Salivary Cotinine Levels in Children with Otolaryngologic Disorders

Christine M. Clark, BA[1]; Jillian N. Printz, BS[1]; Lauren E. Stahl, BS[2]; Brett E. Phillips, PhD[3]; Michele M. Carr, DDS, MD, PhD, FRCSC[2]

[1]Penn State College of Medicine, Hershey, PA
[2]Department of Surgery, Division of Otolaryngology-Head & Neck Surgery, Penn State Health, Hershey, PA
[3]Department of Surgery, Penn State Health, Hershey, PA

Introduction

Environmental tobacco smoke (ETS) exposure is correlated with a higher incidence of otitis media (OM) in children during the first three years of life.[1] ETS exposure has also been linked to recurrent tonsillitis and obstructive sleep apnea (OSA) in children.[2,3]

The goal of this study is to determine if elevated salivary cotinine levels are correlated with a higher incidence of recurrent tonsillitis or OSA requiring tonsillectomy. We also aim to compare the cotinine levels among these patients to those in healthy controls and children meeting criteria for tympanostomy tubes.

Methods

Subjects: Children under 14 years of age were enrolled in outpatient otolaryngology and general pediatrics clinics. Subjects were divided among three groups: Group 1 served as healthy controls. Group 2 was comprised of patients meeting criteria for tympanostomy tube insertion, and Group 3 consisted of patients meeting tonsillectomy criteria. A sample size of 110 children/group was used to detect a difference of 25% in incidence between the control group and each of the study groups with a power of 85% and an alpha of 0.05.

Data collection: Demographic data were collected during each subject's outpatient clinic visit. Saliva samples were obtained using SalivaBio Swabs and measured using a quantitative enzyme immunoassay (Salimetrics, PA). The assay's lower limit of sensitivity was 0.15 ng/mL, and all values below this cutoff were recorded as 0.0 ng/ml. A salivary cotinine concentration of 1.0 ng/ml or higher constituted secondhand smoke exposure.

Statistical analyses: Data analysis was performed in SPSS 22 (IBM, Armonk, NY). Kruskal-Wallis tests were used to compare the frequencies and skewed continuous data among the three groups. Mann-Whitney U testing was performed to make pairwise comparisons between each group.

Results

Demographics: 331 subjects were included. There was a significant age difference between the three groups, with younger subjects in Group 2 (mean: 4.1 years; p<0.001) compared to Groups 1 (6.7 years) and 3 (6.8 years). There were also significant differences in medical co-morbidities between groups, with a higher percentage of subjects with asthma in Group 3 (23.4%; p=0.010) compared to Groups 1 (8.3%) and 2 (17.9%). Subjects in Groups 2 (27.7%; p=0.003) and 3 (31.5%) compared to Group 1 (13.0%).

ETS exposure: There were no differences in ETS exposure by history, smoker's identity, salivary cotinine level, or frequency of positive cotinine results. The frequency of positive cotinine tests was greater than expected from the history provided by parents.

Among subjects with positive cotinine levels, 93 had no ETS exposure, and 64 had ETS exposure by history alone. The only significant difference between these groups was that the cotinine level was lower in children with no ETS exposure by history (**Table 1**).

Results (cont'd.)

Table 1. Positive salivary cotinine levels by environmental tobacco smoke exposure history

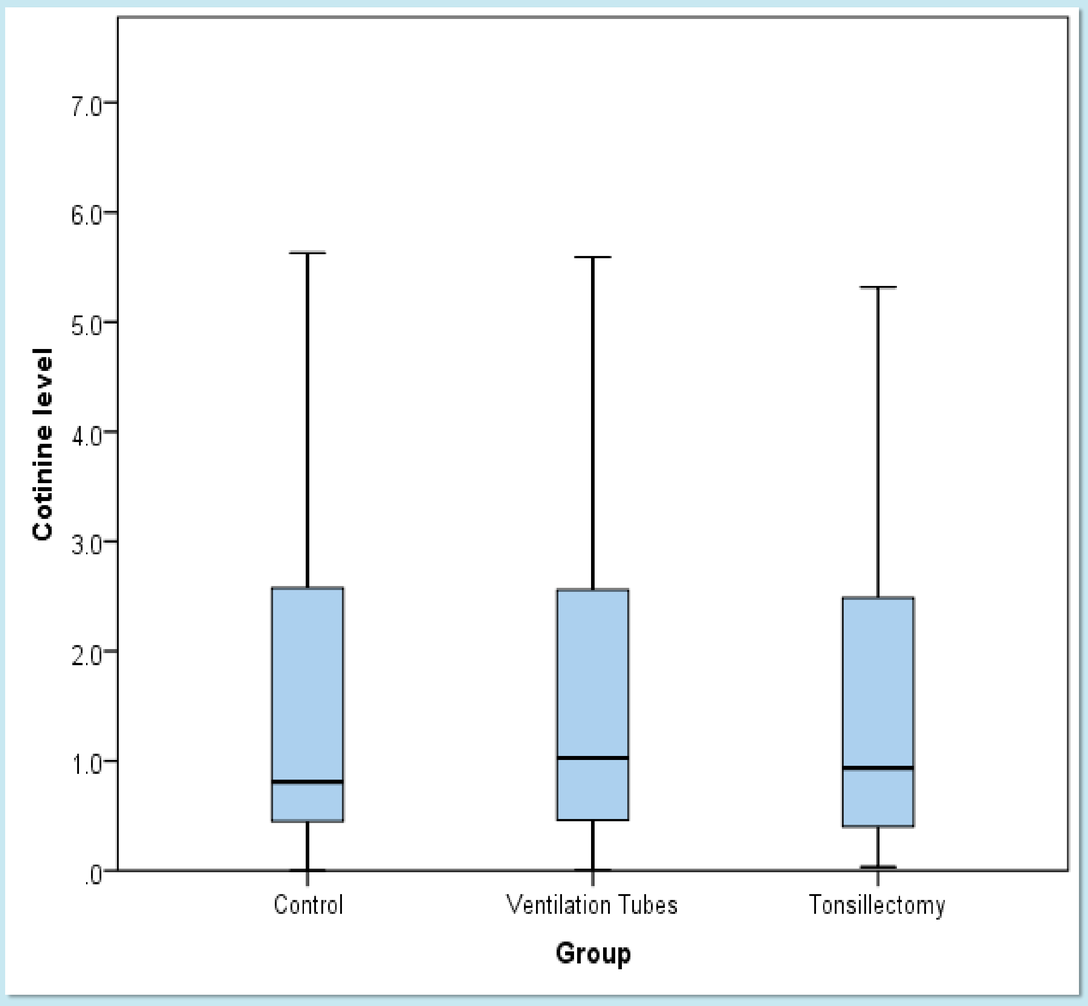
	Denied ETS exposure	Positive ETS exposure	P value
Group (N)	93	64	
Control	31	15	0.155
Tympanostomy tubes	36	22	
Tonsillectomy	26	27	
Adult providing history (N (%))			
Mom	79 (84.9)	58 (90.6)	0.742
Dad	10 (10.8)	3 (4.7)	
Other	4	3	
Age (years)	5.1	5.7	0.304
Average cotinine level (ng/ml)	3.65	6.6	0.006*

