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Ambient air pollution and semen quality

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ABSTRACT

Background: Ambient air pollution is associated with systemic increases in oxidative stress, to which sperm are particularly sensitive. Although decrements in semen quality represent a key mechanism for impaired fecundability, prior research has not established a clear association between air pollution and semen quality. To address this, we evaluated the association between ambient air pollution and semen quality among men with moderate air pollution exposure.

Methods: Of 501 couples in the LIFE study, 467 male partners provided one or more semen samples. Average residential exposure to criteria air pollutants and fine particle constituents in the 72 days before ejaculation was estimated using modified Community Multiscale Air Quality models. Generalized estimating equation models estimated the association between air pollutants and semen quality parameters (volume, count, percent hypo-osmotic swollen, motility, sperm head, morphology and sperm chromatin parameters). Models adjusted for age, body mass index, smoking and season.

Results: Most associations between air pollutants and semen parameters were small. However, associations were observed for an interquartile increase in fine particulates ≤ 2.5 μm and decreased sperm head size, including -0.22 (95% CI -0.34, -0.11) μm^2 for area, -0.06 (95% CI -0.09, -0.03) μm for length and -0.09 (95% CI -0.19, -0.06) μm for perimeter. Fine particulates were also associated with 1.03 (95% CI 0.40, 1.66) greater percent sperm head with acrosome.

Conclusions: Air pollution exposure was not associated with semen quality, except for sperm head parameters. Moderate levels of ambient air pollution may not be a major contributor to semen quality.

1. Introduction

Air pollution has been associated with a broad array of health effects, including cardiovascular disease morbidity and mortality (Langrish et al., 2012; Shah et al., 2015), even at the relatively moderate levels observed in the United States (Kaufman et al., 2016). Ambient air pollution exposure is associated with systemic increases in inflammation and oxidative stress (Chin, 2015), which may underlie prior reproductive health findings regarding the relation between air pollution and pregnancy loss and reduced fecundability (Checa Vizcaino et al., 2016). However, prior research has not determined whether reproductive effects of air pollution are due to male and/or female factors, as partners are typically exposed to similar levels of ambient air pollution. Semen quality is a sensitive marker for exposure to environmental pollution, as evidenced by associations with exposure to heavy metals, pesticides and phthalates (Gabrielsen and Tanrikut, 2016), and air pollution may affect male fecundability through adverse effects on semen quality.

While reactive oxygen species play a crucial role in spermatogenesis and fertilization, sperm are particularly sensitive to adverse impacts of oxidative stress (Du Plessis et al., 2015). Excesses in oxidative stress are associated with damage to sperm chromatin, peroxidation of sperm

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membranes, impaired motility and increases in apoptosis (Aitken et al., 2015; Du Plessis et al., 2015). Although systemic inflammation may directly lead to poorer semen quality through obstruction of sperm transport, impaired accessory gland functions and dysregulation of spermatogenesis, a key mechanism linking inflammation to poorer semen quality is the production of free radicals by leukocytes, contributing to oxidative stress (Azenabor et al., 2015). In a review of randomized trials of antioxidant supplementation among men with abnormal semen parameters, Ahmadi et al. noted a strong possibility of efficacy of supplementation in improving semen quality parameters (Ahmadi et al., 2016).

Prior epidemiologic research has reported inconsistent associations between air pollution and semen quality. A recent systematic review noted suggestive evidence of an association between air pollution and poorer sperm morphology, a weak association with DNA fragmentation and inconclusive associations with sperm motility and sperm count (Lafuente et al., 2016). Another meta-analysis found no statistically significant associations between air pollutants and semen quality parameters, although air pollutants appeared to be associated with a trend of decreased semen concentration and motility (Deng et al., 2016). Although several individual studies have reported impaired semen quality associated with particulate matter (Hammoud et al., 2010; Radwan et al., 2016; Wu et al., 2017; Zhou et al., 2014) and occupational exposure to vehicle exhaust (Calogero et al., 2011; Guven et al., 2008), the variation between studies in geographic region, study population and methods of assessment of both air pollution and semen quality parameters limits generalizability of findings.

More research is needed to determine whether air pollution adversely affects semen quality, and whether moderate levels of air pollution in countries such as the United States that fall below the World Health Organization air quality guidelines (World Health Organization, 2006) may be associated with decrements in semen quality. To date, studies in areas with moderate air pollution exposure have mostly utilized data from ambient air monitoring to assess exposure, which may lead to misclassification, and have only assessed the association of air pollution with a few semen quality endpoints (Hammoud et al., 2010; Hansen et al., 2010; Sokol et al., 2006). To address the need for additional research, we evaluated the association of residential exposure to ambient air pollutants, estimated using the Community Multiscale Air Quality (CMAQ) model, with 35 semen quality measures among men enrolled in a longitudinal time-to-pregnancy study exposed to moderate levels of air pollution. We hypothesized that greater exposure to ambient air pollutants would be associated with adverse effects on semen quality.

