

Original Article

The Impact of Anti- Asthmatic Medications On Salivary pH And Dental Caries Pattern In A Group of Egyptian Children With Bronchial Asthma: A Cohort Study

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Abstract

Aim:The study aimed to assess the oral condition in a group of Egyptian children with bronchial asthma in terms of salivary pH and dental caries pattern. And, assessment of the medications taken by those children (Aironyl and Apidone) in terms of pH and total sugar content.

Subjects and methods:A sample of 60 children was divided into two groups (30 asthmatics ,30 asthmatic-free). A questionnaire was used to record history of asthma, snacking habits and frequency of tooth brushing. Dental caries surface index was measured using DMFs/defs index. The saliva samples were collected for measuring salivary pH. Anti-asthmatics (Aironyl and Apidone) were evaluated in terms of pH and total sugar content

Results:The asthmatics had a significantly higher value regarding (defs) than the control ($p<0.001$). Concerning the pH value, the asthmatics had a significantly lower value than the control($p<0.001$).But there was no significant difference between both groups regarding DMFs ($p=0.260$). Both drugs (Apidone and Aironyl) are acidic where their pH values are 5.3 and 5.1 respectively. While, the total sugar content of Apidone is higher than Aironyl as the values are 17g% and 0.5g% respectively.

Conclusions: Asthmatic children have more caries experience than healthy controls. Salivary pH value is less in asthmatics than controls.

Key words: Bronchial Asthma; Anti-asthmatic medications; Salivary pH; Dental caries

Introduction

Asthma is a chronic inflammatory condition characterized by an obstruction of the airflow¹.

Asthma is a significant public health issue with global variations in incidence and severity².

The aim of asthma treatment is to reduce symptoms while maintaining normal lung function and preventing permanent changes in the airways³.

Long-term treatment is needed for children with chronic medical conditions. As a result, they are at an increased risk of dental diseases in general, and dental caries in particular⁴. This increased risk of caries is either a result of their disease or as a side-effect of their drugs.

Some authors suggest that children with asthma showed lower salivary flow rate and pH than healthy one⁵. Tooth demineralization is worsened by a low salivary pH. Reduced salivary flow rate was found to be linked to lower salivary pH as well⁶.

In Children, consuming sweetened drugs causes plenty of oral health problems⁷. The amount of sucrose in the drug, its acidity, and the person's salivary flow rate and buffering efficiency are all variables to consider when assessing the drug's cariogenicity⁸.

Subjects and Methods

The study consists of clinical part and Invitro part for analysis of some drugs used in treatment of asthma.

Trial Registration

ClinicalTrials.gov ID: NCT03877874

Ethical approval

The Research Ethics Committee at the Faculty of Dentistry, Cairo University, Egypt, granted ethical approval. **Code number (19-6-6)**.

Clinical part:

The study design was a Retrospective Cohort study. The sample size calculation was approved by **Medical Biostatistics Unit (MBU) at Faculty of dentistry, Cairo University**. The sample was (60) child i.e. (30) for each group. **Group (A)**; Asthmatic group selected from Abu El-Reesh Japanese

Hospital for Children's Asthma and Allergy Outpatient Clinic. **Group(B)**; Asthmatic-free control group picked from the Pediatric Dentistry and Dental Public Health Department of Faculty of Dentistry, Cairo University.

Inclusion criteria:

-Egyptian children aged 6-12 years old previously diagnosed with Bronchial asthma, taking regular medications for the treatment of asthma for at least 1 year back and didn't have any other systemic diseases to be included in group(A).

-A matched group of healthy asthmatic-free Egyptian children to be included in group(B).

1-Questionnaire items:

A questionnaire chart was used to record the personal data, parameters of the asthmatic medications (Duration, Dose, and Frequency of Drug Administration), snacking habits (Type, Frequency of consumption), frequency of tooth brushing, the use of mouth wash and flossing.

For recording the snacking habits and its potential cariogenicity, we used a scoring system designed by⁹. The diet's cariogenic potential was determined as follows:

- Based on its putative cariogenicity, each carbohydrate was given an arbitrary value as follows:

○ Sugared Soda	1
○ Tea, coffee with 2 or more spoons of sucrose	1
○ Bread, whole wheat bread, sugarless cookies	2
○ Candy, ice cream, jam, chocolate	3
○ Cake, cookies with sugars, sugared pastry	4
○ Honey, sugared cereals, toffee, sticky candy	5
- Frequency of consumption was calculated as following, the sugar-containing food was given a score of 0, 1, 2 or 3; depending on whether it was eaten occasionally, two or more times a week, daily or more than twice per day respectively.
- The Occasion Score was determined as follows: a cariogenic food was given a score of 1 or 5;

depending on whether it was eaten with main meals or between meals.