*Significant difference (p<0.05)

Table 2. Positive salivary cotinine levels within each group

	Control	Tympanostomy Tubes	Tonsillectomy
Positive salivary cotinine (%)	42.6	51.8	47.7

Figure 1. Salivary cotinine levels in each group



Discussion

- Cotinine provides an objective measure of ETS exposure that reflects recent ETS exposure of up to 4 days preceding sample collection[4]
- ETS exposure is an accepted risk factor for recurrent OM and OM with effusion
- Though previous studies have linked elevated serum and salivary cotinine with recurrent OM and OM with effusion, we found no significant differences in positive salivary cotinine levels between groups[5,6]
- The 5-10% difference we encountered is smaller than what has been previously reported and casts doubt on the importance of ETS in these otolaryngologic disorders
- We found that cotinine levels were more frequently positive than expected by history alone, which has important implications, as prior studies have shown an increased risk of respiratory complications in children with history of ETS exposure during the perioperative period[7]
- Our study is novel in that it is the first to relate salivary cotinine levels to otolaryngologic disorders in children
- Salivary cotinine measurements are easy to collect and have an available point of care, which may be of clinical utility

Conclusion

Children presenting for tonsillectomy are just as likely to have objective evidence of ETS exposure as children presenting for tympanostomy tube insertion. Whether this is a significant contributor to otolaryngologic disease in children is not clear from our results. About half of these patients have objective evidence of ETS exposure, twice as many as predicted by parental history. This can impact perioperative care since ETS can result in respiratory issues following general anesthesia, and it is important for clinicians to keep this in mind when managing these populations.

References

1. Etzel RA, Pattishall EN, Haley NJ, Fletcher RH, Henderson FW. Passive smoking and middle ear effusion among children in day care. *Pediatrics.* 1992; 90(2); 228-32.
2. Straight CE, Patel HH, Lehman EB, Carr MM. Prevalence of smoke exposure amongst children who undergo tonsillectomy for recurrent tonsillitis. *Int J Pediatr Otorhinolaryngol.* 2015; 79(2): 157-60.
3. Said G, Zalokar J, Lellouch J, Patois E. Parental smoking related to adenoidectomy and tonsillectomy in children. *J Epidemiol Community Health.* 1978; 32: 97-101.
4. Martínez-Sánchez JM, Sureda X, Fu M, Pérez-Ortuño R, Ballbé M, López MJ. Secondhand smoke exposure at home: assessment by biomarkers and airborne markers. *Environ Res.* 2014; 133: 111-6.
5. Strachan DP, Jarvis MJ, Feyerabend C. Passive smoking, salivary cotinine concentrations, and middle ear effusion in 7 year old children. *BMJ.* 1989; 298(6687): 1549-52.
6. Ilicali OC, Keleş N, Değer K, Sagun OF, Güldíken Y. Evaluation of the effect of passive smoking on otitis media in children by an objective method: urinary cotinine analysis. *Laryngoscope.* 2001; 111(1): 163-7.
7. Skolnick ET, Vomvolakis MA, Buck KA, Mannino SF, Sun LS. Exposure to environmental tobacco smoke and the risk of adverse respiratory events in children receiving general anesthesia. *Anesthesiology.* 1998; 88(5): 1144-53.

Funding

Supported by a grant from the Groff Foundation

PennState College of Medicine