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Personal exposure to particulate matter and inflammation among patients with periodontal disease

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HIGHLIGHTS

- Adults with periodontal diseases are sensitive to $PM_{2.5}$-induced effects.
- $PM_{2.5}$ can induce greater inflammatory responses among female adults.
- Adults with BMI over 25 are at higher risk of PM-induced inflammation.

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ABSTRACT

The association between particulate air pollution and high-sensitivity C-reactive protein (hs-CRP) has been well documented in epidemiological studies. Periodontitis has been linked to elevated hs-CRP levels in recent studies. It is still unknown whether patients with periodontal infections are more susceptible to particulate air pollution. The aim of this study was to investigate whether particles with aerodynamic diameters of less than 2.5 μm ($PM_{2.5}$) had greater effects on increasing hs-CRP among patients with periodontal infections compared to periodontally healthy individuals. We conducted a cross-sectional study on two panels of adult subjects, 100 adult patients with chronic periodontitis and 100 periodontally healthy adults, in order to evaluate the association between particulate matter (PM) and hs-CRP. We collected blood samples from each subject, measured hs-CRP and monitored average exposure to $PM_{2.5}$ over 24 h four times during 2010 to 2012. We used mixed-effects models to estimate the association between $PM_{2.5}$ and hs-CRP and adjusted for cardiovascular risk factors. We found that a 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 3.22% (95% confidence interval, CI: 1.21, 5.23; $p < 0.01$) increase in hs-CRP among all adult subjects. The effect of $PM_{2.5}$ in patients was significantly higher than the effect in healthy participants. In the healthy adult panel, a 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 1.17% (95% CI: 0.54, 1.80; $p < 0.01$) increase in hs-CRP. For adults in the patient group, a 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 9.62% (95% CI: 7.05, 12.19; $p < 0.01$) increase in hs-CRP. We concluded that personal exposure to $PM_{2.5}$ was associated with increases in hs-CRP among adult subjects. The presence of periodontal disease led to a considerably increased effect magnitude by more than eight fold.

1. Introduction

The association of particulate air pollution with cardiovascular morbidity and mortality has been demonstrated in previous epidemiological studies (Pope and Dockery, 2006; Samet et al., 2000). The main proposed mechanism linking particulate air pollution to cardiovascular diseases is the effect of particulate matter (PM) on cardiopulmonary systems through pulmonary inflammation that develops into a systemic inflammatory response (Book et al., 2010). High-sensitivity C-reactive

Abbreviations: 8-OHdG, 8-hydroxy-2-deoxyguanosine; CI, confidence interval; hs-CRP, high-sensitivity C-reactive protein; $PM_{2.5}$, particles with aerodynamic diameters of less than 2.5 μm.

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protein (CRP) is released in response to diverse inflammatory stimuli; it is recognized as a biomarker of systemic inflammation (Salzberg et al., 2006) and a predictor for cardiovascular disease risk (Paraskevas et al., 2008). Several studies explored the relationship between hs-CRP and particulate air pollutants and reported that elevated hs-CRP was associated with increased levels of particles with aerodynamic diameters of less than 10 μm (PM_{10}) and 2.5 μm ($PM_{2.5}$) in human subjects (Chuang et al., 2007; Hoffmann et al., 2009; Schwartz, 2001). The elderly and patients with cardiopulmonary diseases tend to be more susceptible to PM-induced inflammatory responses (Goldberg et al., 2000; Sunyer et al., 2000; Zanobetti et al., 2000).

Recently, several epidemiological findings showed that patients with periodontal diseases had higher CRP levels compared to periodontally healthy subjects (Loos et al., 2000; Noack et al., 2001; Slade et al., 2000). Periodontal diseases are destructive inflammatory diseases of the tissues that support the teeth and are classified into three main types, including aggressive periodontitis, chronic periodontitis and periodontitis as the manifestation of systemic disease (Picolos et al., 2005). Periodontal diseases and particulate air pollution have each been linked to an increased risk of systemic inflammation; however, the interactions among periodontal infection, particulate air pollution exposure and systemic inflammation are poorly understood. It is biologically plausible that patients with periodontal infections might be susceptible to particulate air pollution. Accordingly, we designed this study to investigate whether $PM_{2.5}$ had greater effects on increasing hs-CRP among patients with periodontal infections compared to periodontally healthy individuals.

