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To cite this article: Arlene M. Butz, Mona Tsoukleris, Mary Elizabeth Bollinger, Mandeep Jassal, Melissa H. Bellin, Joan Kub, Shawna Mudd, C. Jean Ogborn, Cassia Lewis-Land & Richard E. Thompson (2018): Association between second hand smoke (SHS) exposure and caregiver stress in children with poorly controlled asthma, Journal of Asthma, DOI: [10.1080/02770903.2018.1509989](https://doi.org/10.1080/02770903.2018.1509989)

To link to this article: <https://doi.org/10.1080/02770903.2018.1509989>



Published online: 11 Oct 2018.



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Association between second hand smoke (SHS) exposure and caregiver stress in children with poorly controlled asthma

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ABSTRACT

Objective: Urban children with asthma experience high rates of second hand smoke (SHS) exposure. The objective was to examine whether SHS exposure is associated with symptom frequency in children with poorly controlled asthma. **Methods:** Children were enrolled in a RCT to test the efficacy of an environmental control behavioral intervention versus an attention control group and followed over 12 months. SHS exposure assessed using salivary cotinine measurement. Frequency of child asthma symptoms, healthcare utilization, household smoking and caregiver daily life stress were obtained via caregiver report. Time of enrollment was recorded to assess seasonal factors. Symptom days and nights were the primary outcomes. Multivariable models and odds ratios examined factors that best predicted increased frequency of daytime/nighttime symptoms. **Results:** Children ($n = 222$) with a mean age of 6.3 (SD 2.7) years, were primarily male (65%), African American (94%), Medicaid insured (94%), and had poorly controlled asthma (54%). The final multivariable model indicated symptoms in the fall (OR 2.78; 95% CI 1.16, 6.52) and increased caregiver daily life stress (OR 1.13, 95% CI 1.02, 1.25) were significantly associated with increased symptom days when controlling for cotinine level, intervention status, child age and home and car smoking restrictions. **Conclusions:** There was no impact of SHS exposure on increased symptom frequency. High caregiver daily life stress and symptoms in fall season may place children with asthma at risk for increased day/nighttime symptoms. Close monitoring of symptoms and medication use during the fall season and intervening on caregiver life stress may decrease asthma morbidity in children with poorly controlled asthma.

ARTICLE HISTORY

Received 25 January 2018
Revised 31 July 2018
Accepted 5 August 2018

KEYWORDS

Pediatric; asthma; second hand smoke exposure; caregiver stress

Introduction

Asthma affects approximately 7 million children in the U.S. and remains the most common chronic illness in children [1]. Inner-city children continue to experience high asthma morbidity and burden of disease [2]. Identifying individual, family and environmental risk factors associated with high asthma morbidity in inner-city children is complex, however a range of multilevel factors are suspected to contribute to uncontrolled asthma in inner-city children, including exposures to second hand smoke (SHS), viral illness, indoor allergens and high caregiver stress [2]. High urine cotinine concentrations, a biomarker

of SHS exposure, have been associated with increased number of asthma symptom days in young urban children residing with a smoker [3] and increased SHS exposure are reportedly associated with an increased risk of developing asthma, asthma prevalence and poor asthma control [4–8]. Increased symptom days are likewise noted during the fall season because of heightened exposure to viral illnesses with children returning to school and increased seasonal allergens [9,10]. Exposure to specific indoor allergens such as cockroach and mouse, commonly found in poor housing conditions, may elevate risk for increased symptom days, particularly among children

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with positive allergen sensitization to these exposures [11]. Growing attention has also been placed on the influence of caregiver daily life stress on child asthma morbidity [12]. The stress described by urban caregivers is multifaceted in nature (poverty, housing, unemployment, neighborhood violence and trauma) and may result in ineffective home asthma management and ultimately heightened risk for increased symptoms and healthcare utilization for acute asthma care [12].

Examining SHS exposure is a critical public health concern with over half of low-income children with asthma exposed to SHS based on self-report and biomarkers of tobacco exposure [13–17]. Moreover, reducing SHS exposure is a key component of national and international guidelines for asthma management [18,19]. Although daily SHS exposure is associated with increased asthma severity, more severe asthma exacerbations, and overall asthma morbidity in school aged children [4], the association between SHS exposure based on cotinine measurement and impact on asthma symptoms in young urban children is less well understood. The objective of this study was to examine if an association exists between SHS exposure, based on salivary cotinine levels, and frequency of day and night time symptoms in low-income, minority children with poorly controlled asthma. We hypothesized that increased SHS exposure would be associated with higher day and night asthma symptom frequency. A secondary aim was to explore associations between other individual, family and environmental risk factors including season, allergen sensitization, indoor allergen exposure, child age, and caregiver stress with increased day and night symptoms.

