Dental caries in children with asthma undergoing treatment with short-acting β2-agonists

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ABSTRACT: Aim This study sought to evaluate possible higher risk for dental caries among asthmatic children undergoing treatment with short-acting β2-agonists. Methods Dental clinical assessments, saliva analysis and a questionnaire survey were carried out on 60 children aged 6-12, of whom 30 were asthmatic subjects undergoing treatment with short-acting β2-agonists and 30 were used as controls. The obtained data for DMFT/dmft scores, Silness-Löe plaque index, buffer capacity and bacteria counts for Streptococcus mutans and Lactobacillus in the saliva, oral hygiene and dietary habits were compared using Student t-test and Pearson chi-square test. Results We registered a higher DMFT score among asthmatics of 1.2±1.8 (SD) and 0.3 ± 0.8 among non-asthmatic patients (p<0.05), while comparison of dmft scores between the examined groups showed not significant (Student t-test). Saliva analysis revealed lower buffer capacity in 43.3% of the asthmatic children, followed by higher cariogenic bacteria counts in their saliva (p<0.05 Student t-test). These results show the lower plaque index in the asthmatic group (1.6 ± 0.4) compared with the control (2.1 ± 0.3). Asthmatic children expressed better oral-health habits with more frequent tooth-brushing and usage of fluorides. Conclusion The results from our study suggest a higher caries-susceptibility among asthmatic children undergoing treatment with short-acting β2-agonists, but a clear association between these drugs, salivary changes and dental caries among children, still remains to be demonstrated.

KEYWORDS: Caries; Asthma; Short-acting β2- agonists; Paediatric patients.

Introduction

Asthma is one of the most common chronic diseases in industrialised countries and its prevalence is constantly increasing throughout the world [Haahr et al., 1990; Burney et al., 1990; Upton et al., 2000]. Some of the studies report that the disease affects approximately 3-5% of the adult population and as much as 10% of children [Pearce et al., 2000]. Both asthma and dental caries are defined as chronic conditions with very complex aetiologies, variable clinical presentations and challenges in the diagnosis that complicate attempts to study them.

Relatively few studies exist on oral health of asthmatic patients. We find conflicting results in the previous reports on the association between asthma and oral disease [Hyyppä and Paunio, 1979; Bjekanbork et al., 1987; Storhaug, 1985; Kankaala, 1998]. Findings, indicating an increased risk of oral diseases in asthmatic patients are mainly obtained from studies on children and adolescents. According to most published reports, young asthmatic patients suffer more from caries and/or periodontal diseases than non asthmatic subjects [Mc Derra et al., 1998; Ryberg et al., 1991; Arnup et al., 1993; Wierchola et al., 2006]. These findings were mainly obtained from small scale studies. Shulman [Shulman, 2001] found no association between dental caries and childhood asthma, Meldrum [Meldrum, 2001] found no
association over time between asthma and caries increase and Eloot et al. found no dose-response relationship between the severity and duration of asthma and caries [Eloot et al., 2004].

Ryberg et al. [Ryberg et al., 1991; Ryberg, 1987; Ryberg et al., 1990] reported a link between increased incidence of dental caries and regular use of inhaled β2-agonists used in the treatment of asthma. These studies suggested that asthmatics may have altered salivary composition and flow rates due to the presence of specific auto-antibodies to β2-agonists adrenergic receptors. These receptors are affected by the administration of β2-agonists anti-asthmatic drugs [Ryberg et al., 1991; Ryberg, 1991; Ryberg et al., 1990].

Other authors observed decreased salivary and plaque pH in asthmatic children who were using inhalers [Kargul, 1998].

Taking into consideration the controversial conclusions found in the previous literature on a possible higher risk of dental caries among asthmatic children, we defined the objective of our study: to evaluate the prevalence of dental caries and gain further insight on dietary and hygiene habits among children with asthma undergoing treatment with short-acting β2-agonists.

