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Association between ambient particulate matter exposure and semen quality in Wuhan, China

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ABSTRACT

Background: Health effects of exposure to particulate matter (PM) on male reproductive health remain unclear. Only a limited number of studies have investigated the effects of $PM_{2.5}$ or PM_{10} exposure on semen quality, and the results were largely inconsistent.
Objectives: To quantitatively assess the exposure-response association between PM exposure and semen quality in Chinese men who were exposed to a wide concentration range of PM.
Methods: We investigated 1759 men from Wuhan, China, who were partners of women undergoing assisted reproductive technology procedures, and had semen examined at least once between 2013 and 2015. Individual $PM_{2.5}$ and PM_{10} exposures during 0–90, 0–9, 10–14 and 70–90 days before each semen examination (corresponding to the entire and three key periods of sperm development, respectively) were retrospectively estimated by inverse distance weighting interpolation. Linear mixed models were used to assess exposure-response relations of PM exposure with sperm concentration, count and motility.
Results: $PM_{2.5}$ exposure during 0–90 lag days ranged from 27.3 to 172.4 μg/m^3. It was linearly and inversely associated with sperm concentration (β: −0.20; 95% CI: −0.34, −0.07) and count (−0.22; −0.35, −0.08). For the three key exposure periods, only $PM_{2.5}$ exposure during the 70–90 lag days was significantly associated with sperm concentration (−0.12; −0.22, −0.03) and count (−0.12; −0.21, −0.02). Sensitivity analyses for a subgroup ($n = 1146$) excluding subjects with abnormal sperm concentration, count or motility yielded similar results. Compared with $PM_{2.5}$, we found generally similar associations for PM_{10} exposure in relation to sperm concentration and count, except that the associations appeared to be nonlinear with inverted J-shaped relationships. Neither $PM_{2.5}$ nor PM_{10} exposure was significantly associated with sperm motility (all $p > 0.05$).
Conclusions: Our results suggest that ambient PM exposure during sperm development adversely affects semen quality, in particular sperm concentration and count.

1. Introduction

The health effects of ambient particulate matter (PM) have drawn much public health concern globally. China is currently suffering from severe air pollution due to its rapid socioeconomic development. In 2015, the annual mean $PM_{2.5}$ (particulate matter < 2.5 μm in aerodynamic diameter) and PM_{10} concentrations in 74 cities in China were 55 and 93 μg/m^3 respectively, which were 5 and 4 times more than

Abbreviations: $PM_{2.5}$, particulate matter < 2.5 μm in aerodynamic diameter; PM_{10}, particulate matter < 10 μm in aerodynamic diameter; IDW, inverse distance weighting; WHO, World Health Organization; AQI, air quality index; BMI, body mass index; SD, standardized deviation; 95% CI, 95% confidence interval; IQR, interquartile range; df, degree of freedom; FDR, false discovery rate; ROS, reactive oxygen species.

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those recommended by the World Health Organization (WHO) air quality guidelines for $PM_{2.5}$ (10 μg/m^3) and PM_{10} (20 μg/m^3) (Ministry of Environmental Protection of China, 2015; World Health Organization, 2005). PM exposures have been associated with a variety of adverse effects, ranging from subclinical outcomes to deaths (Brook et al., 2013; Dominici et al., 2006; Rice et al., 2015; Zhou et al., 2016). The effects of PM on reproductive health have gained increasing interest recently (Cao et al., 2015; Hansen et al., 2010; Trasande et al., 2016). As an important cause of infertility, poor semen quality has been suggested to be associated with PM exposure *in vivo* (Cao et al., 2015; Pires et al., 2011). However, the association has only been investigated in a very limited number of epidemiological studies, and the results remain largely inconsistent.

In 2006 and 2010, two studies in the US reported no significant effects of $PM_{2.5}$ or PM_{10} on any semen quality outcome (Hansen et al., 2010; Sokol et al., 2006). Another study by Hammoud et al. reported that $PM_{2.5}$ exposure was significantly related to reduced sperm motility 2–3 months after exposure (Hammoud et al., 2010); in contrast, two studies in China and Poland found significant associations between PM and decreased sperm morphology (Radwan et al., 2016; Zhou et al., 2014). Due to the inconsistent results and study limitations such as selection bias, inaccurate individual PM exposure assessment and small sample size, all these studies emphasized the needs for further research. Another important limitation of the current studies is that they have assumed a linear exposure-response association between PM exposure and semen quality, which means that the incremental effect of an increase in PM on semen quality is the same for all PM exposure (Hansen et al., 2010; Radwan et al., 2016; Santi et al., 2016; Sokol et al., 2006; Zhou et al., 2014). In many occasions, the assumption of linearity may not be met (Greenland, 1995). Understanding the shape of exposure-response association is crucial for public health assessment, and departures of the association from linearity may have important consequences (Levy, 2003).