Methods

Design and study setting

The data for this longitudinal study were derived from a randomized controlled trial testing the efficacy of an emergency department (ED) and home-based environmental control intervention for young inner city children who had frequent ED visits for asthma [20]. Families of children aged 3–12 years with persistent asthma were recruited and enrolled from two urban pediatric EDs (Johns Hopkins Hospital and University of Maryland Hospital) during an asthma ED visit from August 2013 through February 2016. Inclusion criteria were physician diagnosed persistent and uncontrolled asthma based on current national asthma guidelines [18] and caregiver report of asthma symptom frequency at enrollment, having two or

more ED asthma visits or ≥ 1 hospitalization over the past 12 months, and residing in the Baltimore metropolitan area. Children were excluded if they had significant other nonasthma respiratory conditions including cystic fibrosis, bronchopulmonary dysplasia or lung cancer. The Johns Hopkins Medical and the University of Maryland Institutional Review Boards approved the study and the study is registered with ClinicalTrials.gov (NCT01981564). Each child's caregiver provided written informed consent and all children over age 8 years provided verbal assent to participate. Out of the 554 child/caregivers screened for study enrollment, 117 children were ineligible for enrollment and another 215 caregivers declined to participate. This resulted in enrollment of 222 children with 204 available with cotinine results for analysis at the 12-month follow-up visit, i.e. 18 children had missing cotinine data at 12 months. At the baseline and 12-month follow-up visit, trained research assistants, blinded to study group assignment, conducted all surveys with caregivers via face-to-face interviews ascertaining frequency of child asthma symptoms, health care utilization, indoor allergen exposure and information regarding household and car smoking behavior. At the same time points, the RAs collected saliva from the child for cotinine analysis. Season of enrollment was recorded to assess seasonal factors associated with asthma symptom frequency.

Description of interventions

Asthma express intervention (INT)

$n = 107$ (48.2%) was an ED-home based environmental control educational and remediation program [20] delivered by trained nurses and nurse practitioners (NP) to the child and caregiver within 2 months of ED visit. Children randomized to the intervention group received a medical asthma follow-up visit in the Pediatric ED to monitor symptoms, review of allergen sensitization and cotinine results using educational graphs presenting the child's allergen sensitization and cotinine concentration results, two home nurse visits for targeted environmental control education with remediation based on allergen profile (i.e. positive mouse allergy: set up mouse traps; positive cockroach allergy: set up cockroach bait and delivered kitchen trash cans), a brief motivational interview to implement a total home smoking ban and smoking cessation referral for caregivers of children with positive cotinine (≥ 1.0 ng/mL) results [21] and assistance with scheduling primary care provider (PCP) asthma care

follow-up. A specially trained nurse with integrated pest management education provided all home INT visits.

Control families (CON) or attention control group

$n = 115$ (51.8%) received three home nurse visits to provide standard asthma education, basic environmental control education (with no home remediation) and assistance with scheduling PCP follow-up asthma care. A community health nurse conducted CON home visits. The child's primary care provider and caregiver were mailed the results of their child's allergen sensitization and cotinine test results with low-literacy written recommendations. Basic environmental control education was provided however, no home remediation was conducted for positive allergen sensitizations. Referrals to smoking cessation programs were provided to caregivers with a smoker in the home.

Measures

Asthma morbidity and health care utilization

Measurement of asthma severity and asthma symptom frequency was based on items from the National Asthma Education and Prevention Program (NAEPP) guidelines [18]. Symptom days were assessed by asking "How many days over the past 14 days has your child had asthma symptoms during the day including cough, wheeze, chest tightness, difficulty taking a breath or shortness of breath?" Concurrently, symptoms nights were assessed with "How many nights over the past 30 nights has your child had asthma symptoms that woke him/her up at night with cough, wheeze, chest tightness, and difficulty taking a breath or shortness of breath?" Asthma severity was determined using an algorithm based on frequency of symptom days and nights, frequency of short-acting β_2 -agonist use, level of limitation of activity and use of long-term control medications [18]. Number of ED visits and/or hospitalizations for asthma over the past 12 months, limitation of activity and use of rescue medication over the past 2 weeks were all based on caregiver report. ED visits and hospitalizations were verified using electronic medical record review.

Household smoking and indoor pest exposure

The child's SHS exposure in the home was based on caregiver report of number of household smokers and relation of smoker to child, if caregiver smoked in home and type of household and car smoking restrictions. E-cigarette and Vaping use were ascertained at

baseline and 12 months. Brand of cigarettes or Cigarillo use was not ascertained. Level of household smoking restriction was ascertained by asking: "How is cigarette smoking handled in your home?" Caregiver's responses included choosing one of the three categories: "No restrictions (people are allowed to smoke anywhere in my home), some restrictions (only special guests are allowed to smoke in my home or people are allowed to smoke only in certain areas in my home) or Total home smoking ban (No one is allowed to smoke in my home)". Smoking restrictions while the child was riding in a car were ascertained by asking "How is cigarette smoking handled when you child rides in a car?" Caregiver response options (No, Some or Total restrictions) were comparable to home smoking restriction responses. Household indoor exposure to mice and/or cockroach was ascertained at baseline and 12 months by asking the caregiver (1) "Over the past 3 months, have you seen roaches or water bugs in your home?" and (2) "Over the past 3 months, have you seen mice in your home?" Type of housing such as row home or multiunit apartment and ownership of a car were not ascertained.

