Nitrogen dioxide exposure in school classrooms of inner-city children with asthma

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Background: Ambient and home exposure to nitrogen dioxide (NO_2) causes asthma symptoms and decreased lung function in children with asthma. Little is known about the health effects of school classroom pollution exposure.

Objective: We aimed to determine the effect of indoor classroom NO_2 on lung function and symptoms in inner-city school children with asthma.

Methods: Children enrolled in the School Inner-City Asthma Study were followed for 1 academic year. Subjects performed spirometry and had fraction of exhaled nitric oxide values measured twice during the school year at school. Classroom NO_2 was collected by means of passive sampling for 1-week periods twice per year, coinciding with lung function testing. Generalized estimating equation models assessed lung function and symptom relationships with the temporally nearest classroom NO_2 level.

Results: The mean NO_2 value was 11.1 ppb (range, 4.3-29.7 ppb). In total, exposure data were available for 296 subjects, 188 of whom had complete spirometric data. At greater than a threshold of 8 ppb of NO_2 and after adjusting for race and season (spirometry standardized by age, height, and sex), NO_2 levels were associated highly with airflow obstruction, such that each 10-ppb increase in NO_2 level was associated with a 5% decrease in FEV_1/forced vital capacity ratio ($\beta = -0.05$; 95% CI, -0.08 to -0.02; $P = .01$). Percent predicted forced expiratory flow between the 25th and 75th percentile of forced vital capacity was also inversely associated with higher NO_2 exposure ($\beta = -22.8$; 95% CI, -36.0 to -9.7; $P = .01$). There was no significant association of NO_2 levels with percent predicted FEV_1, fraction of exhaled nitric oxide, or asthma symptoms. Additionally, there was no effect modification of atopy on lung function or symptom outcomes.

Conclusion: In children with asthma, indoor classroom NO_2 levels can be associated with increased airflow obstruction. (J Allergy Clin Immunol 2017;■■■:■■■-■■■.)

Key words: *Asthma, indoor air pollution, obstructive lung disease, nitrogen dioxide, spirometry, exhaled nitric oxide*

Exposure to ambient air pollutants has been associated with asthma development, asthma exacerbations, and reduction in lung function.[1-8] Moreover, home-based measurements of nitrogen dioxide (NO_2) and other pollutants with indoor sources have been associated with asthma symptom severity[9] and lower lung function[2,10,11] in children, even at modest exposure levels.[10]

NO_2, a gaseous pollutant generated from fossil fuel combustion, has emerged as one of the most notable pollutants associated with health effects. In urban environments NO_2 is generated by traffic-related combustion, home heating and cooking with fossil fuels (gas, oil, and coal), and tobacco smoke.[12,13] It is a prevalent indoor pollutant in homes, where heating and cooking are common activities, and during these exposures, asthma symptoms worsen.[11,14] However, little is known about the effect of NO_2 in indoor environments aside from the home.

Urban schools represent a unique and important micro-environment for indoor pollution. In most schools there is no cooking, tobacco smoke is prohibited, and the centralized furnace

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Abbreviations used

FEF_{25-75}: Forced expiratory flow between the 25th and 75th percentile of forced vital capacity
FENO: Fraction of exhaled nitric oxide
FVC: Forced vital capacity
NO_2: Nitrogen dioxide

system minimizes the combustion exposure to any individual classroom. However, exposure to combustion-related pollutants from outside sources can enter through traditional ventilation and intrusion through doors, windows, and structural imperfections of the school building. The school classroom represents the occupational setting for children (ie, the environment in which they spend 6 to 10 hours per day). Therefore exposures encountered in this environment can have a substantial health effect.

Several studies have cataloged indoor air quality in schools[15-19] and associations with respiratory[19-21] and neurodevelopmental measures.[22] However, variation in the source and type of pollutants is significant based on geographic region,[16] and few studies have focused on US inner-city schools.[23] Furthermore, few studies have specifically evaluated lung function in relation to school-based exposure.[24] In this study we examine the symptomatic effects of NO_2 and objective assessment of lung function in inner-city children with asthma.

We hypothesized that exposure to NO_2 in schools would be associated with lung function deficits and higher rates of asthma symptoms in children with asthma.

METHODS

Study population

The School Inner-City Asthma Study is a single-center epidemiologic study of the effect of school classroom environmental exposures on asthma morbidity in inner-city schoolchildren with asthma, with methods that have been published previously.[25] Briefly, children with asthma were recruited from inner-city school classrooms from 2008 to 2013 for participation. Screening surveys were distributed schoolwide to participating schools the spring before the study year. Children with a physician's diagnosis of asthma or with a report of signs and symptoms consistent with persistent asthma and at least 1 asthma symptom within the past year were invited to participate. This study was approved by the Boston Children's Hospital Institutional Review Board. Written informed consent was obtained from the subject's guardian, and assent was obtained from the subjects before enrollment.

