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Allergens, air pollutants, and childhood allergic diseases

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ABSTRACT

Background: The synergistic effect of allergens and air pollutants on the risk of allergic diseases is unclear.
Objective: To evaluate the joint effect of outdoor pollutants and indoor allergens on the risk of allergic diseases.
Methods: We enrolled 2661 kindergarten children from the CEAS cohort. Data on allergic diseases and environmental exposure were collected. Skin prick tests were performed. Individual exposure to air pollution was estimated using a geographic information system with the mean concentration of air pollutants. Multiple logistic regression analysis was performed to estimate the association between air pollutants, allergen exposure and the risk of allergic diseases with adjustments for potential confounders.
Results: Overall, 12.6% of the children had asthma, 30.0% had allergic rhinitis (AR), and 14.4% had atopic dermatitis (AD). Mite sensitization significantly increased the risk of AD, AR, and asthma (OR (95%CI) 2.15 (1.53–3.03), 1.94 (1.46–2.58), and 2.31 (1.63–3.29), respectively). Exposure to PM_{10}, $PM_{2.5}$, CO, and O_3 was associated with asthma (OR (95% CI) 1.39 (1.03–1.87), 1.45 (1.07–1.97), 1.36 (1.01–1.83), and 0.68 (0.51–0.92), respectively). $PM_{2.5}$ may have increased the risk of AR (OR (95% CI) 1.54 (1.03–2.32). Mite sensitization showed a synergistic effect with $PM_{2.5}$ on the development of asthma ($p < 0.001$). Moreover, mite allergens may modify the effect of air pollutants on allergic diseases.
Conclusion: Dust mites and $PM_{2.5}$ play an important role on the risk of asthma and AR. Exposure to $PM_{2.5}$ and mite allergens had a synergistic effect on the development of asthma. Avoiding co-exposure to allergens and air pollutants is important.

1. Introduction

Levels of traffic-related pollutants (TRAP) are increasing rapidly across many Asian countries in parallel with the level of urbanization and economic development (Leung et al., 2012). Air pollution increases asthma symptoms, the use of medication, bronchoconstriction, emergency room admissions and hospitalizations due to pollutants such as ozone (O_3), nitrogen dioxide (NO_2) and particulate matter (PM) (Sandström and Kelly, 2009). Prenatal exposure to $PM_{2.5}$ was reported to increase susceptibility to respiratory infections and may program respiratory morbidity in early childhood (Jedrychowski et al., 2013). Children appear to be most vulnerable to the harmful effects of ambient air pollutants. As their lungs have not completely developed, they may experience greater exposure to environmental pollutants than adults, and a higher amount of these pollutants may remain in their lungs for a greater duration (Tzivian, 2011). Particulate and gaseous pollutants can act on both the upper and lower airways to initiate and exacerbate cellular inflammation through interactions with the innate immune system (Bonay and Aubier, 2007).

In addition to air pollution, early and persistent allergic sensitization is known to be a risk factor for the development of asthma (Sly, 2011). Indoor allergens from dust mites, cockroaches and cats have been associated with asthma exacerbation in children (Sly, 2011). It has also been reported that allergen sensitization is associated with allergic diseases and also with air pollutants (Pénard-Morand et al., 2005). While many studies have focused on the association between TRAP and exacerbations of existing respiratory conditions, few studies have reported the impact of TRAP

Abbreviations: SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone; CO, carbon monoxide; PM_{10}, particulate matter $\leq 10\,\mu m$; $PM_{2.5}$, particulate matter $\leq 2.5\,\mu m$; $8hO_3$, 8-h average ozone concentration; AD, atopic dermatitis; AR, allergic rhinitis.

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Table 1
Comparison of basic demographics of the study population.

Characteristics	Study population ($n = 2661$)	All participants ($n = 3246$)
Age (years)[a]	5.5 ± 1.1	7.7 ± 1.6
Gender (male) (%)	54.1	54.1
Weight (kg)[a]	18.8 ± 3.9	19.6 ± 6.4
Height (cm)[a]	107.6 ± 8.5	108.9 ± 11.5
BMI (kg/m^2)[a]	16.2 ± 2.0	16.3 ± 2.3
Sleep duration (h)[a]	9.0 ± 1.2	8.9 ± 1.2
ETS exposure (%)	64.1	57.8
Family history of atopy (%)	55.9	55.0
Breast feeding (%)	75.8	74.7
Family income per year (%)		
<1,000,000 NT$	69.7	69.4
>1,010,000 NT$	30.3	30.6
Maternal age (years)[a]	34.2 ± 4.3	29.3 ± 4.5
Maternal education (%)		
<High school	27.6	27.4
≥High school	31.5	35.0
>College	40.8	37.7

Abbreviations: BMI, body mass index; ETS, environmental tobacco smoke; NT$, Taiwan dollar.
[a] Mean ± SD.

on the development of asthma and allergies over time. In addition, most of the studies on the relationship between exposure to air pollutants and the risk of asthma in children have been cross-sectional (Evans et al., 2014; Bowatte et al., 2015; Zhang et al., 2002).