**Materials and methods**

Our study population comprised 60 children aged 6-12, of whom 30 (14 females and 16 males) were asthmatic subjects, enrolled among the patients visiting the Paediatric Clinic of Pulmonary Diseases, University of Padua Hospital. All children were diagnosed with asthma, undergoing treatment with short-acting β2-agonists (salbutamol) in a form of oral inhalator, associated with a corticosteroid (fluticasone dipropionate), for at least 6 months before examination.

The classification of diagnosed asthma was done according to its severity [NHLBI/WHO, 1995]. Duration of the treatment with short-acting β2-agonists (salbutamol) was expressed in months.

All patients with diagnosed asthma who were not following regular/continuous therapy (the minimum of six months before the examination), diagnosed with other pulmonary diseases or other health disturbances, treated with short-acting β2-agonists or diagnosed with lung diseases other than asthma, were excluded from the study.

The control group comprised 30 subjects (12 females and 18 males) aged 6-12 enrolled among patients who came for regular check-ups at the Clinical Department of Paediatric Dentistry, University of Padua. All subjects were clinically healthy; none of them was under any medical treatment and had never been under treatment with β2-agonists.

To avoid bias of the saliva analysis, all subjects were asked not to drink, eat, brush their teeth or eat chewing gums for at least one hour before examination.

All subjects that had been under antibiotic treatment in the last two weeks before the examination were excluded from the study.

From the study, we excluded the patients undergoing orthodontic treatment, fixed or removable, to avoid bias of the oral hygiene conditions assessment.

**Clinical assessment**

Oral examinations were carried out according to the WHO guidelines [WHO, 1987]. The examinations were performed in a dental chair, under a good light using a plane mouth mirror n. 5, and an explorer n. 23. The examinations were performed by one person in an blind manner.

The following data were registered.
- DMFT/dmft - Decayed (D/d), missing or extracted (M/e) and filled (F/f) teeth, for permanent and deciduous teeth respectively.
- General condition of oral mucous membranes (cheeks and tongue) and lips.

**Saliva analysis**

Collection and treatment of saliva samples were performed using a standardised kit CRT Ivoclar Vivadent, composed by CRT Buffer e CRT Bacteria. The CRT Buffer Test [CRT® Bacteria and Buffer Test (Vivadent Ets., Lichtenstein)] was used to determine the buffer capacity of saliva using a colorimetric test strip. The CRT Bacteria Test measured the Streptococcus mutans and Lactobacilli count in saliva by means of selective culture media.

Paraffin-stimulated whole saliva was collected in calibrated sterile tubes. CRT Buffer Test was stripped from the package without touching the yellow test field. The entire yellow test field was wetted with saliva using a pipette. To determine the buffer capacity of saliva, the color of the test field was compared with the color samples after exactly 5 minutes of reaction time. High, medium, and low salivary buffer capacities are indicated by blue, green, and yellow test.
fields, respectively.

The saliva collected for the CRT Buffer Test was also used for the CRT Bacteria Test. The agar carrier was removed from the test vial, and a NaHCO₃ tablet was placed at the bottom of the vial. Using a pipette, both agar surfaces were wetted with saliva. The agar carrier was placed back into the vial and closed tightly.

After incubation at 37°C for 48 hour, the density of S. mutans and Lactobacilli colonies was assessed using the corresponding evaluation pictures provided with the kit. The presence of bacteria colonies over 10⁵ indicates a high risk for dental caries.

After obtaining an informed consent from each child and parent, according to the biomedical ethics guidelines, the parent answered to a questionnaire dealing with the following data:
- background information (age, gender, place of residence);
- information on oral care habits (frequency of tooth brushing and usage of fluoride tablets);
- information on dietary habits (intake of sweets and candies, soft and sweetened beverages).

All patients included in the study came from the city of Padua, Italy, that does not have community water fluoridation.

**Statistical procedures**

Comparisons between asthmatic children and control group were made using the Pearson’s chi-square and Student t-test. The significance level was set at p<0.05. All analysis was performed with SPSS for Windows (version 12.0).

**Results**

**Clinical findings**

The mean ± Standard Deviation (SD) age was 9±2.0 in asthmatic and 8.5±1.7 in non-asthmatic children. We encountered different types of asthma among the children of the asthmatic group. Table 1 presents the classification criteria for asthma categories with the number of subjects affected. Most of the subjects affected by asthma (80%) were undergoing treatment for a period between 6 and 12 months.

