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24-h Nitrogen dioxide concentration is associated with cooking behaviors and an increase in rescue medication use in children with asthma

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ABSTRACT

Exposure to nitrogen dioxide (NO_2), a byproduct of combustion, is associated with poor asthma control in children. We sought to determine whether gas-fueled kitchen appliance use is associated with 24-h indoor NO_2 concentrations and whether these concentrations are associated with asthma morbidity in children. Children aged 5–12 years old with asthma were eligible. Mean 24-h NO_2 concentration was measured in the kitchen over a four-day sampling period and gas stove use was captured in time activity diaries. The relationship between stove and oven use and daily NO_2 concentration was analyzed. Longitudinal analysis assessed the effect of daily NO_2 exposure on symptoms, inhaler use, and lung function. Multivariate models were adjusted for age, sex, season, and maternal education. Thirty children contributed 126 participant days of sampling. Mean indoor 24-h NO_2 concentration was 58(48) ppb with a median (range) of 45(12–276) ppb. All homes had gas stoves and furnaces. Each hour of kitchen appliance use was associated with an 18 ppb increase in 24-h NO_2 concentration. In longitudinal multivariate analysis, each ten-fold increase in previous-day NO_2 was associated with increased nighttime inhaler use (OR = 4.9, p = 0.04). There were no associations between NO_2 and lung function or asthma symptoms. Higher previous-day 24-h concentration of NO_2 is associated with increased nighttime inhaler use in children with asthma.

1. Introduction

Asthma affects nearly 25 million people in the United States, including 10% of children (Centers for Disease Control and Prevention, 2011), and is the most common noncommunicable disease among children worldwide (World Health Organization, 2010). The current therapeutic strategy focuses on control of the illness through medications and avoidance of factors that exacerbate the disease, including allergens, tobacco smoke, irritants, and air pollution (NHLBI, 2007). Long term exposure to elevated concentrations of nitrogen dioxide (NO_2), a byproduct of consumption, may contribute to development of asthma (United States Environmental Protection Agency, 2016). Several epidemiologic studies have shown associations between exposure to NO_2 and increased asthma symptoms, including chest tightness, shortness of breath, wheeze, and cough, an increase in rescue inhaler use, and an increased number of asthma attacks among children with established disease (United States Environmental Protection Agency, 2016; Belanger et al., 2006; Hansel et al., 2008; Garrett et al., 1998; Hasselblad et al., 1992; Gillespie-Bennett et al., 2011). Because of the adverse health effects of NO_2 exposure, in the United States, outdoor concentrations of NO_2 are regulated by the EPA Clean Air Act (United States Environmental Protection Agency, 2016), and the 2005 World Health Organization (WHO) air quality guidelines suggest limits for indoor NO_2 concentrations worldwide (World Health Organization, 2006).

The indoor residential environmental may contain several sources of NO_2, and prior studies have shown that presence of a gas cooking appliance (gas stove and oven; herein referred to as gas stove) in the home is associated with higher NO_2 concentrations (Hansel et al., 2008; Hasselblad et al., 1992; Levy, 1998; Neas et al., 1991; Kattan et al., 2007). Across the United States, 35% of homes report using gas stoves, and use is particularly concentrated in urban areas (U.S. Energy Information Administration (EIA), 2015). These indoor sources of NO_2 are used intermittently, resulting in highly fluctuating NO_2 concentrations, and real-life studies quantifying the effect of stove use on indoor NO_2 concentrations are limited. Furthermore, the multi-day averaging

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concentration data commonly used in health outcomes research often fail to reflect the short-term concentrations and temporal variability in exposures produced by indoor sources (Brauer et al., 1990; Franklin et al., 2006). Short-term increases in NO_2 concentrations, including daily concentrations, may reflect independent risk to adverse respiratory outcomes, in addition to adverse effects noted with longer-term average exposures (Kattan et al., 2007; Nitschke, 1999; Smith et al., 2000). In this study, we investigate the relationship between use of gas stoves and 24-h NO_2 concentrations, and how daily NO_2 concentration impacts asthma morbidity in a cohort of children living in Baltimore city, where gas stove use is common (83% in prior studies) (Hansel et al., 2008).

2. Methods

2.1. Study design

Thirty participants living in homes with gas stoves were recruited from the ASTHMA-DIET study, a longitudinal cohort with the aim to examine how diet influences susceptibility to environmental exposures in children with asthma. Eligibility criteria included 1) Age 5–12 years, 2) Physician diagnosis of asthma, 3) Symptoms of asthma and/or reliever medication use in past 6 months, and 4) Residence in catchment area of East Baltimore. Exclusion criteria included a current diagnosis of another major pulmonary disease and planning to relocate residence during the study period. 24-h NO_2 monitoring occurred daily in the home over a period of 4–7 days during one of the three, seven-day monitoring periods part of ASTHMA-DIET. The Johns Hopkins Medical IRB approved the protocol and Informed consent was obtained from all individual participants included in the study.