- The Frequency Score(FS) and Occasion Score(OS) were determined by multiplying the frequency and occasion scores by the snack food values, respectively.
- Diet's Cariogenic Potential(CP) was calculated by adding the FS and OS.
- The values were turned into a three-category scale;
 - Low: 10-33score
 - Moderate: 34-79score
 - High: 80-144score

2-Dental Examination:

All Children were examined clinically for dental caries by using dental mirrors and dental explorer no.23 under daylight conditions with the aid of light cure fiber optic transillumination (WOODPECKER,RTA Light Cure (1000-1200 watt),China). Dental caries surface index was measured using DMFs/defs index. Caries was evaluated according to WHO guidelines¹⁹⁸⁷; a tooth was classified as carious whether it had a softened floor, undermined enamel, or softened wall, caries around any restoration, or a tooth with a temporary restoration.

3-Salivary Examination:

To assess the salivary pH, a saliva sample was taken. 1–2 hours after breakfast, a resting saliva sample was taken. The child was asked to sit motionless in an upright position and lean his head slightly forward, as per the guidelines of collecting the saliva¹⁰. The child was instructed to spit into a plastic cup. This process was repeated until a volume of 3-5ml was obtained. A digital pH electrode meter was used to determine the salivary pH. (ATC, Pen Type pH Meter- pH-009 (I) A,Guangdong,China).

Invitro part:

The oral drugs used by those asthmatic children were(Apidone and Aironyl). These drugs are oral syrups used for long periods. These drugs were tested for their pH and Total sugar content. The drug's pH was measured using a digital pH electrode meter. A glass beaker containing 20 mL of each drug was put in a water bath set at 37°C. A glass electrode was dipped into the syrup, and the pH was shown on the meter's panel. Each sample was checked three times in order to obtain a mean value¹¹.For measuring the total sugar content of drug ,The Fehling method was used¹². The following equation was used to determine the sugar percentage:

$$\text{Total sugars[\%]} = \frac{\text{FEQ} \times \text{dilution} \times 100}{V \text{ TITRATION}}$$

V TITRATION

Where, FEQ-equivalence factor

V TITRATION-titration volume required

Statistical analysis:

Categorical data were expressed as frequencies (n) and percentages (%) and were analyzed using Fisher's exact test. Quantitative data were tested for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests. Parametric data of age were represented as mean and standard deviation values and were analyzed using independent t-test. Ordinal data were expressed as interpolated median and interquartile range values and were analyzed using Kruskal–Wallistest followed by pairwise comparisons utilizing Dunn's post hoc test. The significance level was set at $p \leq 0.05$ for all tests. Statistical analysis was performed with IBM® SPSS® (SPSS Inc., IBM Corporation, NY,USA)Statistics Version 26 for Windows.

Results

The study was conducted on 60 children (30 asthmatics ,30 asthmatic-free controls). (70.0%) of the asthmatics were males (30.0%) were females with mean age of (7.70±1.84). The control group consisted of (60.0%) males and (40.0%) females

with mean age of (7.17±1.37) years. There was no significant difference in sex and age between both groups (p=0.598 and p=0.208) respectively.

Table(1) showed the Frequencies(n) and percentages(%) of asthma drugs parameters; type, form, dose, duration of intake and frequency of administration.

Table (2) showed the snacking cariogenic potential intake and oral hygiene habits of each group. There was a significant difference between both groups regarding snacking cariogenic potential (p=0.024). While, There was no significant difference regarding oral hygiene habits (p=0.538).

Table(3) showed the Interpolated median and interquartile range (IQR) values of (defs/ DMFs and salivary pH) scores for both groups. The findings revealed that there was a significant difference between both groups regarding **defs and salivary pH** (p<0.001). While, There was no significant difference between both groups regarding **DMFs** (p=0.260).

Table(4) showed the Interpolated median and interquartile range (IQR) values of (defs, DMFs and salivary pH) scores for different parameters of the drugs (dose, frequency of administration and duration of administration).

Regarding the dose of the drug, the findings revealed that there was a significant difference between values of different doses and defs and DMFs (p=0.040), (p=0.002) respectively. While, There was no significant difference between values of different doses and salivary pH (p=0.720).

Regarding frequency of administration, There was a significant difference between different drug intake frequency and defs, DMFs and salivary pH (p=0.002), (p=0.023) and (p=0.002) respectively.