Study procedures

Fig 1 shows the study schema. Baseline characterization of study subjects was performed at a formal research clinic visit during the summer before the academic year, during which sociodemographic information, medical history, and baseline symptom profiles were assessed by means of questionnaire. Subjects performed spirometry with a Koko spirometer (Ferraris Respiratory, Louisville, Colo) using American Thoracic Society guidelines,[26] fraction of exhaled nitric oxide (FENO) measurement with the NIOX MINO device (Aerocrine, Solna, Sweden), and aeroallergen sensitization testing by means of allergy skin testing (MultiTest device, Lincoln Diagnostics, Decatur, Ill) and/or serum specific IgE measurement (ImmunoCAP; Phadia AB, Uppsala, Sweden). Sensitization was defined by a wheal 3 mm or larger than that elicited by the negative saline control on skin prick tests or a specific IgE level of 0.35 kU/L or greater. The tested allergens included tree pollen, grass, ragweed, dust mites, cat, dog, mouse, rat, cockroach, and molds (Greer Laboratories, Lenoir, NC).

Subsequently, questionnaire-based symptom assessments were performed up to 4 times throughout the academic school year by telephone interviews at 3, 6, 9, and 12 months. Spirometric and FENO values were assessed at 2 in-school visits that coincided with school environmental assessments approximately 6 months apart. Testing occurred throughout the day, with 90% of tests occurring after 10 AM and the majority occurring between 10 AM and 3 PM.

Exposure assessment

Classrooms of participating students were sampled twice during the academic year while school was in session approximately 6 months apart. NO_2 was collected by means of passive monitoring with Ogawa samplers[27] for 1-week periods. NO_2 analysis was performed with ion chromatography. Average NO_2 levels per assessment period were determined and used for analyses.

Outcome measures

The FEV_1/forced vital capacity (FVC) ratio was chosen as the primary spirometric outcome of interest because it is the most sensitive marker of airflow obstruction in children with asthma.[28,29] FEV_1 percent predicted, FVC percent predicted, and forced expiratory flow between the 25th and 75th percentile of forced vital capacity (FEF_{25-75}), a measure of medium- and small-caliber airways, were also assessed. All spirometric measures were assessed for acceptability and repeatability by study physicians per American Thoracic Society guidelines.[26,30] Reference values were derived from the National Health and Nutrition Examination Survey III[31] reference equations, which account for age, race, and sex. FENO was measured per standardized methodology. Both spirometric and FENO measurements were performed in the school during the same season (fall or spring) of exposure measurement.

Symptom outcomes were measured as maximum symptom days, as used in prior urban home-based[32,33] and school[34,35] studies. To define this outcome, 3 variables of symptoms in the 2 weeks before each survey were evaluated: (1) number of days with wheezing, chest tightness, or cough; (2) number of days on which the child had to slow down or discontinue play activities because of wheezing, chest tightness, or cough; or (3) number of nights with wheezing, chest tightness, or cough leading to disturbed sleep. The greatest result of these 3 variables was used as the asthma symptom days outcome. As such, this outcome was a score of from 0 to 14 days.

Statistical analysis

Characteristics of the cohort are expressed with descriptive statistics. Variability of NO_2 levels between schools and between classrooms within schools was determined with random-effects linear regression. All clinical outcomes were linked to the temporally closest measured exposure during the academic school year. Only outcome measures obtained during the academic school year were used for analysis. The relationship between NO_2 levels and lung function test results was evaluated with locally weighted regression (Lowess) to examine possible nonlinear relationships. On the basis of these smoothers, we then fit a linear spline of NO_2 with a single knot at 8 ppb to be used in all subsequent models. Relationships between NO_2 levels and lung function outcomes are presented as the effect of a 10-ppb change in NO_2 levels of greater than the threshold of 8 ppb. The exposure-outcome relationship was evaluated by using generalized estimating equations with an exchangeable correlation structure and robust variance estimates, with clustering defined at the participant level. We considered clustering at the school level in addition to the participant level within a multilevel random-effects model containing both subject and school random effects, but this was deemed unnecessary because there was little to no between-school variability in all outcomes (intraclass correlations between 0.00 and 0.04). All models included linear and quadratic terms for the number of days since school started to address the time variation of asthma activity across the study period. Symptom outcomes were adjusted for age, race, and sex because of *a priori* assumptions that these might be important