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Parental phenols exposure and spontaneous abortion in Chinese population residing in the middle and lower reaches of the Yangtze River

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HIGHLIGHTS

- We focused on parental phenol exposure and spontaneous abortion.
- Urinary parental concentrations of phenols were detected.
- Paternal PCP exposure increased the risk of spontaneous abortion.
- Maternal AP exposure increased the risk of spontaneous abortion.

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ABSTRACT

Widespread use of phenols has led to ubiquitous exposure to phenols. In experimental animals, phenols increased resorptions, reduced live litter size and fetal body weights. However, there are limited epidemiological evidences of the relationships between exposure to phenols and pregnancy outcomes. We evaluated the associations between parental urinary levels of various phenols and spontaneous abortion in a Chinese population residing in the middle and lower reaches of the Yangtze River. A case-control study was conducted that included 70 case couples with medically unexplained spontaneous abortion and 180 control couples who did not have a history of spontaneous abortion and had at least one living child. Both parental urinary phenols were measured by ultra-high performance liquid chromatography-tandem mass spectrometry including bisphenol A (BPA), benzophenone-3 (BP-3), 2,3,4-trichlorophenol (2,3,4-TCP), pentachlorophenol (PCP), 4-*n*-octylphenol (4-*n*-OP) and 4-*n*-nonylphenol (4-*n*-NP). Compared with the low exposure group, there was an increased risk of spontaneous abortion with high paternal urinary PCP concentration [odds ratio (OR) = 2.09, 95% Confidence Interval (CI), 1.05–4.14], and maternal exposure to 4-*n*-OP and alkylphenol(s) also significantly increased the risk of spontaneous abortion (OR = 2.21, 95% CI, 1.02–4.80; OR = 2.81, 95% CI, 1.39–5.65, respectively). Our study firstly provides the evidence that paternal PCP exposure, maternal 4-*n*-OP and alkylphenol(s) exposure are associated with spontaneous abortion in humans.

1. Introduction

Human reproduction is not considered a highly efficient biological process (Gupta et al., 2007). Spontaneous abortion, which is the termination of pregnancy before 20 completed gestational weeks from the last menstrual period, or less than 500 g fetal weight (WHO, 1977), is the most common complication of human pregnancy. 15–20% of clinical pregnancies end in spontaneous abortion (Gupta et al., 2007; Nowak et al., 2011). The etiology of spontaneous abortion is complicated and remains unclear so far. The known main cause of spontaneous abortion is chromosomal

Abbreviations: BPA, bisphenol A; BP-3, benzophenone-3; 2,3,4-TCP, 2,3,4-trichlorophenol; PCP, pentachlorophenol; 4-*n*-OP, 4-*n*-octylphenol; 4-*n*-NP, 4-*n*-nonylphenol; APs, alkylphenols; APEs, alkylphenol polyoxyethylene ethers; UPLC–MS/MS, ultra high performance liquid chromatography-tandem mass spectrometry; LODs, limits of detection; CR, creatinine; WHO, World Health Organization; BMI, body mass index; ORs, odds ratios; CI, confidence interval.

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abnormality. Further etiological factors have been reported including maternal uterine anatomic anomalies, infection, immunologic disorders such as antiphospholipid antibody syndrome and clotting disorders (Regan and Rai, 2000; Fritz et al., 2001; Bottomley and Bourne, 2009; Zhang et al., 2010). As we know, the male gamete contributes one-half of the genomic content to the embryo. Therefore, the male factor also plays an important role in embryonic development and may lead to spontaneous abortion or birth defects. Some studies have reported that paternal age and sperm DNA damage may increase the risk of spontaneous abortion (Slama et al., 2005; Bhattacharya, 2008; Zini et al., 2008). Recently, there is a growing body of evidence that exposure to some environmental chemicals may be associated with spontaneous abortion. It was reported that maternal exposure to pesticides may increase the risk of spontaneous abortion (Arbuckle et al., 2001). Some studies have demonstrated that paternal exposure to solvents and pesticides were associated with spontaneous abortion and birth defects (Magnusson et al., 2004; Logman et al., 2005; Slama et al., 2005; Hooiveld et al., 2006). Thus, simultaneous determination of both maternal and paternal exposure to chemicals will enable us to more comprehensively understand how chemicals induce spontaneous abortion.

