ORIGINAL PAPER

doi: 10.5455/medarh.2015.69.247-250

Med Arh. 2015 Aug; 69(4): 247-250
Received: June 15th 2015 | Accepted: July 19th 2015

Published online: 04/08/2015 Published print:08/2015

Cariogenic Potential of Inhaled Antiasthmatic Drugs

Amela Brigic, Sedin Kobaslija, Amila Zukanovic

Pediatric Clinic, University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina

Corresponding author: Amela Brigic, MD. Pediatric clinic. University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina. E-mail: amela.brigic@gmail.com

ABSTRACT

Introduction: The organism of children with asthma is exposed to the effects of the disease but also the drugs for its treatment. Antiasthmatic drugs have different modes that promote the caries formation which varies according to their basic pharmacological composition. Namely, these drugs have a relatively low pH (5.5), can contain sweeteners such as lactose monohydrate in order to improve the drug taste or both. Frequent consumption of these inhalers in combination with reduced secretion of saliva increases the risk of caries. **Material and methods**: The study sample consisted of 200 patients, age from 7-14 years, divided into two groups: control group (n1 = 100) consisted of healthy children and the experimental group consisted of children suffering from asthma (n2 = 100). In both groups of respondents are determined the DMFT index, plaque index value and hygienic-dietary habits using the questionnaire. The subjects in the control group had significantly higher DMFT index than subjects in the experimental group ($p = 0.004$). It is determined that there are no significant differences in the values of plaque index ($p>0.05$). **Conclusion:** The effect of different diseases or medications from their treatment, diet and fermentable carbohydrates in the etiology of dental caries cannot be observed outside the living conditions of subjects, their social epidemiologic status, age, habits, oral hygiene, fluoride use, etc.

Key words: asthma, caries, inhalers.

1. INTRODUCTION

There are reasonable indications that in children with asthma who are on long-term therapy of inhaled antiasthmatic drugs (IAD) there is an increased risk of caries. In various studies that have investigated the impact of IAD on oral health has been demonstrated increased prevalence of caries in asthmatic compared to healthy children (1, 2, 3) while Meldrum et al. in his study 2001 refuted this view, because they did not observed a statistically significant difference in terms of the dental caries prevalence among children with asthma and healthy children (4). The body of children with asthma is exposed to the action of the disease and the drugs for its treatment. Most of these drugs are inhaled and thus it is impossible to prevent contact of the drug with the hard dental tissues and oral mucosa, which is exacerbated by the fact that most children incorrectly uses inhalers and the majority of drug are scattered in the oral cavity. In this way, in addition to antiasthmatic drugs inhalation undesired side effects also can cause local adverse effects in the oral cavity (5, 6).

Some inhalers containing fermentable carbohydrates such as lactose monohydrate in order to improve the taste of the drug and thus the tolerance of the patient to the same. Frequent consumption of these inhalers in combination with reduced secretion of saliva has a further negative effect of these drugs or increases the risk of caries (7). O'Sullivan et al in their study demonstrated that certain types of inhalers, particularly inhalers with drug in the form of a powder (Dry Powder Inhalers DPI) having a pH lower than the critical value of pH at which dissolution of the hydroxyapatite of the enamel starts, which increases the risk of erosion (8). Most patients used inhalers incorrectly and instead that most of the drug is applied at the upper airways are scattered in the oral cavity. This improper way of using the inhaler further potentiates their cariogenic effect. Kargul and colleagues in their study compared the pH of plaque interdental spaces after inhaler use, the consumption of water and chewing gum and reach the conclusion that inhaled antiasthmatics can cause significant reduction in plaque pH, which increases the risk of caries. This study also demonstrated that 30 minutes after the first use of the inhaler there is significant decrease of the saliva pH value and plaque pH below a critical value for the demineralization of enamel as it has a pH of 5.5 (9). It is also noted that children suffering from asthma, which use inhalers everyday have a frequent need for rehydration because the inhaled medications create a feeling of dryness in the mouth and often use sweetened

drinks, which further creates conditions for the formation of cavities (10).