Salivary cotinine for second hand smoke (SHS) exposure

Saliva samples were collected at each time point (baseline and 12 months) using a 3-cm cotton swab that was placed under the child's tongue for 1 min to absorb 1 ml of saliva (Salimetrics, State College, PA). The cotton roll was placed in a 2 mL vial, stored at -20°C within 30 min of collection and batched for testing (up to 4 weeks). Transport of samples to the lab occurred within 10 min. During processing, the saliva samples were thawed to room temperature, centrifuged for 15 min and then nondiluted saliva samples were analyzed at the Johns Hopkins Institute for Clinical and Translational Research (ICTR) laboratory using high sensitivity salivary cotinine quantitative enzyme immunoassay (ELISA) test kits. Unopened kits were stored at $2-8^{\circ}\text{C}$ for stability. The cotinine analysis served as a biomarker of nicotine exposure that has a half-life of 17–20 h [21]. The lower limit of cotinine sensitivity was .05 ng/mL and average intra and inter-assay coefficients of variation were less than 5.8% and 7.9%, respectively. Although serum cotinine is the gold standard, there is high correlation between plasma, urine and salivary cotinine [13,22]. Salivary cotinine tests were selected over urine and blood tests since (1) saliva is noninvasive and easier to obtain in children and (2) salivary cotinine levels are highly

correlated with blood cotinine levels [22]. Consistent with prior research, positive SHS exposure was based on a salivary cotinine cutoff level ≥ 1.0 ng/mL [23].

Caregiver daily stress scores (life stress and asthma stress)

Caregiver daily life stress over the past month was measured using a visual analog scale (VAS). Anchors included “1” defined as no stress at all, and “10” reflecting the highest level of stress. Caregivers selected the number between 1 and 10 to indicate their level of daily life stress to include stress associated with poverty, unemployment, neighborhood stress, trauma or other experiences. Concurrently, a separate asthma daily stress score was measured by asking the caregiver to rate their daily stress associated with care of their child with asthma. A score of 6–7 suggested moderate stress, and a score of 8 or above was regarded as a high level of stress. In a previous study, the construct validity of the VAS was moderate to high based on correlations with standardized measures of psychological stress [24].

Serologic allergen specific IgE test

Serum specific IgE testing, collected during the enrollment ED visit, was performed by a private commercial laboratory using the (ImmunoCap[®]) fluorescent enzyme immunoassay (FEIA) and measured specific IgE to ten common environmental allergens: mouse, cockroach, cat, dog, timothy grass, *Alternaria* and *Aspergillus* molds, oak tree, common ragweed and house dust mite. The degree of sensitization ranged from <0.35 to >100 kU/L of specific IgE to any of the allergens tested and results of >0.35 kU/L were considered as an increased likelihood of presence of clinical allergy and considered as “positive”.

Statistical methods

Standard frequencies, means and standard deviations were used to describe sociodemographic, child health and environmental exposures, i.e. household smoking, pest exposure characteristics of all children and their caregivers ($n=222$). Asthma symptom days were summed and categorized as low (≤ 2 days/14 days) versus high (>2 days/14 days) as were night symptoms (low ≤ 2 nights/30 nights versus high or >2 nights/30 nights) based on NAEPP guidelines [18]. Because a moderate correlation between caregiver daily life and asthma daily stress was observed (Spearman's $r=0.394$, $p<0.001$) and mean caregiver daily life stress was higher than asthma daily stress at

baseline and 12 months, only caregiver life stress variable was included in the analysis.

Initially, we examined if high SHS exposure was associated with child health outcomes. Chi-square tests were used to examine the risk of SHS exposure (cotinine level ≥ 1.0 ng/mL) with number of asthma ED visits and hospitalizations over the past 12 months and limitation of activity and rescue medication use during the past 2 weeks. Varying cotinine levels were then examined for association with high symptom days and nights. Presence of high symptom days or nights were plotted across the range of cotinine levels (0–10 ng/mL) and lowess smoothing line was fit for these data.

Next odds ratios were calculated for select health, sociodemographic, SHS exposure status, season, intervention group status for association with high day and nighttime symptom frequency at 12 months. ANOVA was used to examine association between continuous variables and symptom frequency. For the season variable, summer served as the reference category. Finally, multivariable models and odds ratios were conducted to examine factors that best predicted increased frequency of daytime/nighttime symptoms at 12 months. Variables indicating a trend towards statistical significance (i.e. $p<0.10$) in the bivariate analyses for association with high day and nighttime symptom frequency at 12 months were included in the final model as were variables that were clinically or theoretically significant [i.e. intervention group status (INT or CON), change in cotinine level over 12 months, and type of home smoking ban]. Significance was set at $p<0.05$. Analyses were conducted using STATA Version 15 software [25].

