

A Cross-Sectional Study of Medication-Related Factors and Caries Experience in Asthmatic Children

Michael Milano, DMD¹ Jessica Y. Lee, DDS, MPH, PhD² Katherine Donovan³ Jung-Wei Chen, DDS, MS⁴

Abstract

Purpose: The purpose of this study was to examine the relationship between the specific types of medication, length of use, frequency of use, and dosing time of day on the dental caries of children diagnosed with asthma.

Methods: Using a patient list from a previous study, surveys were mailed to the parents of 179 asthmatic children. The survey itself consisted of a table that asked 4 questions: (1) What combination of asthma medications was used by the subject? (2) How long were the medications used? (3) How often were the medications used? (4) What time of day were the medications used?

Results: Of the 179 surveys that were mailed out, 156 were returned. Children who used their medication greater than twice daily were significantly more likely to experience dental disease in both the primary (odds ratio [OR]=2.56, 95% confidence interval [CI]=1.45-6.29) and mixed dentitions (OR=3.56, 95% CI 2.45-5.94).

Conclusions: Increased frequency of asthma medication use was associated with increased likelihood of caries experience. The time of day asthma medication was used was associated with increased likelihood of caries experience in children in the primary dentition. Duration of asthma medication use was associated with a decreased likelihood of caries experience in children in the mixed dentition. (Pediatr Dent 2006;28:415-419)

KEYWORDS: DENTAL CARIES, CHILDREN, ASTHMA

Received January 26, 2006 Revision Accepted May 16, 2006

Asthma is defined as an inflammatory disorder of the bronchioles, in which contractions of the bronchial smooth muscle and increased mucous secretion lead to reversible airway obstruction in the patient. These asthmatic episodes can be evoked by genetic or a number of different environmental stimuli and are characterized by: (1) wheezing; (2) coughing; (3) shortness of breath; and/or (4) chest tightness.¹ Often starting in early childhood, bronchial asthma is a growing public health concern, affecting 100 to 150 million people worldwide.² With the exception of dental caries, asthma is the most common chronic childhood disease in the United States, affecting 5% to 10% of all children.³

As the prevalence of asthma rises in the pediatric population, it is necessary to examine how this disease affects other areas of health care, most notably oral health. In recent years, the correlation between asthma and oral health has been evaluated, producing varying results. A number of studies have found asthmatic children to have higher caries rates than nonasthmatic children,⁴⁻⁸ while others have not.⁹⁻¹¹

The increased risk of dental caries in asthmatic children is most often associated with the decrease in salivary flow and increase in lactobacilli and *Streptococcus mutans* due to medication, as explained by Ryberg et al.^{7,8,12} The flow rates of whole and parotid saliva in asthmatic children treated with β_2 agonist inhalers were 26% ($P<.05$) and 36% ($P<.05$) lower, respectively, compared to the control group. This diminished flow rate jeopardizes the protective ability of saliva to clear the oral cavity of fermentable substance and decreases its buffering capacity.

Kargul et al found that, in asthmatic children 30 minutes after treatment with a β_2 agonist inhaler, there was a significant decrease in pH to below the critical value of 5.5 for enamel demineralization in saliva ($P<.001$).¹³ In

¹Dr. Milano is clinical associate professor and graduate program director, Department of Pediatric Dentistry, ²Dr. Lee is assistant professor, Departments of Pediatric Dentistry and Health Policy, and ³Ms. Donovan is fourth-year undergraduate student, School of Public Health, all at the University of North Carolina at Chapel Hill, Chapel Hill, NC; ⁴Dr. Chen is clinical assistant professor, Department of Pediatric Dentistry, University of Texas Dental Branch at Houston, Houston, Tex.
Correspond with Dr. Milano at Michael_Milano@dentistry.unc.edu

a 4-year follow-up study, Ryberg noted that asthmatics treated with β_2 agonist inhaler had a significantly higher DFS score (mean=17.6 \pm 9.4) compared to the control group (mean=11.9 \pm 7.9; $P<0.01$).⁸ Similarly, in a cohort study of 3- to 7-year-old asthmatic children receiving both inhaled β_2 agonist and inhaled corticosteroids, the relative risk of developing new caries lesions in permanent teeth was 1.62 (95% confidence interval (CI)=1.03-2.56; $P=.04$), although no increased risk was determined in the primary dentition.⁵