The statistical analysis revealed that there is a significant difference in DMFT values between the two examined groups (asthmatic and control group), while the dmft values were not significantly different (Student t-test p<0.05). The mean Standard Deviation (SD) DMFT score was 1.2±1.8 in asthmatic and 0.3±0.8 in non-asthmatic patients.

A significant difference was noted comparing the plaque index between the two groups, where a lower plaque index was registered among the asthmatic children.

**Analysis of the saliva**

The buffer capacity and bacteria load of the saliva showed a significant difference in the two groups (p<0.05 Student t-test). For the asthmatic children group the buffer capacity was notably lower and we registered a low buffer capacity of the saliva in 43.3%

<table>
<thead>
<tr>
<th>Classification and clinical features #</th>
<th>n.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild Intermittent</td>
<td>2</td>
</tr>
<tr>
<td>Symptoms ≤ two times per week</td>
<td></td>
</tr>
<tr>
<td>Brief exacerbations (from few hours to few days)</td>
<td></td>
</tr>
<tr>
<td>Night times asthma symptoms, two times per month</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic and normal lung function between exacerbation</td>
<td></td>
</tr>
<tr>
<td>PEF o FEV₁ ≥ 80% of predicted values; variability &lt; 20%</td>
<td></td>
</tr>
<tr>
<td>Mild Persistent</td>
<td>13</td>
</tr>
<tr>
<td>Symptoms &gt; two times per week, but &lt; one time per day</td>
<td></td>
</tr>
<tr>
<td>Exacerbations that may affect activity</td>
<td></td>
</tr>
<tr>
<td>Night times asthma symptoms &gt; two times per month</td>
<td></td>
</tr>
<tr>
<td>PEF o FEV₁ ≥ 80% of predicted values; variability 20%–30%</td>
<td></td>
</tr>
<tr>
<td>Moderate Persistent</td>
<td>13</td>
</tr>
<tr>
<td>Daily symptoms</td>
<td></td>
</tr>
<tr>
<td>Exacerbations that affect activity</td>
<td></td>
</tr>
<tr>
<td>Night times asthma symptoms &gt; one time a week</td>
<td></td>
</tr>
<tr>
<td>Daily use of inhaled short-acting β-agonists</td>
<td></td>
</tr>
<tr>
<td>PEF o FEV₁ ≥ 60% e &lt; 80% of predicted values; variability &gt; 30%</td>
<td></td>
</tr>
<tr>
<td>Severe Persistent</td>
<td>2</td>
</tr>
<tr>
<td>Continuous symptoms</td>
<td></td>
</tr>
<tr>
<td>Frequent exacerbations</td>
<td></td>
</tr>
<tr>
<td>Frequent nighttimes symptoms</td>
<td></td>
</tr>
<tr>
<td>Limited physical activity</td>
<td></td>
</tr>
<tr>
<td>PEF o FEV₁ &lt; 60% of predicted values; variability &gt; 30%</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1 - Classification of asthma by severity.**

Classification is based on the clinical features of asthmatic patients. Sources: National Heart, Lung and Blood Institute.

# Presence of one of the features of severity is sufficient to place a patient in that category. A person should be assigned to the most severe grade in which any feature occurs. FEV₁ Forced expiratory volume in one second; PEF- Peak expiratory flow; n - Number of subjects.
of the asthmatic subjects (n=13), while no case of a low buffer capacity of the saliva was registered among the controls. Most of the non-asthmatic children 60% (n=16), expressed high buffer capacity of the saliva.

S. mutans and Lactobacilli counts showed as well a significant difference between the two groups (Table 2).

**Oral care and dietary habits**

The results of the questionnaire survey on the oral care and dietary habits of the asthmatic and non-asthmatic children, brought to light a better oral care of the asthmatic children compared with the control group. We noticed that 33.3% (n=10) of the asthmatic children brushed their teeth 3 times a day, while among controls only 6.7% (n=2) do so. Both of the groups showed similar dietary habits and not significantly different.

