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Association of ultrafine particles with cardiopulmonary health among adult subjects in the urban areas of northern Taiwan

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HIGHLIGHTS

- UFPs are associated with increased blood pressure and systemic inflammation.
- The negative trend between UFPs and FEV_1 is observed among healthy adults.
- Effects of UFPs on cardiovascular health are greater than other air pollutants.

GRAPHICAL ABSTRACT

The table shows percentage changes (95% confidence interval) in health data for an interquartile range change in ultrafine particles (0.97 μg/m^3) among 100 adult subjects. All models were adjusted for sex, age, body mass index, day of week, season, temperature and relative humidity.

Health data	Ultrafine particles
Systolic blood pressure	6.3 (2.9, 9.7)*
Diastolic blood pressure	5.6 (4.1, 7.1)*
Forced expiratory volume in 1 second	-1.8 (-3.8, 0.2)†
High sensitivity-C-reactive protein	8.5 (3.9, 13.1)*

† p-value < 0.10 (marginally significant)
* p-value < 0.05 (statistically significant)

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ABSTRACT

The association between short-term exposure to particulate air pollution, especially fine particles, and cardiopulmonary health has been well-established in previous studies. However, previous findings regarding the effect of ultrafine particles (UFPs) on cardiopulmonary health are inconsistent. We repeatedly measured the mass concentrations of UFPs using a Micro-Orifice Uniform Deposit Impactor (MOUDI) in the apartments of 100 adult participants and collected the participants' health data from the pulmonary outpatient unit of Shuang-Ho Hospital to investigate the association between short-term exposure to UFPs and cardiopulmonary health using mixed-effects models from January 1, 2014 to August 31, 2017. We also collected ambient air pollution monitoring data from the Taiwan Environmental Protection Administration for data analysis. We observed that an interquartile range increase in the 24-hour mean UFPs (0.97 μg/m^3) was associated with a 6.3% [95% confidence interval (CI) = 2.9, 9.7], 5.6% (95% CI = 4.1, 7.1) and 8.5% (95% CI = 3.9, 13.1) increase in systolic blood pressure, diastolic blood pressure and high sensitivity-C-reactive protein, respectively. We also observed the association of particulate matter less than or equal to 2.5 μm in diameter and nitrogen dioxide with increased blood pressure and ozone with decreased lung function. A negative trend between UFPs and forced expiratory volume in the first

Abbreviations: DBP, diastolic blood pressure; FEV_1, forced expiratory volume in the first second; hs-CRP, high sensitivity-C-reactive protein; IQR, interquartile range; NO_2, nitrogen dioxide; O_3, ozone; PM_{10}, particulate matter less than or equal to 10 μm in diameter; $PM_{2.5}$, particulate matter less than or equal to 2.5 μm in diameter; SBP, systolic blood pressure; UFPs, ultrafine particles.

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second was observed. We concluded that short-term exposure to UFPs was associated with cardiovascular health in adult subjects in the urban areas of northern Taiwan.

1. Introduction

Previous epidemiology studies have established the association between short-term exposure to particulate matter (PM) and cardiopulmonary morbidity and mortality (Li et al., 2016; Lu et al., 2015; Requia et al., 2017). The association seems to be more evident as the PM size is reduced (Schwartz et al., 1996). The biological mechanism linking PM, especially particulate matter less than or equal to 2.5 μm in diameter ($PM_{2.5}$), and adverse health effects has been partially elucidated in previous *in vitro*, *in vivo* and controlled human exposure studies (Book et al., 2010). Ultrafine particles (UFPs), defined as particulate matter less than or equal to 0.1 μm in diameter, comprise the greatest number but the least mass concentration compared with coarse and fine particles (Nel et al., 2006). It has been hypothesized that this size fraction could be a uniquely toxic matter for adverse health effects (Seaton et al., 1995) according to a previous *in vivo* study. The study demonstrated that titanium dioxide (TiO_2) with an average particle diameter of approximately 20 nm induced greater lung inflammatory responses than equal mass concentrations of TiO_2 with an average particle diameter of approximately 250 nm. However, the fate, toxicity and cellular mechanisms of UFPs have not been thoroughly elucidated to date. The findings regarding UFP-induced adverse effects from recent *in vitro* and *in vivo* studies are also inconsistent (Meldrum et al., 2017).