Phenolic compounds are widely used in industrial agricultural production and people's daily lives. Bisphenol A (BPA), an essential additive in plastic industry, is important raw material for the production of polycarbonate and epoxy resins which is widely used in baby bottles, lunch boxes and many other food and beverage packaging materials (Vandenberg et al., 2007). BPA is one of the highest volume chemicals produced worldwide, with >8 billion pounds produced each year and >100 tons released into the atmosphere by yearly production (Vandenberg et al., 2010). Alkylphenols (APs), such as octylphenol (OP) and nonylphenol (NP), are the major degradation products of alkylphenol ethoxylates (APEs) which are most widely used classes of nonionic surfactants in industrial, agricultural application and household detergents (Vandenberg et al., 2007). Chlorophenol (CP) is a halogenated phenolic compound that has been used extensively as a biocide and preservative in cosmetics, ropes, paints, adhesives, canvas (Proudfoot, 2003; Yamarik, 2004; Cooper and Jones, 2008). The ability of benzophenone-3 (BP-3) to absorb and dissipate ultraviolet radiation facilitates its use as sunscreen agent, fragrance and flavor enhancer, photoinitiator, ultraviolet curing agent as well as indirect food additive (Calafat et al., 2008). The general population is widely exposed to these phenolic compounds through air, drinking water, soil, food and personal care products (Vandenberg et al., 2007). Meanwhile, phenolic compounds can be detected in human blood, urine, breast milk, amniotic fluid, follicular fluid, placental tissue, semen, umbilical cord blood, fetal serum and adipose tissues in many countries (Vandenberg et al., 2010; Li et al., 2011).

Some studies have suggested that phenolic compounds may pose potential risks on human health including cancer, cardiovascular disease, diabetes, immunization, reproduction and endocrine (Bredhult et al., 2007; Lang et al., 2008; Zorrilla et al., 2009; Barrett, 2010). In experimental studies, exposure to phenols can lead to abortion and increase arrest of early embryonic development (LeBlanc et al., 2000; Tachibana et al., 2007). In epidemiological studies, Sugiura-Ogasawara stated that maternal high exposure to BPA may be associated with recurrent miscarriage (Sugiura-Ogasawara et al., 2005), but the association of maternal BPA exposure and miscarriage is still controversial (Berkowitz, 2006). To our knowledge, there were no epidemiological studies regarding the relationships between parental exposure levels of various phenols and spontaneous abortion.

Phenols are mainly excreted in urine and feces by the means of glucurondiation and sulftation (Wu et al., 2010). Urine is considered to be the most appropriate matrix for biomonitoring phenols (Dekant and Volkel, 2008). Therefore, total (conjugated and free) phenols measured in human urine can reflect individual internal exposure level and urinary phenols have been widely used in exploring phenols exposure and human disease as well as laboratory abnormalities (Lang et al., 2008; Wang et al., 2012).

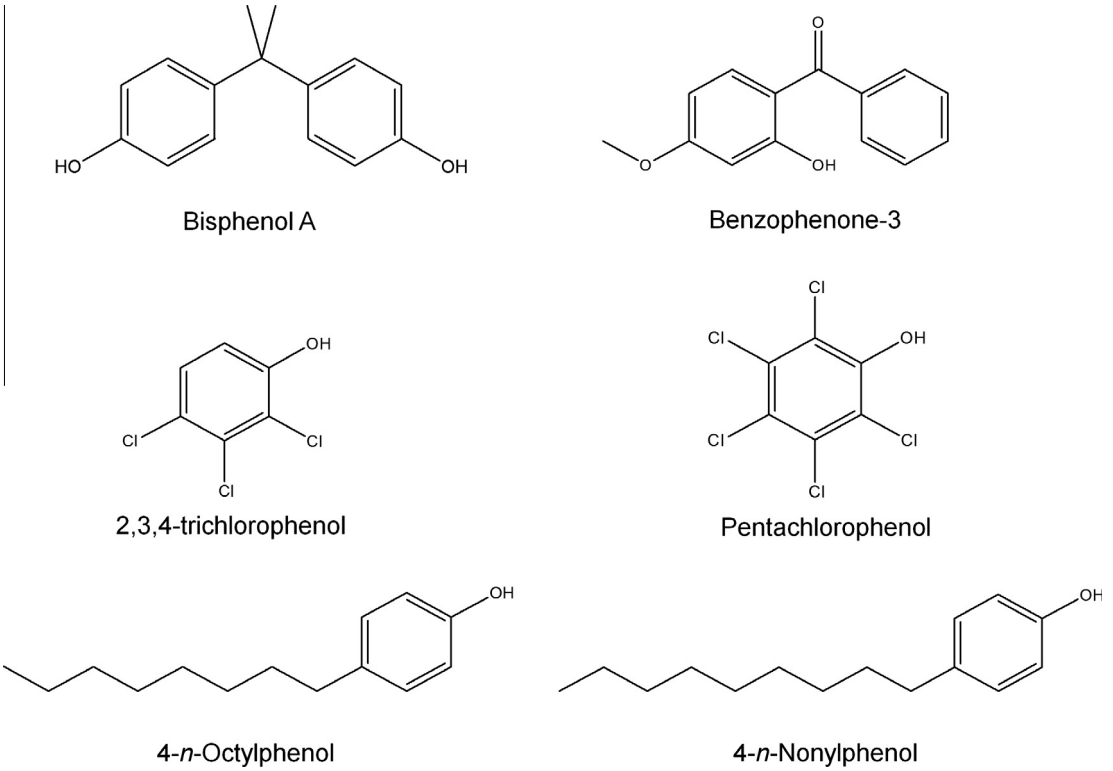

Fig. 1. Chemical structures of phenols determined in this study.

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