**Discussion**

The results from our study supported the hypothesis that asthma may increase the risk of caries among children undergoing treatment with short-acting β2-agonists. We registered a higher DMFT score, lower buffer capacity and higher cariogenic bacteria counts in the saliva of the asthmatic children, in spite of the results of better oral hygiene and lower plaque index registered among the asthmatic group compared with the controls.

Our findings that the asthmatic children have higher DMFT scores than controls are in accordance with the results reported by Milano [Milano, 1999]. Similar to our study, Milano’s study was conducted in a region which does not have community fluoridation and has less than 0.3 ppm natural fluoride (Texas Dpt. Of Health 2000, for the city of San Antonio, US) [Texas Dpt Of Health, 2000], as our study was conducted in the region of the city of Padua that lacks community fluoridation.

The different approach between our study and the one of Milano [Milano, 1999] lies in the fact that in this study we included the subjects who were taking dietary fluoride supplements. Although more asthmatic children were taking fluoride supplements, the difference between the two groups was not significant. On the other side, our findings differ from those reported by Kankaala [1998] and McDerra et al. [1998], who found significant differences in dfs and dft scores between asthmatics and controls. Kankaala et al. [1998] found that asthmatic children had more restorations and more extractions of primary molars due to caries than the controls. Our study showed no significant difference in the dmft scores among the examined groups. A possible explanation for the difference between our findings and those of McDerra et al. and Kankaala [Kankaala, 1998; McDerra et al.,1998] might be that most of the subjects included in our study were in the mixed dentition phase and the

<table>
<thead>
<tr>
<th>Bacterial counts</th>
<th>Buffer capacity of saliva</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Streptococcus mutans</td>
</tr>
<tr>
<td></td>
<td>&lt;10⁵ CFU/L</td>
</tr>
<tr>
<td>Asthmatic children</td>
<td>5</td>
</tr>
<tr>
<td>controls</td>
<td>24</td>
</tr>
<tr>
<td>SD</td>
<td>13.4</td>
</tr>
<tr>
<td>St Err</td>
<td>9.5</td>
</tr>
<tr>
<td>p</td>
<td>&gt;0.05*</td>
</tr>
</tbody>
</table>

**Table 2 - Saliva analysis: Buffer capacity and density of S. mutans and Lactobacilli colonies**

CRT® Bacteria and Buffer Test (Vivadent Ets., Lichtenstein). The CRT Buffer Test was used to determine the buffer capacity of saliva. High, medium, and low salivary buffer capacities are indicated. The density of Streptococcus mutans and Lactobacilli colonies was assessed using the corresponding evaluation pictures provided with the kit (CRT Bacteria Test). The presence of bacteria colonies over 10⁵ indicates a high risk for dental caries. Values with a superscript * in the table are significantly different P < 0.05 (Student t-test). n - Number of cases; CFU - Colonies Formed Unit; SD - Standard Deviation; St Err – Standard Error.
first molars were often decayed or filled. A possible
drawback of our study might be that the dental check-
ups were performed in an unmasked manner, which
may bias the results.

There are evident discrepancies in the previous
reports on the prevalence of dental caries among
asthmatic children.

Recently, Shulman and Meldrum [Shulman, 2001;
Meldrum, 2001] questioned the association between
caries and asthma and our results clearly differ from
those reported in their studies. The study design and
approach in time are as well different, taking into
consideration that these studies are long-term studies
and included more subjects.

The results of saliva analysis revealed lower buffer
capacity and an increased bacteria load in the saliva of
the asthmatic children compared with the control
group. The alteration in the saliva buffer capacity and
increase of Streptococcus mutans and Lactobacilli
counts in the saliva of the asthmatic children
undergoing treatment with short-acting β2-agonists
could be attributed to the diminished salivary
production and secretion associated to the prolonged
use of β2-agonists, reported in some previous studies
[Arnup et al., 1993]. The effect of reduced salivary
flow has been elucidated in both human and animal