Results

Characteristics of the study population ($n=222$) at baseline

Of the 222 study participants enrolled in the original controlled trial (RCT), 204 (92%) had complete cotinine data at 12 months. Children were primarily male (65%), African American (94%) and Medicaid insured (94%) (Table 1). Child mean age was 6.3 (SD 2.7) years and 49.5% were living in poverty based on household income at less than the 2015 Federal Poverty Level. Caregivers were the child's biological mother (94%), high school graduates or higher educated (81%), single (75%) and had a mean age of 31.4 (SD 7.5) years. Mean caregiver daily life stress scores were higher than caregiver

Table 1. Baseline characteristics of child and caregiver participants. *n* = 222.

Characteristic	<i>n</i> (%)
<i>Child sociodemographic characteristics</i>	
Age in years (mean, SD)	6.3 (2.7)
Gender	
Male	144 (64.9)
Race/ethnicity	
African American	208 (93.6)
White or Hispanic	7 (3.2)
Other	7 (3.2)
Medicaid insured	209 (94.1)
Poor ^a	110 (49.5)
Season of enrollment	
Summer	43 (19.4)
Fall	77 (34.7)
Winter	57 (25.6)
Spring	45 (20.3)
<i>Caregiver sociodemographic characteristics</i>	
Biological mother	205 (92.3)
Education	
High school graduate or higher education	178 (80.2)
Marital status	
Single	164 (73.9)
Caregiver age in years (mean, SD)	31.4 (7.5)
Employment	
Yes	122 (54.9)
Caregiver daily life stress score (range 0–10) (mean, SD)	6.06 (2.98)
Caregiver daily asthma stress score (range 0–10) (mean, SD)	4.35 (3.24)
<i>Child health characteristics</i>	
Asthma severity (<i>n</i> = 221)	
Mild persistent	56 (25.3)
Moderate persistent	101 (45.7)
Severe persistent	64 (29.0)
Asthma control (<i>n</i> = 221)	
Well controlled	0 (0)
Not well controlled	102 (46.2)
Very poorly controlled	119 (53.8)
Symptom days over past 14 days (mean, SD)	5.88 (4.8)
Symptom nights over past 30 nights (mean, SD)	6.95 (8.7)
ED asthma visits past 3 months <i>n</i> = 219	
0	67 (30.6)
1	80 (36.5)
2 or more	72 (32.9)
Hospitalization for asthma past 12 months <i>n</i> = 215	
0	191 (88.8)
1 or more	24 (11.2)
Allergen sensitization (atopy status) <i>n</i> = 201	
0 (no allergy)	35 (17.4)
1 or more positive	166 (82.6)
Indoor pest exposures (caregiver report)	
Mice (yes)	105 (47.3)
Cockroach (yes)	70 (31.5)

^aPoor defined by household income and number of persons in household as less than the federal poverty level.

daily asthma stress at both time points (Mean caregiver daily life stress: baseline = 6.06 (SD 2.98), 12 months: 5.21 (SD 2.97); Mean caregiver daily asthma stress: baseline = 4.35 (SD 3.24), 12 months: 4.30 (SD 3.12). Children were categorized with moderate persistent asthma (46%) and the majority had poorly controlled (54%) asthma. Over two-thirds of children had an asthma ED visits within the prior 3 months. Atopy was positive in 83% of children. Indoor exposure to mice and cockroach was high (mice: 47%, cockroach: 32%) and fall was the primary season of enrollment (Fall: 34.7%, Winter: 25.6%, Spring: 20.3%, and Summer: 19.4%).

Description of child secondhand smoke exposures

As seen in Table 2, mean child cotinine levels were high and did not differ over the 12-month study period. Over 50% children tested positive for SHS exposure at each time point (baseline: 54.5%; 12 months: 58.3%). Correlation between baseline and 12 month cotinine levels was moderate (Pearson $r = 0.37$, $p < 0.001$). Rate of maternal smoking in the home was consistent over the 12 months (baseline: 42.9%, 12 months: 44.2%). Child cotinine levels significantly increased with increased number of household smokers at baseline (mean, SD: no smokers: 1.89 (4.2) ng/mL, 1 smoker: 3.07 (4.1) ng/mL,

Table 2. Characteristics of child SHS exposure at baseline and 12 months.