Table (1): Frequencies (n) and percentages (%) of bronchial asthma drugs parameters

Regarding drug duration intake, There was no significant difference between different durations of drug intake and defs, DMFs and salivary pH (p=0.057), (p=0.135) and (p=0.607) respectively.

In vitro part; the results shows that both drugs (**Apidone and Aironyl**) are acidic where their pH values are 5.3 and 5.1 respectively. While the total sugar content of **Apidone** is higher than that of **Aironyl** as the values are 17g% and 0.5g% respectively.

Discussion

Bronchial asthma is a critical threat that affects millions of people. Several studies have been conducted to understand the effect of asthma and its medications on oral health.

The results of this study revealed that the asthmatic group had a significantly higher value of (defs) than the control group (p<0.001). While, there was no significant difference between both groups regarding DMFs (p=0.260). These results are in agreement with^{4, 13, 14, 15}. While,^{16, 17, 18} found that there was no correlation between asthma and caries. This controversy may be due to the difference in the medication (types, dose, frequency, and duration), water fluoridation, lifestyle, snacking habits and oral hygiene habits.

Regarding the drugs frequency, the results showed that there was a significant difference between drug frequency and DMFs (p=0.023) and defs (p=0.002). This comes in accordance with^{19, 20, 21, 4}. This result could be attributed to many reasons. Firstly; Frequent use of conventional sugar-containing medications raises the risk of caries due to the simple carbohydrates and the low endogenous pH of these drugs²². Secondly; If doses are administered too close together, they remain in contact with the tooth surface for longer periods of time, causing the drug concentration level in the oral

Parameter

Asthmatic

p-value

	Parameter		Asthmatic	p-value
Drug type	Bronchodilator and Corticosteroids	n(%)	30(100%)	—
Drug form	Inhalation and oral	n(%)	30(100%)	—
Drug dose	2.5 ml/ 2 puffs	n(%)	17 ^A (56.7%)	0.014*
	3 ml/ 3 puffs	n(%)	4 ^B (13.3%)	
	5 ml/ 3 puffs	n(%)	9 ^{AB} (30.0%)	
Duration of drug intake	1-2years	n(%)	2 ^B (6.7%)	<0.001*
	3-5 years	n(%)	21 ^A (70.0%)	
	≥ 6 years	n(%)	7 ^B (23.3%)	
Frequency of drug intake	Twice/day	n(%)	5 ^B (16.7%)	0.002*
	3 times/day	n(%)	19 ^A (63.3%)	
	4 times/day	n(%)	6 ^B (20.0%)	

Different superscript letters indicate a statistically significant difference within the same vertical column and parameter*; significant ($p \leq 0.05$), ns; non-significant ($p > 0.05$)

Table(2): Frequencies (n) and percentages (%) of snack cariogenic potential intake and oral hygiene habits of each group

	Parameter		Asthmatic	Control	p-value
Snack-cariogenic potential intake	No	n(%)	4 ^A (13.3%)	0 ^B (0.0%)	0.024*
	Low	n(%)	19 ^A (63.3%)	15 ^A (50.0%)	
	Moderate	n(%)	7 ^A (23.3%)	15 ^B (50.0%)	
	High	n(%)	0(0%)	0(0%)	
Frequency of teeth brushing	None	n(%)	23(76.7%)	19(63.3%)	0.538ns
	Once/day	n(%)	2(6.7%)	3(10.0%)	
	Twice/day	n(%)	1(3.3%)	0(0.0%)	
	Once/week	n(%)	3(10.0%)	6(20.0%)	
	Twice/week	n(%)	1(3.3%)	0(0.0%)	
	3 times/week	n(%)	0(0.0%)	1(3.3%)	
	Once/month	n(%)	0(0.0%)	1(3.3%)	
	Flossing	No	n(%)	30(100%)	
	Yes	n(%)	0(0%)	0(0%)	
Mouthwash usage	No	n(%)	30(100%)	30(100%)	
	Yes	n(%)	0(0%)	0(0%)	

Different superscript letters indicate a statistically significant difference within the same vertical column *; significant ($p \leq 0.05$) ns; non-significant ($p > 0.05$)

Table (3): Interpolated median and interquartile range (IQR) values for (defs ,DMFs and salivary pH)for both groups

Score	Interpolated median(IQR)		p-value
	Asthmatic	Control	
defs	22.50(20.25)	15.00(7.75)	<0.001*
DMFs	2.00(5.50)	1.60(1.00)	0.260ns
Salivary pH	6.00(0.55)	6.90(0.00)	<0.001*

Different superscript letters indicate a statistically significant difference within the same horizontal row*; significant ($p \leq 0.05$) ns; non-significant ($p > 0.05$)

Table (4): The Interpolated median and interquartile range (IQR) values of (defs, DMFs and salivary pH) scores for different parameters of the drugs(dose, frequency of administration and duration of drug intake).