Reddy et al, however, found a significant difference in both the primary ($P<.05$) and mixed dentitions ($P<.009$) of asthmatic children treated with various anti-asthma medications.⁴ Reddy et al also illustrated the statistically significant association between increasing prevalence of caries with increasing severity of asthma, most likely due to the increased dosage and frequency of medication required to treat more severe asthma.⁴ A significant difference in mean dmfs ($P<.01$) and dmft ($P<.05$) in the primary dentition and dmfs and DMFS in the mixed dentition of asthmatic children when compared to a control group was displayed by Milano in 1999. No significant difference was found, however, in dmft and DMFT of the mixed dentition.⁶

By comparison, Bjerkeborn et al found only a slight increase in the prevalence of caries and gingival bleeding in asthmatic children treated with β_2 agonist inhalers, although the increase was not statistically significant.⁹ Similarly, a population-based case-control study using data from the Third National Health and Nutrition Examination Study did not recognize a significant increase in df/DMF scores in asthmatics compared to their controls. NHANES III, however, did not report information on medication dosage or compliance.¹⁰

Adequate management of asthma is often achieved through continuous pharmacotherapy. The complexity of asthma and asthmatic stimuli often leads to an individualized disease management plan for each patient. Due to varying results of medications on individual patients, bronchodilators, inhaled corticosteroids, and/or cromolyn and nedocromil are often used in combination.

Bronchodilators and the use of β_2 agonist inhalers or theophylline inhalers aim to control an asthmatic episode before exposure to stimuli or the onset of symptoms. β_2 agonist inhalers, usually containing an aerosol such as albuterol, are prescribed to control acute asthmatic attacks quickly. Inhaled corticosteroids like prednisone are prescribed to control a higher severity of asthma, while cromolyn sodium and nedocromil are used in preventive therapy rather than to combat an attack.¹

The differences in the previous studies and their findings on the relationship between asthma and dental caries can be partially attributed to the different types of pharmacotherapy used during treatment of the patients. While it is evident that there may be an association between prevalence of dental caries in asthmatic patients, the individualistic nature of asthma poses the question of which combinations of asthma medications, if any, are attributable to increased caries risk.

This study's purpose was to examine the relationship between the specific types of medication, length of use, frequency of use, and dosing time of day on the dental health of children diagnosed with asthma.

Methods

Using a patient list from a previous study which examined the caries rate in asthmatic children,⁶ surveys were mailed to the parents of 179 asthmatic children. These children were active dental patients at the Postgraduate Pediatric Dentistry Program of the University of Texas Health Science Center at Houston, and had participated in the previously cited study. In addition to the survey, a cover letter describing the study was also mailed to the parents. By returning the survey, the parents gave consent to use the information provided within the context of the study. This study was approved by the Institutional Review Board of the University of Texas Health Science Center at Houston and was funded by a pilot research grant through the University of Texas Dental Branch at Houston.

The survey and cover letter was written in both English and Spanish, with all of the parents receiving both versions. The survey was mailed to the study participants within 30 days of completion of the previously cited study.⁶ Included in the survey mailing was a self-addressed stamped envelope to be used to return the completed survey. A second mailing was done to reach nonresponders. The survey itself consisted of a table of 9 asthma medication choices and asked 4 questions:

1. What combination of asthma medications were used by the subject?
2. How long were the medications used?
3. How often were the medications used?
4. What time of day were the medications used?

In addition, each of the questions had answer choices for the parents to choose from. For example, the question that asked what time of day the medication was used had the answer choices of "morning," "afternoon," "evening," and "bedtime." Prior to its use, the survey instrument was reviewed by the grant committee of the University of Texas Dental Branch at Houston that helped to fund this project.

Once the completed survey was returned, it was paired with the information used in the first study and previously recorded from the patient's dental chart. The information specifically included the patient's: (1) age; (2) gender; and (3) ethnic group. Also, decayed, missing, or filled teeth and surfaces scores were recorded for the primary (dmft, dmfs) and the permanent (DMFT, DMFS) dentitions.

Variable definitions

The principal outcome variable was caries experience—defined as decayed, missing, and filled surfaces/teeth (dmfs[t]/DMFS[T]) that were collected previously from the patients' dental records. The missing (m/M) component of the scores included only those teeth that were extracted due to dental caries and not due to exfoliation.