<table>
<thead>
<tr>
<th>Frequency of tooth brushing</th>
<th>Asthmatic children</th>
<th>Controls</th>
<th>SD</th>
<th>St Err</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once/day</td>
<td>12</td>
<td>14</td>
<td>1.4</td>
<td>1.0</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Twice/day</td>
<td>6</td>
<td>14</td>
<td>5.7</td>
<td>4.0</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>3 times/day</td>
<td>10</td>
<td>2</td>
<td>5.7</td>
<td>4.0</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>After each meal</td>
<td>2</td>
<td>-</td>
<td>1.4</td>
<td>1.0</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Usage of fluoride tablets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>20</td>
<td>16</td>
<td>2.8</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10</td>
<td>14</td>
<td>2.8</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>Intake of sweets and candies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 times/day</td>
<td>29</td>
<td>29</td>
<td>0.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 times/day</td>
<td>1</td>
<td>1</td>
<td>0.0</td>
<td></td>
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</tr>
<tr>
<td>10 times/day</td>
<td>-</td>
<td>-</td>
<td>0.0</td>
<td></td>
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</tr>
<tr>
<td>&gt;10 times/day</td>
<td>-</td>
<td>-</td>
<td>0.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intake of soft and sweetened beverages</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 times/day</td>
<td>27</td>
<td>24</td>
<td>2.1</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>5 times/day</td>
<td>3</td>
<td>6</td>
<td>2.1</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>10 times/day</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
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<tr>
<td>&gt;10 times/day</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3 - Survey of oral care and dietary habits**
Results from a questionnaire filled in by the parents of the examined children containing information on oral care habits
(frequency of tooth brushing and usage of fluoride tablets) and dietary habits (intake of sweets and candies, soft and sweetened
beverages). Values with a superscript * in the table are significantly different P < 0.05 (Student t-test). SD - Standard Deviation;
St Err – Standard Error.
studies [Ryberg et al., 1991; Arnup et al., 1993; Ryberg et al., 1988; Johansson and Ericson, 1987]. Ryberg et al. [1987] demonstrated a reduction of whole and stimulated saliva of 26% and 36% respectively. Our results of lower buffer capacity of the saliva and increase in cariogenic bacteria may be due to the anti-asthmatic medications, containing fermentable carbohydrate and sugar, as suggested in some previous studies [Holbrook et al., 1989; Storhaug, 1985; Maguire et al., 1996; Tootla et al., 2005].

The inhaled drugs as salbutamol are delivered in a carrier powder which contains sugar. Some authors showed that almost all inhalant powders have a pH lower than 5.5 [O’Sullivan and Curzon, 1998]. Lactose, that is commonly used as a carrier for salbutamol sulphate, a is less cariogenic than other common sugars, but it has caries promoting potential when associated with reduced salivary flow [Pearce and Sissons, 1987].

Since our analysis does not include the analysis of saliva flow, and certain chemical components, our data are limited to the cariogenic bacteria counts and buffer capacity of the saliva, just as a possible indicator for a higher caries-susceptibility.

However it remains to be demonstrated that there is a clear association between the suggested beta-agonists, salivary changes and dental caries among children.

The data of our survey suggested that the asthmatic children, used to a continuous medical observation, follow the dental recommendations better and practice more frequent tooth-brushing and usage of fluorides.

The two groups of children followed almost identical dietary regime consuming sweets and sweetened beverages.

However this study shares the same problem as many previous studies in children and adolescents, considering that the measurements were carried out on fairly small number of subjects.

Conclusion

The published reports give somewhat contradictory picture on the association between asthma and dental caries.

The current study found supporting evidence for the higher caries-susceptibility among asthmatic children undergoing treatment with short-acting β2-agonists. We registered lower buffer capacity and higher cariogenic bacterial load in the saliva of the asthmatic subjects undergoing treatment. The results of higher DMFT scores, in spite of a lower plaque index and better oral hygiene habits, can lead us to a conclusion that the undergoing treatment with short-acting β2-agonists may influence the caries-susceptibility among the asthmatic children. Nevertheless, the oral physiological changes may be due to both disease and medications and it remains very difficult to determine the effects of the drugs and the disease itself.

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