. via use of medical devices containing DEHP, due to the fact that numerous bags and tubes used in hospitals are made of PVC and these PVC polymers leach phthalate plasticizer DEHP (Koch et al., 2005). PAEs hazards on professional workers in PVC industries are the most concern. DEHP is released to the atmosphere as respirable workplace dust (PM_{10}, particulate matter with aerodynamic diameter $\leqslant 10\ \mu m$) contaminated with high PAE levels, which cause bronchial obstruction and asthma if inhaled by the professional workers (Gaudin et al., 2011). This workplace dust can penetrate effectively into the respiratory system and deposit deeply in the bronchioles and alveoli of the lungs. The association of workplace dust with these chemicals may contribute to adverse health effects or potentially result in long-term health hazards (Wang et al., 2008).

Adverse human effects of PAEs depend upon their potential toxicity, as well as levels and exposure duration. Toxicological evaluation of these chemicals has shown that prolong exposure to high PAE levels can affect multiple organs including liver and kidney functions (Heudorf et al., 2007). DEHP is the most commonly used phthalate plasticizer in the production of PVC. It is suspected to be endocrine disrupting chemicals exhibiting carcinogenic action (Calafat and McKee, 2006). As a result, DEHP has been added to the list of "chemicals of concern" by the US Environmental Protection Agency (EPA). Although many studies were carried out to investigate the possible toxicity of PAEs including DEHP, their health hazards were observed in laboratory animals, mainly in rats (Andrade et al., 2006; Grande et al., 2007; Christiansen et al., 2010), there remain questions about human health effects of these chemicals (Latini et al., 2003; Gaudin et al., 2011).

Clinically, occupationally exposed chemical workers are more likely to represent with potential adverse symptoms (David and Gans, 2003). Biomarkers may be used to detect the hazardous effects of chemicals before clinical adverse events occur (Manno et al., 2010). In the late 20th century, several epidemiological studies have shown an association between high DEHP exposure and adverse effects on human endocrine or reproductive system (Andrade et al., 2006; Benson, 2009; Eveillard et al., 2009; Gaudin et al., 2011). At present, DEHP has widely spread in our environment. Does occupationally exposure to high dose DEHP cause adverse poison symptoms? There is a concern for estimating the association between high DEHP exposure and human health risks. Information about DEHP pollution in the occupational environment and workforces is limited. In addition, the human exposure to DEHP considering as a health hazard is not well reported. In this paper, we reported the hazardous health effects of occupationally DEHP-exposed workers, by measuring plasma cholinesterase (PChE), DEHP residues, and biochemical markers, with the aims of establishing baseline levels needed for assessing DEHP safety in exposure among populations.

2. Materials and methods

A longitudinal comparative study was conducted to investigate the DEHP health effects on workers from three PVC factories ranging in size, S1 being a large factory (9100 workers), S2 being medium size (4645 workers) and S3 being small (888 workers).

2.1. Subjects

Sampling sites and selected workers are summarized in Table 1. 456 workers from the three PVC factories were identified, 352 workers from the production department normally exposed to airborne dusts were selected as exposed workers and 104 office workers were as control workers. The exposed workers ranged between 20 and 45 years of age: 125 of them from S1, 111 from S2 and 116 from S3. They were full time workers actively involved in PVC manufacturing. The 104 control workers have the comparable socio-economic status as the exposed workers but were seldom exposed to DEHP. Each participant was interviewed with questions about their general status, exposure history, smoking habits, previous medical records, and present symptoms. Medical history and physical examination of the subjects were also carried out before tests. Those with diabetes mellitus, hypertension, and viral hepatitis were excluded. A record of their exposure history, smoking habits and general health conditions were maintained.

2.2. Sample collection

A trained nurse from the factory's Occupational Health Service was assigned to perform blood sampling. Each participant took two blood tests: one when the worker was newly employed and one after the worker had worked in the same place for 3 years. The blood samples were kept in cold chamber while being transported to the analytical laboratory. Blood plasma was separated by blood centrifugation at $1500 \times g$ for 15 min. Samples were stored at $-20\ ^\circ C$ in clean glass vials for biochemical and DEHP analysis.

The studies were conducted in the different period of time. Airborne dust samples were collected from the three factories: 5 samples each from their worksites and 2 samples each from their office areas during the months of January, April, July, and November. Each sampling period was 6 consecutive days every three

Table 1
Detailed information of the sampling sites and selected workers.

Sampling site	Total workers	Selected volunteers	Sampling number		Detail information about the sampling site
			Airborne dust	Serum	
S1	9100	125	$5 \times 6 \times 12 = 360$	$125 \times 2 = 250$	A large-sized worksite producing PVC-products added DEHP as plasticizers, where the work processes during the sampling included mixing procedure and compression molding.
S2	4645	111	$5 \times 6 \times 12 = 360$	$111 \times 2 = 222$	A medium-sized worksite producing PVC-products added DEHP as plasticizers, where the work processes during the sampling included mixing procedure and compression molding.
S3	888	116	$5 \times 6 \times 12 = 360$	$116 \times 2 = 232$	A small-sized worksite producing PVC-products added DEHP as plasticizers, where the work processes during the sampling included mixing procedure and compression molding.
S4	–	104	$6 \times 6 \times 12 = 432$	$104 \times 2 = 208$	104 Office workers from the three office buildings at S1-S3 served as unexposed controls expected to have a background exposure to DEHP.