Table 1. Medication Use among Asthmatic Children

	Primary dentition n=102%		Mixed dentition n=52%	
Medication types				
Albuterol only	76	73	40	77
Albuterol and Intal	16	15	4	8
Albuterol, Intal, and prednisone	12	12	8	5
Medication use duration (ys)				
<1	8	8	4	8
1 to <2	20	19	16	31
2 to <3	12	12	8	15
3 to <4	20	19	4	8
4-5	12	12	0	0
>5	32	31	20	39
Frequency of medication use				
1x/daily	16	15	8	15
2x/daily	36	35	24	46
3x/daily	32	31	12	24
≥4x/daily	20	19	8	15
Time of medication use				
Morning only	4	4	4	8
Afternoon only	8	8	4	8
Morning and afternoon	8	8	8	15
Bedtime only	4	4	4	8
Other combination	80	76	32	61
Sociodemographic characteristics				
Race (African American)	60	58	28	54
Ethnicity (Hispanic)	44	42	24	46
Gender (female)	28	27	16	31
Age in mos (mean)	77		97	

Four asthma-related explanatory variables were used: (1) medication types; (2) duration of medications used; (3) daily frequency of medications used; and (4) time of day when medications were used. To facilitate interpretation of regression estimates, responses were dichotomized. The responses to medications type used were grouped into 2 categories:

1. 1 medication (albuterol); or
2. more than 1 medication (albuterol plus 1 or more other medication).

Duration of medication used was grouped into: (1) <2 years; and (2) ≥2 years. Daily frequency was grouped into: (1) <2 times daily; and (2) ≥2 times daily. Time of day the medication was used was grouped into:

1. in the morning and/or afternoon only; and
2. evening and bedtime in addition to morning and/or afternoon.

An additional 3 sociodemographic explanatory variables were also included in the analysis: (1) patient's age in months; (2) race/ethnicity; and (3) gender.

Data analysis

Descriptive statistics reporting percentage frequency distributions for sociodemographic data were run using SPSS statistical software version 13.0 (SPSS Inc, Chicago, Ill). After an examination of bivariate associations of explanatory variables and dental caries experience (dmfs/DMFS), logistic regression models were developed to test the effects of asthma medication type, duration of use, frequency, and time of day on dental caries experience. Multivariate logistic regression models were used to obtain regression parameter estimates and their variances.

Results

Of the 179 surveys that were mailed, 156 were returned—yielding an overall response rate of 87% (104 for children in primary dentition and 52 for children in mixed dentition). No attempt was made to examine the characteristics of the nonresponders. The results for the children in primary and mixed dentitions are reported separately.

Primary dentition

One hundred four children were included in the evaluation of the primary dentition. The descriptive results are presented in Table 1. The majority of the children in this study's sample were African American (58%) and male (73%). Forty-two percent were of Hispanic ethnicity. The average age of the sample was 77 months (range=31-141±27.1 SD). The most common medication used was albuterol only (73%), while the other 27% used a combination of albuterol and other medications. Nearly one third of the children had been on asthma medication for greater than 5 years (31%), and the majority used their medications more than twice daily (85%). In terms of caries rates, 34% of the children had no disease reported while 66% had at least 1 decayed, missing, and filled surface (dmfs). The average dmfs was 13.4 (range=0-47±15.9 SD).

Following analysis of descriptive results and examination of the distribution, the explanatory variables were dichotomized from the continuous summary scores. For example, due to the skewed distribution of dental caries experience, the measure was dichotomized into no caries experience (dmfs/DMFS=0) and caries experience (dmfs/DMFS>0). Results of the logistic regression analysis are presented in Table 2. Three of the predictor variables were significant ($P<.05$), and 1 was not statistically significant ($P=.054$). Those children who used their medication greater than

Table 2. Results of Logistic Regression Analyses of Asthma Medication Use and Dental Caries

Variables	Primary dentition		Mixed dentition	
	Odds ratio	95% CI	Odds ratio	95% CI
Intercept				
Medication type	1.10	1.02-3.96	1.25	1.12-2.56
Duration of medication use	1.25	0.50-1.45	0.60*	0.30-1.65
Frequency of medication use	2.56*	1.45-6.29	3.56*	2.45-5.94
Time of day of medication use	0.86	0.41-1.52	0.97	1.12-2.78
Gender	2.12*	1.13-3.96	3.12*	1.10-5.67
Race/ethnicity	1.37	0.78-2.42	1.07	0.84-2.15
Age	N/A (linear measure)		N/A (linear measure)	

*Significance level= $P < .05$.

twice daily were more likely to experience dental disease (odds ratio [OR]=2.56; 95% confidence interval [CI]=1.45-6.29). Time of use was also not statistically significant, and children who used their medication in the morning or afternoon only were less likely to have experienced dental disease (OR=0.86; 95% CI=0.41-1.52). Age and gender were also significant in this study's model ($P < .05$).