Characteristic	Baseline <i>n</i> = 222 <i>n</i> (%)	12 months <i>n</i> = 204 <i>n</i> (%)
Cotinine level (ng/mL)		
Mean (SD)	2.84 (4.6)	2.83 (4.03)
Median	1.27	1.41
Range	0-38.8	0-28
Cotinine ≥ 1 ng/mL		
Positive SHS exposure	121 (54.5)	119 (58.3)
Number of smokers in the home	<i>n</i> = 219	<i>n</i> = 195
None	105 (47.9)	109 (55.9)
1	72 (32.9)	66 (33.8)
2 or more	42 (19.2)	20 (10.3)
Mother smokes in the home	<i>n</i> = 114 homes with smokers	<i>n</i> = 86 homes with smokers
(Yes)	49/114 (42.9)	38/86 (44.2)
Home smoking restrictions	<i>n</i> = 219	<i>n</i> = 189
No restrictions	18 (8.2)	11 (5.8)
Partial restrictions	39 (17.8)	23 (12.2)
Total home smoking restriction	162 (74.0)	155 (82.0)
Car smoking restrictions	<i>n</i> = 217	<i>n</i> = 191
No restrictions	17 (7.8)	11 (5.8)
Partial restrictions	21 (9.7)	23 (12.0)
Total car smoking restriction	179 (82.5)	157 (82.2)
E-cigarette use/vaping		
Yes	4 (1.8)	3 (1.6)

2 smokers: 5.82 (6.0) ng/mL, 3 smokers: 4.25 (2.7) ng/mL, ≥ 4 smokers: 4.10 (3.1) ng/mL; $F = 4.56$, $p = 0.002$). Use of E-cigarettes and/or vaping was very low (baseline: 1.8% and 12 months: 1.6%). Total home and car smoking bans were reported by most caregivers at both time points (total home smoking ban: baseline = 74%, 12 months = 82%; total car smoking ban: baseline = 83%, 12 months = 82%). Notably, child cotinine and caregiver daily life stress levels were not significantly correlated at baseline or 12 months (baseline: $r = 0.11$, $p = 0.10$; 12 months: $r = 0.06$, $p = 0.46$).

Impact of child SHS exposure on asthma health outcomes at 12 months

In the bivariate analysis, no significant associations were observed between positive SHS exposure (salivary cotinine ≥ 1.0 ng/mL) at 12 months and increased asthma healthcare utilization over the 12 months (≥ 1 ED visits: OR 1.06; 95% CI 0.59, 1.89), ≥ 1 hospitalization: OR .91; 95% CI 0.45, 1.82), limitation of activity: OR 1.16; 95% CI 0.91, 1.48) or use of rescue medication during the past 2 weeks: OR 1.10, 95% CI 0.88, 1.37). Figure 1 shows that at cotinine levels between zero and 2 ng/mL, the probability for high symptom days or nights was between 0.47 and 0.50. At cotinine levels > 2.0 ng/mL, a linear increase in the probability of high symptom days and nights was noted.

Factors associated with high day and nighttime symptom frequency at 12 months (unadjusted)

As seen in Table 3, children reporting symptoms in the fall season were almost three times more likely to

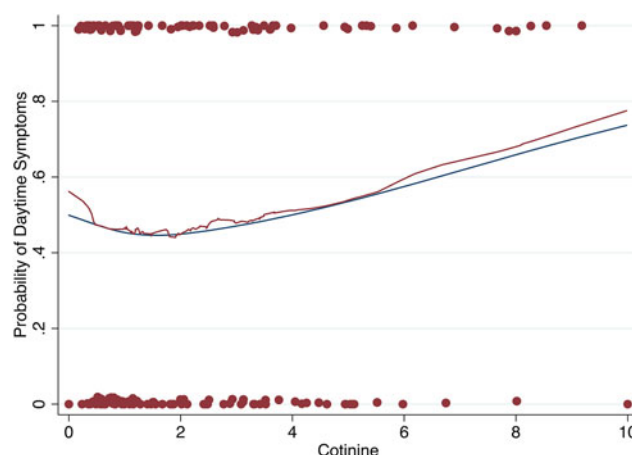


Figure 1. Presence of daytime symptoms (yes = 1, no = 0), jittered (adding random noise to data to prevent over plotting) for visual effect, with estimated probability of symptoms at 12 months across cotinine levels using lowest smoothing (red line) and a regression model with cubic spline terms for cotinine (blue line).

report increased symptom days as compared to children reporting symptoms during the summer months (the reference season). Additionally, mean caregiver daily life stress scores were significantly higher in children with increased symptom days (mean stress scores: ≤ 2 days = 4.67, SD 3.0 and > 2 days = 5.92, SD 2.7; $p = 0.003$) (Table 3). There was no association between higher symptom days and nights with intervention group status (INT vs. CON), cotinine level at 12 months or change in cotinine level between baseline and 12 months, type of car smoking restrictions, or positive child atopy. A trend was noted between partial home smoking

Table 3. Unadjusted analysis of factors associated with high day symptoms (>2 vs. ≤2 days over past 14 days) at the 12-month follow-up: *n* = 203.