Another factor that is associated with an increased prevalence of dental caries in patients suffering from asthma is nitric oxide. It is known that the concentration of single exhaled nitric oxide increased in cases of inflammatory airway disorders. Nitrous oxide in contact with water turns into nitric acid, and taking into account the fact that the oral cavity is rich with water it can be concluded that there is a great risk of demineralization of hard dental tissues (11).

2. GOALS

Collect data on eating habits of the children, oral hygiene and its frequency by applying the questionnaire for the parents.

Evaluate the level of oral hygiene in the experimental and control groups.

Determine the prevalence of dental caries in the experimental and control groups.

3. MATERIAL AND METHODS

Retrospective–prospective study included 100 children with asthma, of both sexes, aged from 7 to 15 years, who are treated at the Clinic for children's diseases in Tuzla. Basic criteria for inclusion in the study is that all children are treated with antiasthmatic drugs for at least two years and that they are children with persistent asthma, which requires long-term therapy. A secondary source of data, for children suffering from asthma will be medical records of the Department of Pulmonology and Outpatient Clinic for children's diseases in Tuzla.

The control group is composed of 100 healthy children who do not suffer from asthma or other systemic disease and which by age, sex and socioeconomic status correspond to the experimental group. A secondary source of data for the control group will be class diaries of the Elementary School Banovici pupils. Subjects in both are randomly selected. Before The clinical examination, the parent of every child fulfill a survey in which, in addition to data on the identity, place of residence, age and sex of the child, are provided answers to the questions which refer to the eating habits of the child, including the number of daily meals, taking sweets and sweet drinks during the day and questions about the measures of oral hygiene and their frequency. Survey which is filled out by the participants of the experimental group contain questions about the need of the child for rehydration after taking inhalation drug with sweetened beverage, questions about the number of daily meals and daily intake of sweets and questions concerning measures of oral hygiene and its frequency. The dental status of each child's is determined by clinical exam trough registration the number of carious and extracted teeth and teeth with fillings of any kind. By clinical exam is also determined the level of oral hygiene by plaque index according to Silness and Loe, 1964 (12). For the experimental and control group the following parameters are analyzed:

- The frequency of teeth brushing;
- The number of daily meals;
- The frequency of eating sweets;
- Consumption of sugar-sweetened beverages;
- Plaque index;
- DMFT INDEX (with an analysis of the D, M, F components)

In accordance with the set goals and hypotheses of the study the data will be analyzed by the following statistical methods: a) For each parameter the descriptive statistics is made which includes measures of central tendency (mean, median and mode), measures of dispersion (standard deviation, interquartile range), measures of asymmetry (curvature with standard error). Results are displayed as text and bar charts; b) Before hypothesis testing will be performed normality distribution testing by Kolmogorov-Smirnov test.

4. RESULTS

Results of descriptive statistics for the parameters D, M, F, DMFT for the control and experimental groups:

- DMFT Index for the control group is 7.46 (±4.08). On average, respondents had a 6.46 (±4.44) decayed, 0.24 (±0.74) extracted and 0.78 (±1.24) tooth with a filling.
- DMFT Index for the experimental group was 5.99 (±3.62). On average, respondents had a 4.65 (±3.93) decayed, 0.15 (±0.6) extracted and 1.19 (±1.76) tooth with a filling (Figure 1).

Testing of distribution normality for D, M, F, DMFT is performed by the Kolmogorov-Smirnov test. All studied variables showed a significant variation from the normal distribution (p = 0.000) except for DMFT index for the experimental group (p = 0.001). Significance of differences between the control and experimental groups for DMFT index and D, M and F components is carried by the non-

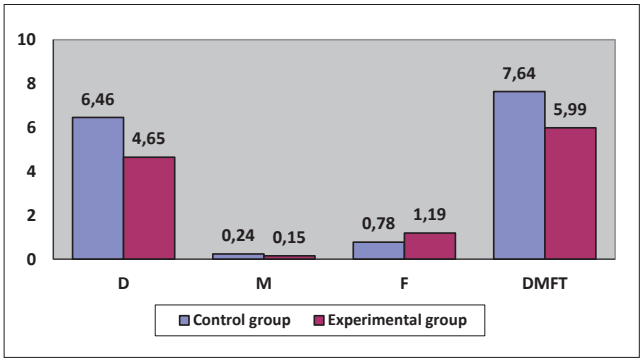

Figure 1. Review of D, M, F and DMFT percent value for the control and experimental group

parametric Mann-Whitney test for independent samples.