2. Materials and methods

2.1. Study participants and study design

This panel study was designed to monitor changes in blood markers and particulate air pollution exposure in study participants from 2010 to 2012. There were 100 adult patients with chronic periodontitis and 100 periodontally healthy adults in this study. These participants were recruited from colleges and universities in the Taipei metropolitan area. The selection criteria for study participants with chronic periodontitis were as follows: probing depth of ≥5 mm and/or clinical attachment loss in more than 8 teeth with varying degrees of disease severity, local factors concomitant with the amount of destruction and a moderate rate of progression. The selection criterion for periodontally healthy subjects was no evidence of attachment loss. The exclusion criteria for all study participants were as follows: smoking (current and former), drinking (current and former) and cardiopulmonary diseases such as coronary artery disease, diabetes mellitus, chronic obstructive pulmonary disease (COPD), asthma and influenza associated with increased inflammatory response. A dental examination was performed by a dentist for each potential study participant and each patient's medical history was recorded by a professionally trained study nurse. Three hundred fifty-four subjects responded to our recurring advertisement for adult patients with chronic periodontitis in the campus bulletin board system, 100 of them (28%) met the criteria and were willing to participate in this study after our protocol had been explained.

The protocol included four visits that entailed continuous 24-hour monitoring of $PM_{2.5}$ and the collection of a blood sample from each study participant between February and November of 2010, 2011 or 2012. We collected one blood sample per 3 month period; collections occurred in February, May, August, and November. The average time between visits was approximately 90 days. The sampling date and time were recorded for each study participant to match with $PM_{2.5}$ and weather data. In case of a failed measurement such as equipment failure or unable to follow participant, the measurement was repeated on another day. The ethics committee at the St. Mary's Medicine Nursing and Management College in Yilan County, Taiwan approved this study. Written informed consent was obtained from each study participant before the study began.

2.2. Blood markers of inflammation and oxidative stress

The study nurse took a 10-ml fasting blood sample every visit from each study participant at the end of the sampling day (0800 h the next day) and kept the sample on ice until centrifugation. All blood samples were centrifuged in a refrigerated centrifuge and stored at −80 °C before being assayed. The inflammatory marker hs-CRP was detected in serum with a two-site chemiluminescent enzyme immunometric assay (IMMULITE hs-CRP; Diagnostic Products Corp., CA). The oxidative stress marker oxidative DNA adduct 8-hydroxy-2-deoxyguanosine (8-OHdG) was also measured by an enzyme-linked immunosorbent assay (ELISA) based on monoclonal antibody N45.1 (Japan Institute for the Control of Aging, Fukuroi City, Japan).

2.3. Personal exposure measurements of particulate matter and meteorological conditions

Personal exposure to $PM_{2.5}$ was measured using a personal dust monitor (DUST-check Portable Dust Monitor model 1.108; temperature and humidity sensor, model 1.153FH; Grimm Labortechnik Ltd., Ainring, Germany), which measured and recorded 1-minute mass concentrations of $PM_{2.5}$ and ambient temperature and humidity. To measure our participants' personal PM exposure, a well-trained technician carrying a DUST-check monitor was asked to accompany each participant from 0800 h to 0800 h the next day. After sampling, we summarized 1-minute $PM_{2.5}$, temperature and humidity measurements with 24-hour averages and obtained 800 segments of 24-hour averages of $PM_{2.5}$, temperature and humidity for all study participants (i.e., four measurements of PM and meteorological measurements for each study participant) for the data analysis.

2.4. Statistical analysis

A Student's t-test was used to compare $PM_{2.5}$ concentrations, meteorological conditions, hs-CRP and 8-OHdG levels between the two panels. A generalized additive mixed model (Dominici et al., 2002) was applied to examine the association between $PM_{2.5}$ and HRV using the R statistical software, version 3.0.3. We treated each subject's sex and age as time-invariant variables, whereas body mass index (BMI), 24-hour mean $PM_{2.5}$, temperature and humidity, and blood markers were time-varying variables in all models. The outcome variables were hs-CRP and 8-OHdG and the exposure variables were 24-hour average $PM_{2.5}$. The study participants' sex, age, BMI and 24-hour mean $PM_{2.5}$ were considered fixed effects and participant identity was a random effect. The models also adjusted for 24-hour mean temperature (5 degrees of freedom), 24-hour mean humidity (4 degrees of freedom) and visit date (6 degrees of freedom), as fit by penalized cubic regression splines, to reflect possible nonlinear effects of continuous covariates and control for the potential confounding effect of weather and seasonality.

Effect modification by periodontal disease (Yes vs. No), BMI (>25 (overweight) vs. ≦25 (normal)) (WHO, 2009) and sex (Female vs. Male) was assessed in a separate generalized additive mixed model by including interaction terms between $PM_{2.5}$ effect and each potential effect modifier among all participants. Model selections were based on minimizing Akaike's Information Criterion (AIC). Effects of 24-hour mean $PM_{2.5}$ on hs-CRP and 8-OHdG were expressed as percent changes per 10 $\mu g/m^3$ ($[\beta \times 10 \div M] \times 100\%$), where β and M are the estimated regression coefficient and the mean of each blood marker, respectively.