Characteristic	OR (95% CI)	SE	<i>p</i> value
Intervention group status			
Intervention group	1.58 (0.90, 2.77)	0.45	0.12
Control group (reference)	—	—	
Change in cotinine from baseline to 12 months (<i>n</i> = 182)			
	1.02 (0.96, 1.09)	0.03	0.73
Cotinine status at 12 months			
Positive	1.27 (0.70, 2.29)	0.30	0.43
Type of home smoking restrictions ^a			
Partial restriction	1.06 (0.33, 3.42)	0.63	0.09
Total restriction	1.57 (0.56, 4.42)	0.83	0.39
No restriction (references)	—		
Type of car smoking restrictions ^b			
Partial restriction	2.44 (0.51, 11.62)	0.80	0.26
Total restriction	1.99 (0.51, 7.77)	0.70	0.32
No restriction (references)	—		
Season			
Fall	2.78 (1.16, 6.52)	1.16	0.01
Winter	1.66 (0.71, 3.87)	0.72	0.24
Spring	1.12 (0.45, 2.75)	0.52	0.81
Summer (references)	—		
Atopy			
Positive (>1 positive allergen test)	1.03 (0.47, 2.24)	0.40	0.94
0 Mean (SD) ANOVA			
<i>F</i> = 0.94, <i>df</i> = 1			
Child age (years)			
≤2 days/14 days	6.53 (2.7)		0.33
>2 days/14 days	6.15 (2.6)		
Caregiver daily life stress scores			
<2 days/14 days	4.67 (3.0)	<i>F</i> = 8.97, <i>df</i> = 1	
>2 days/14 days	5.92 (2.7)		0.003

^aTotal home restriction vs. partial/none: OR 1.20 (95% CI 0.56, 2.56) *p* = 0.64.^bTotal car restrictions vs. partial/none: OR 1.06 (95% CI 0.50, 2.26) *p* = 0.87.**Table 4.** Unadjusted analysis of factors associated with high night symptoms (>2 nights vs. ≤2 nights over the past 30 days) at 12 months follow-up; *n* = 202.

Characteristic	OR (95% CI)	SE	<i>p</i> value
Intervention group status			
Intervention group	1.11 (0.64, 1.94)	0.31	0.71
Constant group (reference)	—		
Cotinine change: baseline to 12 months (<i>n</i> = 182)			
	0.98 (0.93, 1.04)	0.03	0.58
Cotinine status at 12 months			
Positive	1.26 (0.70, 2.25)	0.30	0.44
Type of home smoking ban			
Partial restriction	0.47 (0.14, 1.56)	0.29	0.22
Total restriction	0.64 (0.23, 1.82)	0.34	0.41
No restriction (reference)	—		
Type of car smoking ban			
Partial restriction	1.02 (0.30, 3.47)	0.63	0.98
Total restriction	1.10 (0.46, 2.66)	0.45	0.83
No restriction (reference)	—		
Season			
Fall	1.43 (0.64, 3.22)	0.59	0.39
Winter	1.47 (0.62, 3.46)	0.64	0.38
Spring	1.41 (0.56, 3.52)	0.66	0.47
Summer (reference)	—		
Atopy			
Positive (≥1 positive allergen test)	0.65 (0.30, 1.42)	0.40	0.28
Mean (SD) ANOVA			
Child age (years)			
≤2 days/14 days	7.14 (2.8)	<i>F</i> = 15.27, <i>df</i> = 1	<0.001
>2 days/14 days	5.71 (2.4)		
Caregiver daily life stress scores			
≤2 days/14 days	4.37 (2.9)	<i>F</i> = 14.40	<0.001
>2 days/14 days	5.93 (2.8)	<i>df</i> = 1	

restrictions and higher symptom days as compared to no home smoking restrictions. Risk of indoor exposure to mice and/or cockroach was not

associated with level of symptom days (mouse exposure: OR 0.92; 95% CI 0.59, 1.44; cockroach exposure: OR 1.10; 95% CI 0.71, 1.69).

Table 5. Multivariable logistic regression model for high symptom days (>2 vs. ≤2 days over past 14 days)^a; *n* = 176.

Characteristic	OR (95% CI)	SE	Statistic Z statistic	<i>p</i> value
Intervention group status				
Intervention group	1.45 (0.77, 2.74)	0.47	1.14	0.25
Control group (reference)	—	—	—	—
Change in cotinine: baseline to 12 months	1.02 (0.97, 1.09)	0.03	0.91	0.36
Season				
Fall	2.54 (1.04, 6.22)	1.16	2.04	0.04
Winter	2.45 (0.92, 6.57)	1.23	1.79	0.07
Spring	1.05 (0.40, 2.74)	0.51	0.11	0.92
Summer (reference)	—	—	—	—
Caregiver daily life stress at 12 months	1.12 (1.00, 1.26)	0.06	1.96	0.05
Child age (years)	0.92 (0.81, 1.06)	0.06	−1.11	0.27
Type of smoking restriction in home				
Partial restriction	1.27 (0.30, 5.45)	0.94	0.32	0.75
Total restriction	2.05 (0.53, 7.99)	1.42	1.03	0.30
No restriction (reference)	—	—	—	—

^aWald $\chi^2=13.5$, $p=0.14$; the model includes all variables included in the table.

Higher night symptom frequency was significantly associated with higher caregiver stress and younger child age (Table 4). Intervention status (INT vs. CON), cotinine level, type of home or car smoking ban, season of symptom reports, and child atopy were not associated with level of night symptoms.