Mixed dentition

Fifty-two children were included in the analysis for the mixed dentition. The descriptive results are presented in Table 1. The majority of the children in this study's sample were African American (53%) and male (69%). Forty-six percent were of Hispanic ethnicity. The average age of the sample was 97 months (range=58-141±21.8 SD). The most common medication used was albuterol only (77%), while the other 23% used a combination of albuterol and other medications. Nearly one third of the children had been on asthma medication for greater than 5 years (39%), and the majority used their medications greater than twice daily (85%). In terms of caries rates, 23% of the children had no disease reported while 72% had at least 1 decayed, missing, filled surface (dmfs/DMFS). The average dmfs/DMFS was 17.5 (range=0-48±15.1 SD).

Results of the logistic regression analysis are presented in Table 2. Four of the predictor variables were significant ($P < .05$). Those children who used their medications for longer than 2 years were less likely to have dental caries (OR=0.60; 95% CI=0.30-1.65). Additionally, children who used their medication greater than twice daily were more likely to experience dental disease (OR=3.56; 95% CI=2.45-5.94). Age and gender were also significant in this study's model ($P < .05$).

Discussion

This study's major finding was that children who take their asthma medications more frequently are at least 2 times

more likely to experience dental caries. The authors also found that, for children in the mixed dentition, duration of medication use decreased the risk of dental caries. Previous studies examining dental caries risk and asthma have reported mixed results.^{6,9,13} Because the management of asthma is complex and requires planning, individualized factors—such as type of medication used, frequency, and time of day—may play a very important role in dental caries risk. This is the first known study to examine such factors.

The AAPD Caries Risk Assessment Tool¹⁴ (CAT) stipulates that children with chronic conditions and who are taking medications

may be at higher risk for dental disease. This study's findings substantiate this element of the CAT for children taking asthma medications.

All children examined in this study were receiving albuterol, a β_2 agonist, either alone or in combination. The effect of β_2 agonists on decreased salivary flow, a factor in caries formation, is supported by this study's results.⁷ Furthermore, Ryberg et al showed a positive relationship between decreasing saliva secretion rate and an increased dosage of β_2 agonists.¹² As illustrated in this study, children who medicated more frequently, therefore exposing their teeth to a higher dosage over time, were more likely to experience dental caries. Similarly, a previous study significantly linked the increased severity of asthma, which requires greater medication to control, to increased caries prevalence.⁴

The relative difference between caries prevalence in primary and mixed dentitions, as seen in this study's results, has been demonstrated in previous studies. Reddy et al found an increasing prevalence of caries when examining children with primary (70%), mixed (78%), and permanent dentitions (83%), respectively.⁴ The higher risk of caries in the more developed permanent dentition compared to primary dentition is also shown by Wogelius et al.⁵ Although Wogelius et al found that children taking a β -agonists and inhaled corticosteroids had a relative risk of caries in permanent teeth of 1.62 ($P = .04$), no significant risk for caries was shown in the primary dentition.⁵

Although an association was demonstrated, time of day was not significant in the primary dentition; children medicating in the morning or afternoon showed an OR of 0.86 ($P = .54$). One explanation for this could be that medication taken in the evening, before bed, and without rinsing could pose a greater risk for caries since salivation decreases during the night—thereby diminishing the protection against the medication.⁴ This evening dosing time was seen regularly by Reddy et al and, due to lack of instruction of the patient

and parent, little to no oral hygiene was performed after the medication.⁴

It is possible that several of this study's asthma medication variables may be, in fact, measuring interaction effects. For example, frequency and time of day may have some overlap (eg, children who take their medications in the morning and afternoon take their medication twice a day). This study's sample was too small to test these interaction effects, but it should be taken into consideration with future work on larger populations.