2. Materials and methods

The Longitudinal Investigation of Fertility and the Environment (LIFE) Study was conducted among 501 couples attempting pregnancy between 2005 and 2009 in Michigan (n = 104) and Texas (n = 397). Details of the study are fully described elsewhere (Buck Louis et al., 2011). Eligibility criteria include being married or in a committed relationship, being age 18 years or older, being able to communicate in English or Spanish and not having physician-diagnosed infertility. Couples were followed until pregnancy or up to one year of actively trying to become pregnant. This study was approved by the institutional review boards for all collaborating institutions, and couples provided written informed consent.

2.1. Criteria air pollutants and constituents of particulate matter

Ambient air pollution levels were estimated for each participant's residence. Participants' residential addresses were geocoded using ArcGIS software (Redlands, CA). Mean daily exposure to criteria air pollutants (sulfur dioxide [SO_2], nitrogen oxides [NO_X], nitrogen dioxide [NO_2], carbon monoxide [CO], ozone [O_3], particulate matter < 10 μm [PM_{10}] and fine particulate matter < 2.5 μm [$PM_{2.5}$]) and constituents of $PM_{2.5}$ (elemental carbon [AEC], organic compounds [AOC], sulfate [ASO_4], ammonium [ANH_4] and nitrate [ANO_3]) was estimated using modified Community Multiscale Air Quality (CMAQ) models and linked to residential address (Foley et al., 2010). The CMAQ models use the United States Environmental Protection Agency (US EPA) National Emissions Inventory and meteorological data generated by the Weather Research and Forecasting model to predict raw hourly estimates of pollution levels after adjusting for atmospheric photochemical properties of pollutants. To reduce measurement error, raw CMAQ estimates were fused with observed data from air monitors within the US EPA Air Quality System using inverse distance weighting. Performance of the modified CMAQ model has been previously reported (Chen et al., 2014).

Daily air pollution levels were calculated for all days in which the participant was enrolled in the study, and for 30 days prior to enrollment for couples attempting pregnancy for 0–1 months prior to enrollment (409, 81.8%) and for 60 days prior to enrollment for couples attempting pregnancy for two months prior to enrollment (91, 18.2%). Daily air pollution levels were then averaged across the 72 day window prior to ejaculation to evaluate chronic air pollution exposure during spermatogenesis, as well as for 0–14, 15–29, 30–44, 45–59 and 60–72 day windows prior to ejaculation to evaluate timing of exposure during spermatogenesis (Heller and Clermont, 1963). One couple's address could not be geocoded, leaving 500 couples available for analyses.

2.2. Semen quality parameters

A total of 473 participants provided at least one semen sample, and 378 provided a second semen sample approximately one month later. An established at-home collection protocol was used (Buck Louis et al., 2014). Participants were asked to ejaculate into a glass collection jar through masturbation without use of lubricants after abstaining from intercourse for two days. Participants recorded the date and time of collection, their last day of ejaculation and any spillage, and were asked to place a sperm migration straw (Vitrotubes #3520 VintroCom) plugged at one end and filled with hyaluronic acid into the ejaculate to capture sperm motility at the time of sample collection. Semen samples were shipped overnight in insulated containers with cold packs and a temperature data logger (I-Button, Maxim Integrated) and analyzed within 24 h by the National Institute of Occupational Safety and Health (NIOSH) Andrology Laboratory (Cincinnati, OH).

Thirty-five semen quality parameters were assessed. Six general semen quality parameters included semen volume (mL); 24-h motility (%), measured using the HTM-IVOS (Hamilton Thorne) computer-assisted semen analysis system; distance travelled in the migration straw (mm) as a measure of motile sperm at collection; sperm count (millions/mL), measured using the IVOS system and the IDENT stain; total sperm count (millions), calculated as sperm count multiplied by semen volume; and hypo-osmotic swollen (%), using the hypo-osmotic swelling assay. Seven additional motility measures, including average path velocity (μm/sec), straight-line velocity (μm/sec), curvilinear velocity (μm/sec), amplitude of lateral head (μm), beat cross frequency (Hz), straightness (%) and linearity (%), were assessed using the HTM-IVOS. Six sperm head measures, including sperm head length (μm), area (μm^2), width (μm), perimeter (μm), elongation factor width/length (%) and sperm head with acrosome (%), were measured using the IVOS METRIX system.

Fourteen morphology measures, including strict criteria (%), World Health Organization (WHO) normal criteria (%), amorphous (%), round (%), pyriform (%), bicephalic (%), taper (%), megalo head (%), micro head (%), neck and midpiece abnormal (%), coiled tail (%), other tail abnormalities (%), cytoplasmic droplet (%) and immature sperm (# immature) were measured by Fertility Solutions (Rothmann et al., 2013; World Health Organization, 1992). Two sperm chromatin