Published in final edited form as:

Ann Allergy Asthma Immunol. 2016 May ; 116(5): 463–465. doi:10.1016/j.anai.2016.02.012.

Spit Matters: Salivary Cotinine Measurement for All Children with Persistent Asthma

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ClinicalTrials.gov:NCT01970085

Conflict of interest: none for all authors.

Author Contribution:

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Keywords

asthma; cotinine; second hand smoke exposure; children; inner-city

Despite awareness that second hand smoke (SHS) exacerbates asthma symptoms, over half of U.S. children with asthma are exposed to SHS¹ and the parent is the primary source of exposure.^{2,3} Explanations for failure to prevent SHS exposure in the home for children with asthma are multifaceted, not well understood and significant under reporting of SHS exposure occurs.⁴ Further, few providers use biomarkers, i.e. cotinine, as an objective measure of SHS exposure.⁵ There has been minimal effort to examine the factors associated with persistent SHS exposure in a high risk children with asthma. This study aimed to investigate the pattern and factors associated with persistent high cotinine concentrations in a sample of urban children with asthma who had frequent emergency department (ED) visits.

Participants were 116 children aged 3 to 12 years with persistent asthma and high ED utilization. All were enrolled in a RCT testing the effectiveness of a behavioral environmental control intervention.⁶ The Johns Hopkins Medical Institutional Review Board approved the study and written informed consent was obtained. Children were enrolled during an asthma ED visit and followed over 12 months (baseline, 6 and 12 months). Inclusion criteria were physician diagnosed persistent asthma, 2 or more ED asthma visits or 1 hospitalization/past 12 months and residing in local metropolitan area. Salivary cotinine testing, an established biomarker of tobacco smoke absorption with a half-life of 16–24 hours, was conducted at each time point and analyzed using an enzyme immunoassay analysis at the Johns Hopkins Institute for Clinical and Translational Research. SHS exposure was defined as a cotinine concentration ≥ 1.0 ng/ml. Concurrently, caregivers reported household smoking behavior, i.e. number and child relationship of every household smoker and type of home smoking restrictions (total, partial, none).⁷ Other child environments with potential SHS exposure were ascertained. Caregiver stress and healthcare utilization measures including number of asthma ED visits, hospitalizations, and primary care provider (PCP) visits reported over the past 3 months were asked. Pharmacy records were used to identify asthma medications dispensed over the prior 12 months.

Mean (SD) cotinine concentrations were examined across the three time points. Unadjusted analysis was limited to the 6 month time point due to lack of difference in mean cotinine levels between 6 and 12 months. Cotinine status (positive vs. negative) was compared using standard χ^2 tests and ANOVA. Logistic regression models were tested to predict a positive cotinine level at 6 months while adjusting for baseline cotinine status, number SABA fills, number of routine primary care visits for asthma over past 3 months, number of smokers in the home and caregiver daily stress. Two-sided tests were used and p values ≤ 0.05 were considered statistically significant.

Most children were male (63%), African American (95%), enrolled in Medicaid (96%), with a mean age of 6.3 (SD 2.7) years. Caregivers were single (75%), achieved a high school or more education (81.9%), unemployed (44%), with a mean age of 31.4 (SD 7.4) years. Caregiver daily stress was moderately high (mean: 5.8/10 (SD 2.9). Mean symptom days

over past 2 weeks and nights over past 4 weeks were high (5.7/14 days; 6.5/30 nights, respectively). Although 72% reported a total home smoking ban, over half of children had a positive cotinine concentration at each time point (baseline: 53/98 [54%], 6 months: 52/91 [57%] and 12 months: 51/91 [56%]). Cotinine testing identified 17/53 (32%) children with a cotinine concentration ≥ 1 ng/ml but who had no history of a smoker in the home. There was some bidirectional change in cotinine status between baseline and 6 months (positive baseline change to negative: 31%; negative baseline change to positive: 25%). Mean cotinine concentrations significantly increased from baseline to 6 months ($p=0.03$) but not between 6 and 12 months ($p=0.96$). (Figure 1). Factors significantly associated with 6 month positive cotinine (unadjusted analysis) included a higher baseline cotinine, higher mean controller and short acting beta agonist (SABA) fills, increased number of routine PCP and ED visits/past 3 months and increased number of household smokers. Maternal smoking, type of home smoking ban, caregiver stress and season of cotinine collection were not associated with a positive cotinine concentration at 6 months. Factors associated with a positive cotinine at 6 months in the final regression model were a positive baseline cotinine concentration (OR: 6.5; 95% CI: 2.3, 9.2) and an increased number of PCP visits/past 3 months (OR: 1.85, 95% CI: 1.0, 3.4) while controlling for number of SABA fills and smokers in the home.

This study confirms that SHS exposure is common among urban children with asthma⁸ with relative fluctuation in SHS exposure as evidenced by bidirectional change in cotinine levels at 6 months. Perhaps a low baseline (ED visit) cotinine that significantly increased at 6 months reflects some effort to reduce SHS exposure when a child experiences acute asthma symptoms. Yet, caregivers appear challenged to change long-standing behaviors, i.e. quit smoking and enforce a total home smoking ban. Prior reports indicate that child respiratory symptoms were not significantly associated with parental intention to quit smoking.⁹ Our findings indicate that children with a positive 6 month cotinine level had a mean of one PCP visit within the past 3 months indicating recent health care utilization, perhaps a missed opportunity for assessing SHS exposure. Our data suggest that relying on self-report of SHS exposure will misclassify approximately one-third of children as being non-exposed. Although several commercial laboratories provide salivary cotinine testing, few healthcare providers order cotinine tests primarily due a prior authorization requirement from some insurers and prohibitive patient cost (range \$91–\$131 per test).¹⁰ We advocate for a cotinine measurement of every child with persistent asthma during an acute or routine asthma care visit and promote expanding coverage by all insurers for cotinine testing in high risk children with asthma. Study limitations include lack of accounting for all SHS exposures, long term exposure reflected in a one-time salivary cotinine measurement and generalizability reflected in the high risk asthma inclusion criteria. Despite these limitations, the study suggests that using sequential salivary cotinine measurement reduces misclassification of children with asthma reportedly not exposed to SHS.

Acknowledgments

This study was funded by the National Institute of Nursing Research, NIH, grant number R01NR013486, Principal Investigator: Arlene Butz. This publication was made possible by the Johns Hopkins Institute for Clinical and Translational Research (ICTR) which 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. Last, we acknowledge the families for their time and support of this research.

Abbreviations

SHS second hand smoke

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Figure 1.
Mean ($\pm$ 95% CI) Cotinine Levels over 12 months.