2.2. Environmental assessment

Home inspection documenting type of stove and heat source along with general housing characteristics was conducted by a trained home inspector. Mean 24-h NO_2 concentrations were measured using passive samplers (Ogawa badge) in the kitchen. Badges typically were deployed from 4 p.m. on Day 1–4 p.m. on Day 2. Daily mean outdoor NO_2 concentration data was obtained from publically available datasets (US Environmental Protection Agency, 2015). Time activity diaries were filled out by the primary care giver to document whether combustion sources were used over three eight-hour time periods over the course of a day (any/no use during the eight-hour time period) and whether windows were opened in the home for greater than 10 min (yes/no). In a subset of willing participants (n = 18), detailed time activity diaries captured gas stove use in 15-min increments throughout the day.

2.3. Clinical assessment

Asthma symptom burden was assessed using the Pediatric Asthma Diary, a two-part, validated diary that accurately detects clinically important changes in asthma status over a 24-h period. The daytime diary assesses the frequency of breathing problems, activity limitations, bother of daytime symptoms, report of absence from school, unscheduled visits to the doctor, emergency room or hospital along with the number of albuterol puffs used over the course of the day. The nighttime diary examines the number of awakenings caused by asthma symptoms on a 4-point scale of 0 (no awakenings) to 3 (awake all night) along with number of nighttime rescue inhaler puffs (Santanello et al., 1999). Twice-daily spirometry (FEV_1) was assessed using the PiKo-1 Electronic Peak Flow/FEV1 Meter (PiKo-1, nSpire Health, Inc). The nighttime diary questions were answered in the morning shortly after the child awoke, and the daytime diary was completed in the afternoon/early evening prior to the child's bedtime. Following instruction from research coordinators, caregivers completed the daily diary with input from children and supervised daily lung function recordings. Diaries were reviewed by research coordinators during the three home visits over the course of each study week.

2.4. Statistical analysis

Descriptive statistics were analyzed using Spearman correlations, chi square tests, *t*-tests, and Wilcoxon rank-sum tests, as appropriate. Linear regression models were used to estimate the relationship between duration of gas stove use and indoor 24-h NO_2 concentration; in multivariate analysis these models were adjusted for season (cold season November 1- March 31 based on typical home heating patterns in Baltimore city; non-cold season April 1-October 31, Baltimore Gas and Electric), outdoor NO_2 concentration, and window opening. Effect modification was explored by including an interaction term of stove use * season to determine whether season modified the effect of kitchen appliance use on indoor 24-h NO_2 concentration, and a separate analysis included stove use * window opening to determine whether the relationship between stove use and NO_2 concentration varied by window opening. We also created an interaction between stove use, season, and window opening to determine whether season and window use jointly influenced the relationship between duration of cooking and 24-h indoor NO_2 concentration.

To examine the role of NO_2 exposure on asthma outcomes, as the distribution of mean 24-h NO_2 concentration was right skewed, log-transformed 24-h NO_2 concentration was used as the primary exposure variable in generalized estimating equations models (Diggle et al., 2002) to account for repeated measures. Dichotomous yes/no variables were created to capture any report of breathing problems, activity limitations, bother, or nighttime awakenings over the course of the day. Inhaler use was defined as a dichotomous variable (no puffs vs. any puffs for each daytime and nighttime assessment). Analyses captured the odds of reporting any daytime symptom using a combined daytime symptom score (including report of breathing problems, limitation of activity, bother, absence from school, or unscheduled doctor's visit) (Santanello et al., 1999). Models were adjusted for sex, age, education of primary caregiver, and season of sampling. Presence of pets, carpeting in the child's bedroom, and report of smoking in the home were not associated with both exposure and outcomes and thus were not included as covariates. Analyses were performed with StataSE statistical software, version 12.0 (Stata Corp, College Station, TX). Statistical significance was defined as a p value less than 0.05 for main models and 0.1 for interaction terms.

3. Results

3.1. Participant characteristics

30 participants were enrolled in the study and contributed a total of 126 sampling days. Children on average were 9.8 years old and 33% were female, and 97% were African-American. The majority of caregivers had less than a high school education, and 100% of participants had public insurance. Daytime symptoms and albuterol use were reported on 26% and 19% of sampling days, respectively. Overnight albuterol use was reported on 18% of nights. (Table 1).

3.2. Housing characteristics and NO_2 concentrations

The mean(SD) indoor NO_2 concentration per 24-h sampling period was 58 (48)ppb with a median (range) of 45 (12 – 235)ppb (Fig. 1). 47 (37%) and 15 (12%) of sampling days had 24-h indoor concentrations above the EPA mean annual outdoor limit of 53 ppb and one-hour outdoor limit of 100 ppb, respectively. 106 (84%) of sampling days fell above the mean annual indoor guideline of 21 ppb suggested by WHO, and 13 (10%) sampling days fell above the 1-h indoor suggested limit of 106 ppb. All homes had gas stoves and gas furnaces. Stove use at any point over the 24-h period was reported on 72% of sampling days. 37%