The clinical implications of these results are important for the practicing dentist. In both the primary and mixed dentition there was a significant positive correlation between daily frequency of medication use and caries. Although there may be various physiological explanations, for the practicing clinician these results clearly indicate that frequency of asthma medication use must be elucidated so that a proper caries risk assessment can be performed. A child who uses asthma medications more than twice a day is at a higher risk for dental caries and will need a different prevention program than a nonasthmatic child. This individualized program may include: (1) brushing after medication use; (2) daily fluoride rinses; or (3) more frequent recall visits. This more aggressive prevention program, however, may not be needed permanently since this study's results also show that there is a decrease in caries risk in children who have used asthma medications for more than 2 years in duration.

This study's results should be considered in light of a few study limitations. First, results are based on a self-completed questionnaire and, therefore, all responses are subject to self-reporting bias and recall bias. Another limitation is that the study uses a cross-sectional design. Thus, statistical associations between the medication frequency, duration and timing, and dental caries may not be causal and will need confirmation in longitudinal studies. The temporal nature of the caries process was one of the major difficulties encountered in this study and could not adequately be addressed in a "one-time snap shot" or cross-sectional manner. A longitudinal study should begin with children newly diagnosed with asthma and follow them through for a period of time to test the development of dental disease. Lastly, the results might not have external validity. Results are based on a convenience sample of patients from the Postgraduate Pediatric Dentistry Program of the University of Texas Health Science Center at Houston and they may not be representative of a national sample.

Conclusions

This investigation examined individual factors associated with increased caries experience in a cross-sectional sample of asthmatic children. Based on this study's results, the following conclusions can be made:

1. Increased frequency of asthma medication use was associated with increased likelihood of caries experience.
2. Time of day of asthma medication use was associated with increased likelihood of caries experience in children in the primary dentition, but this could have an interaction effect with frequency of medications used.

3. Duration of asthma medication use was associated with decreased likelihood of caries experience in children in the mixed dentition. This may reflect better disease management.

References

1. Steinbacher DM, Glick M. The dental patient with asthma. An update and oral health considerations. *J Am Dent Assoc* 2001;132:1229-39.
2. World Health Organization. Bronchial asthma. Available at: "<http://www.who.int/mediacentre/factsheets/fs206/en/>". Accessed November 26, 2005.
3. Betz CL, Sowden LA. Asthma. In: Schreffer S, ed. *Pediatric Nursing Reference*. 3rd ed. St Louis, Mo: Mosby-Year Book Inc; 1996:25-8.
4. Reddy DK, Hedge AM, Munshi AK. Dental caries status of children with bronchial asthma. *J Clin Pediatr Dent* 2003;27:293-6.
5. Wogelius P, Poulsen S, Sorensen HT. Use of asthma-drugs and risk of dental caries among 5- to 7-year-old Danish children: A cohort study. *Community Dent. Health* 2004;21:207-11.
6. Milano M. Increased risk for dental caries in asthmatic children. *Texas Dent J* 1999;116:35-42.
7. Ryberg M, Moller C, Ericson T. Effect of Beta 2-adrenoceptor agonists on saliva proteins and dental caries in asthmatic children. *J Dent Res* 1987;66:1404-6.
8. Ryberg M, Moller C, Ericson T. Saliva composition and caries development in asthmatic patients treated with Beta 2-adrenoceptor agonists: A 4-year follow up study. *Scand J Dent Res* 1991;99:212-8.
9. Bjerkeborn K, Dahllof G, Hedlin G, Lindell M, Moeder T. Effects of disease severity and pharmacotherapy of asthma on oral health in asthmatic children. *Scand J Dent Res*. 1987; 95:159-64.
10. Shulman JD, Taylor SE, Nunn ME. The association between asthma and dental caries in children and adolescents: A population-based case-control study. *Caries Res* 2001;35:240-6.
11. Meldrum AM, Thomson WM, Drummond BK, Sears MR. Is asthma a risk factor for dental caries? Findings from a cohort study. *Caries Res* 2001;35:235-9.
12. Ryberg M, Moller C, Ericson T. Saliva composition in asthmatic patients after treatment with two dose levels of a Beta 2-adrenoceptor agonist. *Arch Biol* 1990;35:945-8.
13. Kargul B, Tanboga I, Ergeneli S, Karakoc F, Dagli E. Inhaler medicament effects on saliva and plaque pH in asthmatic children. *J Clin Pediatr Dent* 1998;22:137-40.
14. American Academy of Pediatric Dentistry. Caries Risk Assessment Tool. Available at: "http://www.aapd.org/media/policies_guidelines/p_cariesriskassess.pdf". Accessed April 27, 2006.