Risk of health, sociodemographic and SHS exposure factors in relation to high day and night symptom frequency (multivariable models)

Results of the final multivariable model for predicting high daytime symptoms are presented in Table 5. Children reporting asthma symptoms during the fall season were over two times more likely to report higher symptom days than children assessed in the summer (OR 2.54; 95% CI 1.04, 6.22, $p=0.04$), after controlling for intervention group status (INT vs. CON), change in cotinine over 12 months, caregiver stress, child age and home and car smoking restrictions. Further, reporting symptoms during the winter months showed a trend towards increased risk for high daytime symptoms when compared with reporting symptoms during the summer (OR 2.45; 95% CI 0.92, 6.57, $p=0.07$). Higher caregiver daily life stress was significantly associated with increased odds of high daytime symptoms (OR 1.12, 95% CI 1.00–1.26; $p=0.05$) after controlling for intervention group status, change in cotinine level over 12 months, season of reporting symptoms, child age and type of home smoking restrictions. Intervention group status was not associated with risk of high symptom days. As seen in Table 6, children who were younger and caregivers with higher daily life stress were significantly at risk to experience night symptoms after controlling for intervention group status, change in cotinine from baseline to 12 months, season of reporting symptoms

and type of home smoking restrictions. There was a trend noted for children residing in homes with a partial home smoking ban having higher symptom nights as compared to children living in homes with no smoking restrictions. Intervention group status was not associated with risk of experiencing night symptoms.

Multivariable models examining a higher daytime symptom level (≥ 4 days over the past 14 days) indicated comparable results to above reported results with the exception that total home smoking restrictions were associated with increased symptom days.

Discussion

Contrary to our primary hypothesis, we found no impact of SHS exposure on asthma symptom frequency at 12 months in a sample of low-income minority children with poorly controlled asthma. Yet, almost half of all children had objective evidence of SHS exposure at baseline and 12 months indicating the pervasiveness of SHS exposure in this group of high-risk children. Even in homes with partial home smoking restrictions, children experienced high nighttime asthma symptoms as compared to homes with no smoking restrictions. Although this is counterintuitive, it most likely reflects caregiver lack of understanding how or the struggle to enforce total home smoking restrictions even for parents of children with asthma [26]. Lack of control over all sources of the child's SHS exposure, i.e. visitors who smoke, SHS exposure occurring in public areas and adjacent multiunit homes, may explain the constant high SHS exposure in these high-risk children [27]. Implementing a home smoking ban may have been very stressful for the caregiver [28], who may ease up on smoking restrictions to placate all household

Table 6. Multivariable logistic regression model for high night symptoms (>2 nights vs. ≤2 nights over past 30 nights)^a; *n* = 176.

Characteristic	OR (95% CI)	SE	Statistic Z statistic	<i>p</i> value
Intervention group status				
Intervention group	1.05 (0.55, 1.99)	0.34	0.14	0.89
Control group (reference)	—	—	—	—
Change in cotinine from baseline to 12 months	0.97 (0.90, 1.03)	0.03	−0.93	0.35
Season				
Fall	1.14 (0.43, 3.01)	0.56	0.27	0.79
Winter	2.07 (0.71, 6.02)	1.12	1.34	0.18
Spring	1.66 (0.56, 4.88)	0.91	0.92	0.36
Summer (reference)	—	—	—	—
Caregiver daily life stress at 12 months	1.18 (1.05, 1.32)	0.07	2.89	0.004
Child age (years)	0.83 (0.73, 0.94)	0.06	−2.82	0.005
Type of smoking restriction in home				
Partial restriction	0.22 (0.05, 1.05)	0.18	−1.89	0.06
Total restriction	0.37 (0.09, 1.50)	0.26	−1.40	0.16
No restriction (reference)	—	—	—	—

^aWald $\chi^2 = 16.64$, *p* = 0.05. The model includes all variables listed in the table.

members. Residence in multiunit housing, including subsidized housing, often results in shared ventilation through hallways and ventilation systems allowing tobacco smoke to enter most housing areas [29]. This infiltration of passive SHS exposure may be contrary to the caregiver's smoking restriction preferences [30,31]. In a study of 1565 residents residing in multi-unit housing enforcing smoke-free home rule, 50% reported an intrusion of cigarette smoke in their housing unit [29]. Notably, home smoking restrictions for primarily low-income populations will be tested during the implementation of the 2018 HUD policy requiring public housing agencies to implement smoke-free policies [32].

In contrast to the lack of support for SHS exposure as a risk factor for increase asthma symptoms, caregiver daily life stress and symptoms in the fall season were significantly associated with higher risk for asthma symptoms days in children with poorly controlled asthma. Concerning caregiver daily stress, the identified sources of daily life stress include housing instability, food insecurity, poverty, and neighborhood violence [33,34]. Not only are caregivers overwhelmed by the chronicity of their daily stressors but also by the fear of their child struggling to breathe that may intensify their stress [26,27]. Interestingly, stress related to asthma care was consistently lower than daily life stress in this group of caregivers. Although caregiver asthma stress was moderately low, high caregiver life stress is speculated to diminish the caregiver's ability to provide effective asthma home management, i.e. poor symptom recognition, inconsistent medication administration or poor decision-making related to seeking ED treatment for acute asthma [12] all contributing to poorly controlled

asthma and adding to caregiver burden of asthma care.