Mann-Whitney test revealed that: a) There are no significant differences in the values of the M (p = 0.350) and F component (p = 0.238) between the control and experimental groups, b) There is a significant difference in the number of decayed (component D) teeth between the control and experimental group (p = 0.004). Those in the control group had significantly more carious teeth than subjects in the experimental group. The average number of decayed teeth in the control group was 6.46 and in the experimental 4.65.

There is a significant difference in the DMFT values between the control and experimental groups (p = 0.004). Those in the control group had significantly higher DMFT index than respondents in the experimental group. The

average DMFT values in the control group is 7.46 and in the experimental 5.99.

Descriptive statistics results for the frequency of brushing, the number of daily meals, taking sweets, consuming sweet drinks–control and experimental group:

- In The control group respondents most often brushed their teeth twice a day (Mode = 2), taking three meals a day (Mode = 0), sweets consumed 2-3 times a week (Mode = 2) and sweetened drinks consumed also 2-3 times a week (Mode = 2). All examined variables show asymmetric distribution (positive curvature).
- In the experimental group, the respondents most often brush their teeth twice a day also (Mode = 2), eat 4-6 meals per day (Mode = 1), consume sweets every day (Mode = 3) and sweetened drinks are hardly ever consumed (Mode = 0). All examined variables show asymmetric distribution (positive curvature), except eating candy that has a negative curvature.

Tests of normal distribution for variables is performed by Kolmogorov-Smirnov test. All studied variables showed a significant variation from the normal distribution ($p < 0.000$). Testing significance of differences between the control and experimental groups for the frequency of brushing, the number of daily meals, eating candy, sugar-sweetened beverage consumption, due to the deviation from the normal distribution, for each of the individual variables was performed with nonparametric Mann-Whitney test for independent samples.

Results of Mann-Whitney test for independent samples showed that:

- There is no significant difference in the frequency of brushing teeth between the experimental and control groups ($p = 0.053$). Subjects in both groups usually brush their teeth twice a day (Mode = 2 both for the experimental and the control group).
- There is a significant difference in the number of daily meals between the experimental and control groups ($p = 0.000$). Those in the control group usually take 3 meals a day (Mode = 0), while subjects in the experimental group usually take 4-6 meals a day (Mode = 1).
- There is a significant difference in the eating of sweets between experimental and control groups ($p = 0.000$). Those in the control group usually consume candy 2-3 times a week (Mode = 2), while respondents from the experimental group most commonly consumed sweets every day (Mode = 3).
- There is a significant difference in the consumption of sugar-sweetened beverages between the experimental and control groups ($p = 0.000$). Those in the control group usually consume sweetened drinks 2-3 times a week, while participants in the experimental group usually never take sugary drinks (Mode = 0).

Results of descriptive statistics for plaque index:

- In the control group, subjects generally have very good oral hygiene (Mode for plaque index = 0), while in the experimental group, respondents usually have good oral hygiene (Mode of plaque index = 1). In both groups the values of plaque index showed a positive curvature.
- Testing normality of distribution for all the variables is performed by the Kolmogorov-Smirnov test. All studied variables showed a significant variation from the normal distribution ($p = 0.000$).
- Significance of differences testing between the control and experimental groups for plaque index due to the deviation from the normal distribution, for each of the individual variables was performed with nonparametric Mann-Whitney test for independent samples.
- Based on the results of the Mann-Whitney it is found that there is no significant differences in the values of plaque index ($p > 0.05$) between the control and experimental groups.