Most studies focused on air pollution and semen quality considered PM exposure in the recent 90 days before semen collection (Radwan et al., 2016; Selevan et al., 2000; Zhou et al., 2014), because the development of sperm takes approximately 90 days (Johnson et al., 1997). It should be noted that the sperm development included three different key periods: 0–9, 10–14, and 70–90 days before semen ejaculation, which correspond to epididymal storage, development of sperm motility, and spermatogenesis, respectively. It is of interest and importance to identify how much each key period of sperm development was affected by PM exposure. Unfortunately, only two studies have considered different exposure periods (Hansen et al., 2010; Sokol et al., 2006), and the available evidence remains inconclusive.

The aim of this study is to quantitatively examine the potential adverse effects of ambient $PM_{2.5}$ and PM_{10} exposures during the entire and each key period of sperm development on semen quality (sperm concentration, sperm count, and sperm motility) in Chinese men who were exposed to a wide concentration range of PM, and further identify which stage of sperm development PM exposure mainly affects. We conducted relatively accurate exposure assessment on individual PM using the inverse distance weighting (IDW) interpolation, and for the first time examined the nonlinear association between ambient PM exposure and semen quality.

2. Material and methods

2.1. Study design and population

We conducted an observational study at the Reproductive Medical Center, Tongji Hospital in Wuhan, China. Between March 27, 2013 and December 31, 2015, 2065 men living in central Wuhan visited the center and had at least one semen examination, because their partners underwent assisted reproductive technology procedures. To minimize confounding by semen abnormalities unrelated to PM exposure (Hansen et al., 2010), we excluded 306 (14.8%) men with at least one known condition that might be associated with poor semen quality, including sexually transmitted diseases ($n = 4$), mumps ($n = 145$), urethral surgery ($n = 8$), testicular surgery ($n = 8$), epididymis surgery ($n = 2$), vasectomy surgery ($n = 4$), retrieve sperm difficulty ($n = 6$), absent epididymis ($n = 3$), absent vasectomy ($n = 2$), azoospermia ($n = 68$), varicocele ($n = 22$), chromosomal abnormality ($n = 13$), and abstinence period of <2 days or >7 days ($n = 70$) (World Health Organization, 2010). Finally, we included 1759 men as the study subjects who underwent a total of 2184 semen examinations. Ethics approval for this study was obtained from the Ethical Committee of Hubei Provincial Center for Disease Control and Prevention. The requirement for informed consent was waived by the committee, because the data used in this study were generated from previously routine clinical procedures and were anonymous to the research investigators.

2.2. Data sources

We obtained daily average $PM_{2.5}$ and PM_{10} air quality indices (AQIs) that were published daily by the Wuhan Environmental Protection Bureau. The AQIs have been available since December 27, 2012. According to the national standard operating procedures for air quality monitoring (Ministry of Environmental Protection of China, 2012b), we converted the AQIs to concentrations in μg/m^3 to make our results comparable with those from other studies. $PM_{2.5}$ and PM_{10} concentrations were continuously measured at each of 9 fixed state-controlled air quality monitoring stations located in central Wuhan (Fig. 1). Among the 1100 days between December 27, 2012 and December 31, 2015 for the nine monitoring stations, there were 148 (missing rate: 148/9900 = 1.5%) and 183 (1.8%) missing daily average concentrations for $PM_{2.5}$ and PM_{10} respectively. Data on daily ambient average temperature (in Celsius) in Wuhan between the same period (100% complete) were obtained from the Wuhan Regional Climate Center.

Demographic, anthropometric and lifestyle data, including residence address, date of birth, height, weight, ethnic, education, cigarette smoking and alcohol consumption were obtained from the center, which were routinely collected by clinical doctors. For each subject, the information on lifestyle data were collected for the past 6 months prior to semen examination. Body mass index (BMI, in kg/m^2) was calculated as weight divided by the square of height.

The subjects were asked for number of abstinence days and then masturbate into a sterile plastic specimen container in a semen collection room. The samples were then liquefied in a heating chamber within 60 min and tested for semen quality parameters according to the WHO 5th laboratory manual for the examination and processing of human semen (World Health Organization, 2010). Semen volume was measured using a serologic pipette. A computer-aided semen analysis system (CASA, WLJY9000, Weili New Century Science & Tech Dev., Beijing, China) was used to test sperm concentration and sperm motility. The sperm concentration was multiplied by semen volume to calculate sperm count. The sperm motility parameters included progressive motility and non-progressive motility. Total motility was calculated as progressive motility + non-progressive motility.

2.3. Exposure assessment

We retrospectively assessed individual exposures to $PM_{2.5}$ and PM_{10} during the entire (0–90 lag days) and three key periods (0–9, 10–14, and 70–90 lag days) of sperm development for each subject. First, the residence addresses for all subjects at the date of semen examination and the 9 monitoring stations were geocoded by the Baidu Map API (http://lbsyun.baidu.com/) to obtain their longitude and latitude coordinates. The spatial distribution of study subjects' residence addresses and monitoring stations in Wuhan are presented in Fig. 1. The median distance between subjects' residence addresses and the nearest monitoring stations was 3.32 km, ranging from 0.05 to 23.90 km; over 95%