Other environmental exposures may have had a higher impact on symptom frequency than SHS exposure in this group of children. Higher symptom reports during the fall season, as noted in our data, supports the "September asthma epidemic". This trend observed in children with asthma upon return to school is most likely due to increased exposure to viral illnesses and seasonal allergens [9,10]. In the current study, exposure to viral illnesses was not assessed; however, it may have influenced the high symptom days noted during the fall season. Positive allergen sensitization to common indoor and outdoor allergens was high. Although atopy was not associated with increased symptom frequency, this was most likely due to the high rate (83%) of atopy that may have limited our ability to detect a statistical difference between atopic and non-atopic children by level of symptom days. While exposure to mice and/or cockroach was high, these reported exposures were not associated with increased symptom frequency. Perhaps high indoor exposures to multiple irritants and allergens experienced by this group of children, limited our ability to distinguish the exposures that were most likely associated with higher symptom days. Last, younger children had a higher risk of nighttime symptoms. Because young children spend up to 90% of their time in the home as compared to school aged children [35] their exposure time is higher potentially resulting in increased symptom frequency as noted in our data. Stronger endorsement of effective strategies to reduce indoor irritant and allergen exposures should become routine during well and acute care visits for preschool children.

Notably, the environmental control behavioral educational/remediation intervention had no effect on decreasing symptom days or nights over the 12-month study period. The brief 3-month environmental control education/remediation intervention was likely insufficient for sustained reduction of asthma symptoms over 12 months in children with poorly controlled asthma. Targeting multiple asthma triggers in the home including SHS, pest, mold exposure, viral illnesses, and seasonal allergens was likely overpowering to remediate all exposures during a few home visits. The intensity of the environmental control component of the intervention was likely insufficient when compared to prior successful home environmental control interventions such as the Inner-City Asthma Study that provided HEPA air and HEPA vacuum cleaners with ongoing integrated pest management services [36]. However, identification of indoor SHS exposure for children with poorly controlled asthma using biomarkers is a strength of our study. This clinical data could be used to provide objective feedback to parents about their child's SHS exposure levels and inform step-wise therapy. This is especially important for inner-city children with high ED utilization and who were the focus of this study.

Our study should be considered in the context of several potential limitations. SHS exposure patterns for the child in the home and car were based on caregiver report and subject to recall bias or social desirability to conceal all sources of SHS exposure. Not all sources of SHS exposures were assessed including public places, relatives or social network homes. Although cotinine levels were measured, the cotinine levels reflect a "snapshot" of recent SHS exposure (e.g. 24 h) and may account for the lack of association between cotinine and symptom frequency. Additionally, since type of housing was not ascertained, residing in multi-unit housing with shared ventilation [29] may have resulted in an overestimate of SHS exposure in the home. Several factors associated with the collection, storage and analysis of salivary cotinine may resulted in over or under estimates of the cotinine levels. However, our 55–58% rate of positive cotinine levels over the 12 months is consistent with rates reported in prior studies (43–60%) from comparable samples of inner-city children with asthma [15,37]. Generalizability of our results is limited in that we purposely recruited children with poorly controlled asthma and a high frequency of ED visits for our clinical trial in order to maximize our ability to detect a difference in asthma morbidity with our intervention. By study design and ethical

considerations, our control group received asthma education and support in the home as an attention control group and not usual asthma care. This may have resulted in a significant conservative bias in our analyses, since control group caregivers may have benefited from the receipt of basic environmental control education. Despite these limitations, a major strength of this study was the objective measurement of SHS exposure using salivary cotinine and the ability to capture SHS exposure longitudinally over 12 months.

Conclusions

In summary, there was no impact of SHS exposure on increased frequency of asthma symptoms in children with poorly controlled asthma. However, high caregiver daily life stress and experiencing symptoms during the fall season were significantly associated with increased symptom days. Close monitoring of symptoms during the fall season and intervening on caregiver stress may result in decreased symptom days in high-risk children with asthma.

Acknowledgements

We appreciate Mary Gates and Amanda Manning for their work on this project and the families for their participation in the study.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

Funding

This work was supported by the National Institute of Nursing Research (NINR), NIH [Grant number R01NR013486]. The study is registered with ClinicalTrials.gov with number NCT01981564. Our publication was made possible by the Johns Hopkins Institute for Clinical and Translational Research (ICTR) that is funded in part by Grant Number UL1 TR 000424–06 from the National Center for Advancing Translational Sciences (NCATS) a component of the National Institutes of Health (NIH), and NIH Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of the Johns Hopkins ICTR, NCATS or NIH.

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