Both air pollutants and allergens play important roles in the development of allergic diseases, however whether they synergistically increase the risk of developing allergic diseases is unclear. Therefore, the aim of this study was to evaluate the joint effect of long-term exposure to allergens and air pollutants on the risk of developing allergic diseases, and to investigate whether exposure to allergens modifies the effect of air pollutants on allergic diseases.

2. Methods

2.1. Study population

We conducted a school-based survey on allergic diseases in kindergarten children at 11 communities in Taipei in 2010 (Childhood Environment and Allergic Diseases Study cohort). A total of 3246 children were recruited with written informed consent. After excluding those who were multiple births, premature, had congenital and chronic diseases, were unable to answer questions in Chinese, had moved in or out of their current home, lived more than 10 km from air monitoring stations, 2661 children were entered into the analysis (Table 1). Those who lived more than 10 km from air monitoring stations were excluded because of the relative lower correlation between monitoring station data and children's real exposure for those living more than 10 km from air monitoring stations (Clark et al., 2010; Romieu et al., 1996; Rich et al., 2009). The average distance from monitoring stations to the children's addresses was 2.14 ± 0.72 km. The International Study of Asthma and Allergies in Childhood (ISAAC) questionnaires with extra questions on basic demographics, residential environmental factors, and family history of allergic diseases were answered by parents. The study protocol was approved by the Institutional Review Board at our hospital, and this study complied with the principles outlined in the Helsinki Declaration.

2.2. Case definition

Cases of atopic dermatitis (AD) were identified through the questions, "Has your child ever had AD diagnosed by a physician?" and "Has your child ever had recurrent itchy rash for at least 6 consecutive half-month periods over elbows, knees, face, wrists, neck, peri-auricular and eyebrow areas?" Cases of allergic rhinitis (AR) were identified through the questions, "Has your child ever been diagnosed as having AR by a physician?" and "Has your child ever had a problem with sneezing, or a runny or blocked nose, when they did not have a cold or the flu?" Asthma was defined as positive responses to "physician-diagnosed asthma" and the presence of nocturnal cough or exercise wheeze in the past 12 months.

2.3. Exposure measurements

The long-term exposure to background air pollution was estimated by linking the home addresses to six air quality monitoring stations in six districts in Taipei Figure S1. The home addresses and the monitoring stations were geo-coded using a geographic information system. An expert identified the nearest and most representative background monitoring station for each child. The distance between the home and the nearest monitoring station was determined using Google's online maps Figure S1. The temperature and relative humidity in each monitoring site were also recorded. The mean concentrations of sulfur dioxide (SO_2), nitrogen dioxide (NO_2), ozone (O_3), carbon monoxide (CO), and particulate matter $\leq 10\,\mu m$ and $\leq 2.5\,\mu m$ in aerodynamic diameter (PM_{10} and $PM_{2.5}$) from when the children were born to the end of the study were measured at the relevant monitoring station, and averaged to represent long-term cumulative exposure to air pollutants for each child.

2.4. Laboratory methods

Skin prick tests to six common allergens (house dust mites including Der p, Der f, Der m, and Blot allergens, cockroaches, animal dander, milk, eggs, and crab allergens, all from ALK-Abell & Oacute, USA) were performed. The tests were read at 15 min. In the presence of a positive control (>3 mm), a mean wheal diameter of at least 3 mm greater than the negative control was taken to be positive.

2.5. Statistical analysis

The daily average concentrations of each air pollutant (PM_{10}, $PM_{2.5}$, SO_2, NO_2, CO and O_3) were calculated. More than 75% of the data (for at least 18 h in a 24-h period) had to be available to be included in the analysis. We then calculated the average concentration from birth until the end of the study to estimate long-term cumulative exposure. Adjustments were made for temperature and relative humidity at each monitoring site. The air pollutant data obtained from the geographic information system were taken as independent variables in the regression model.

Multiple logistic regression analyses were performed to estimate the association between air pollutants, allergen sensitization, and the development of allergic diseases. Odds ratios (ORs) and a 95% confidence intervals (CIs) were adjusted for important potential confounders. Potential confounders which were selected based on the previous literatures, including age, gender, body mass index, environmental tobacco smoke, maternal history of atopy, maternal education and nationality, family income, duration of breast feeding, duration of sleep, number of siblings, dampness of the house, fungus on the house wall, residence, temperature, relative humidity, and distance from the home to the air monitoring station were all taken into consideration. Variables were included in the model if they changed the univariate point estimate by at least 10% (Beggs and Bambrick, 2005; Jenerowicz et al., 2012; Weiland et al., 2004).

To further assess the joint effect and interactions between air pollutants and allergen sensitization, we stratified our subjects into

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