Human contact with UFPs in the workplace and environment is increasing. Occupational exposure to UFPs during nanomaterial production and handling processes has been well-demonstrated in previous studies (Ding et al., 2017). The effect of UFPs on the respiratory system among workers has also been reported in case reports (Buerke et al., 2002; Journeay and Goldman, 2014). Recently, the association of ambient UFP exposure with cardiopulmonary morbidity and mortality has been investigated in epidemiological studies (Atkinson et al., 2010; Lanzinger et al., 2016a; Lanzinger et al., 2016b). However, the study findings are inconsistent. Several panel studies have explored the association between short-term exposure to UFPs and biological markers for cardiopulmonary diseases (Karottki et al., 2015; Park et al., 2017; Rich et al., 2012; Toledo et al., 2017; Weichenthal et al., 2014). The results are also inconsistent across outcomes. One explanation for the inconsistent results of UFP-induced cardiopulmonary morbidity, mortality or adverse effects could be the measurement error due to high spatial and temporal variability or the distance of monitors from sources of UFPs (Lanzinger et al., 2016a; Zhu et al., 2002). Apparently, more extensive epidemiological studies are needed using air samplers to measure UFP exposure at individual locations. Therefore, we designed this study to measure the daily UFP levels using a high-volume air sampler at individual locations and measured the blood pressure, high sensitivity-C-reactive protein (hs-CRP) and forced expiratory volume in 1 s (FEV_1) related to the increased risk of cardiopulmonary diseases (Book et al., 2010; Ranu et al., 2011) from a panel of adult participants to explore the association between short-term exposure to UFPs and cardiopulmonary health.

2. Materials and methods

2.1. Study participants and health data

The study panel consisted of 100 adult participants from Taipei-Keelung metropolitan area, including Taipei City, New Taipei City, and Keelung City. They were recruited from the pulmonary outpatient unit of Shuang-Ho Hospital from January 2014 to May 2017. The selection criteria were non-smoking adult persons with an age range of 20 to 64 years without asthma, bronchitis, cancer, cardiovascular diseases, chronic obstructive pulmonary disease and obstructive sleep apnea syndrome. Each participant was repeatedly interviewed and examined three times occurring at one-month intervals from January 1, 2014 to August 31, 2017. The health data on sex, age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), FEV_1 and hs-CRP were collected from each participant in the fasting condition in the morning during each time. Blood pressure was calculated as the average of two seated blood pressure readings using a mercury sphygmomanometer. Lung function was examined using the Vitalograph Spirotac V™ system. Enzyme-linked immunosorbent assay (ELISA) was used to determine the levels of hs-CRP (CRP; R&D Systems, Minneapolis, MN, USA). The study protocol was approved by the joint institutional review board at the Taipei Medical University in Taipei, Taiwan (TMU-JIRB No. 201410032).

2.2. Ultrafine particle data

The Micro-Orifice Uniform Deposit Impactor (MOUDI™; MSP Inc., Minneapolis, MN, USA) with a flow rate of 30 L/min was used to repeatedly collect particles with a size range between 0.05 and 0.1 μm (UFPs) in each participant's apartment three times. We placed the MOUDI sampler in front of the entrance (27%), in the living room (73%) or on the roof (10%) of the participant's apartment (second floor: 74%; third floor: 26%) and collected UFPs on 37-mm Teflon™ (polytetrafluorethylene [PTFE]) filters (Pall Corporation, Ann Arbor, MI, USA). One hundred UFP samples were collected from 8:00 am to 8:00 am the next day (24 h) before the measuring date of the health data. A laboratory blank and field blank without a running system were used for each sample to assess any contamination that occurred in the laboratory during the filter conditioning and weighing processes or in the field during the filter assembly and transportation processes.

2.3. Ambient air pollution data

Daily (24-hour mean) particulate matter less than or equal to 10 μm in diameter (PM_{10}), $PM_{2.5}$, nitrogen dioxide (NO_2), ozone (O_3), temperature and relative humidity were collected from air monitoring stations operated by the Taiwan Environmental Protection Administration (EPA) in the Taipei-Keelung metropolitan area. The data from the nearest air monitoring station, which was within 10 km from his/her address, were used to represent the participant's ambient air pollution exposure. Such ambient air pollution data were merged by the date before the measurement date of the health data for statistical analysis.

2.4. Statistical analyses

We employed R Statistical Software, V.3.4.1 (Development Core Team, 2008) to perform summary statistics for air pollution and health data, Pearson's correlation for air pollutants and mixed-effects models to investigate the association between the air pollutants and biological markers for cardiopulmonary diseases. The nlme package was used to fit the mixed-effects model. The dependent variables were SBP, DBP, FEV_1 and hs-CRP, while the independent variables were daily UFPs, PM_{10}, $PM_{2.5}$, NO_2 and O_3. Sex, age, BMI, day of week and season (spring, summer, autumn and winter) were adjusted as confounding variables, while the daily temperature and humidity were fitted using a penalized cubic regression spline and were adjusted in all models. The