Parameter	Dose of the Drug			p-value	Frequency of administration			p-value	Duration of Drug intake			p-value
	Interpolated median (IQR)				Interpolated median (IQR)				Interpolated median (IQR)			
Score	2.5 ml/2 puffs	3 ml/3 puffs	5 ml/3 puffs		Twice/day	3 times/day	4 time/day		1-2years	3-5 years	≥ 6 years	
defs	34.00 (27.00) ^A	24.00 (7.00) ^{AB}	19.75 (6.00) ^B	0.040 *	20.67 (5.00) ^B	21.00 (15.00) ^B	50.00 (6.50) ^A	0.002*	38.50 (17.50) ^A	27.00 (24.00)	19.75 (8.00) ^A	0.057
DMFs	0.75 (2.00) ^B	4.50 (7.75) ^{AB}	6.00 (4.00) ^A	0.002 *	2.33 (2.00) ^{AB}	3.67 (6.50) ^A	0.25 (0.75) ^B	0.023*	1.50 (0.50) ^A	1.62 (4.00) ^A	4.25 (4.50) ^A	0.135
Salivary pH	6.00 (0.50) ^A	6.00 (0.15) ^A	6.00 (0.60) ^A	0.720	6.45 (0.20) ^A	6.00 (0.30) ^{AB}	5.75 (0.10) ^B	0.002*	6.20 (0.50) ^A	5.88 (0.40) ^A	6.25 (0.60) ^A	0.607

Different superscript letters indicate a statistically significant difference within the same horizontal row*; significant ($p \leq 0.05$) ns; non-significant ($p > 0.05$)

cavity to rise, raising the dental caries risk²³. Thirdly; Drugs given in the evening, when there is a drop in salivary flow as well as decreased swallowing reflexes and muscle activity, stay in the oral cavity longer²⁴.

Regarding the drugs doses, There was a significant difference between different doses and DMFs ($p=0.002$) and defs($p=0.040$). However, The highest value of(defs) was found with 2.5 ml/2 puffs while the lowest value was found with 5 ml/3 puffs . So, increasing the dose of the drugs isn't a risk factor in increasing the caries experience. This

comes in accordance with^{25,26} while^{27,28} found positive correlation between drug doses and caries index.

Regarding the drugs intake duration, there was no significant difference between different drug intake durations and DMFs ($p=0.135$) and defs. ($p=0.057$.) This comes in accordance with^{29,20,30,25,26}. On the other hand, ³¹found positive linkage between duration of asthma and the caries indices.

Regarding the salivary pH, the results revealed that the asthmatic group had a significantly lower value of salivary pH than the control

group ($p < 0.001$). There was a significant difference between different drug intake frequency and the salivary pH ($p = 0.002$) as the lowest value was found with 4 times/day while the highest value was found with twice/day which is in accordance with^{32,33,34,35}, while,¹⁴ didn't find any significance difference between asthmatics and control group regarding the salivary pH. This result could be attributed to many reasons. Firstly, the use of β_2 adrenoceptor agonists results in a reduction in salivary secretion. This reduction in salivary secretion is associated with a reduction in salivary pH³⁶. Secondly,¹³ found that combining inhaled β_2 -agonists with glucocorticoids leading to changes in salivary composition and decrease in salivary pH.

But, there was no significant difference between salivary pH and drug doses or drug intake duration while³⁷ found a negative relationship between the duration of drug intake and the salivary pH. They noticed that as the duration of drug intake increased, the salivary pH decreased.

Regarding the measurement of the Total Sugar content of the drugs, it was done using Fehling method. Using this method comes in accordance with^{38,39,11}. Using Fehling method because it is a very reliable method used since the 1800s to determine the amount of glucose.

The results of this study showed that both drugs (Apidone and Aironyl) are acidic. These results are matching with the values reported by many authors who investigated pediatric liquid medicaments (PLMs)^{22,11}.

The total sugar content of **Apidone** is much higher than that of **Aironyl** as the values are 17g% and 0.5g% respectively. These results are matching with the range of values reported by many authors measuring sugar content^{8,39,22,11}.

These results showed that **Apidone** and **Aironyl** are acidic and contain sugar in their content so; it

supports our results of high caries experience and low salivary pH in asthmatics.

Conclusions:

Caries is more common in asthmatic children than in healthy children. Asthmatics have a lower salivary pH than healthy people.

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