5. DISCUSSION

In this study in not proven a statistically significant difference in terms of tested parameters between the control and experimental groups, which is consistent with the results of the other studies (13-17).

The obtained results are unexpected results in terms of the dental caries prevalence, which is has proven statistically significant difference between the control and experimental groups, but in the opposite direction than expected. The respondents of the control group had a statistically significantly higher DMFT index than respondents in the experimental group. There is no significant difference in the frequency of brushing teeth between the experimental and control groups ($p = 0.053$). Subjects in both groups usually brush their teeth twice a day (Mode = 2 both for the experimental and the control group). Since that statistically significant difference has not been proven in terms of plaque index between the control and experimental groups, we cannot explain the results in terms of differences in DMFT index by false testimony of children in terms of oral hygiene habits. There are two possible reasons that could explain these results. Although the one of the inclusion criteria for the respondents of both groups is that they must be of a similar socioeconomic status, there is a possibility that the subjects of the control group had lower socioeconomic status in relation to the experimental group. Numerous studies have shown a positive correlation between poor dental and socioeconomic status (18, 19). Another reason that explains these unexpected results is that parents of children with asthma, faced with a serious chronic illness of their child still pay enough attention to the other aspects of their overall health and that differences in socioeconomic status was not of crucial importance for this unexpected result. Although it can be expected that underlying disease will not allocate time for periodic dentist examinations and given the importance of oral care it seems that asthmatic status does not necessarily mean worse dental status. Rather Shulman et al. in their study demonstrated that asthma is associated with a lower prevalence of dental caries (20). Similar results were obtained in one regional study in Japan (21).

Some studies have shown that people with asthma more often consume sweetened drinks to neutralize the taste of the drug in the mouth, which increases the daily intake of fermentable carbohydrates and therefore the risk of

caries. Another possible reason for frequent consumption of sugar-sweetened beverages is a feeling of dryness in the mouth, which creates oral inhalers, characteristic for most patients suffering from asthma. However, respondents' answers to the questions in the survey conducted in our research have shown conflicting results. In the experimental group 99% of respondents, after taking the drug never consume sweetened drinks, but following the instructions of the physician wash mouth with pure water.

Taking into account the fact that statistically significant difference between the control and experimental groups has been proven in terms of the frequency of eating the candy and the number of daily meals, which are one of the leading major etiological factor for caries ($p = 0.000$), it is expected that the DMFT values and component D (the number of carious teeth) to be higher in the experimental group compared to the control. But there is a significant difference in the number of decayed (component D) and DMFT index between the control and experimental groups ($p = 0.004$). Those in the control group had significantly more carious teeth and higher DMFT index than subjects in the experimental group. These results are one of the many evidence for multifactorial etiology of dental caries and cannot be explained by the difference in the oral hygiene habits, between the experimental and control groups. Subjects in both groups usually brush their teeth twice a day, and there is no statistically significant difference according to this parameter.

König is in his study proved that diet and daily intake of carbohydrates are important determinants of caries risk, but not the decisive factor. On the results of their study explains the widespread use of toothpaste containing fluoride, developing consciousness regarding oral hygiene and thus good plaque control and the development of preventive measures in dentistry (23). His position was supported by the studies done in the United States, Canada and England which also proved that frequent consumption of carbohydrates is not crucial determinant for the development of caries as opposed to the level of oral hygiene, which is the most important risk factor in terms of caries (24, 25). A review of studies on this subject made during the last 20 years, pointed to little or no connection between carbohydrates and caries prevalence in developed countries. That is not the case with developing countries, where carbohydrates have a greater role in the development of tooth decay due to low socioeconomic status and health education of the population, which means a lower oral hygiene and fluoride availability (26).

6. CONCLUSION

The results of this research have once again confirmed that the dental caries is disease with multifactorial etiology in which mutual relationships and interactions between numerous etiological factors contribute even more to the complexity to estimate the of cavities risk problem. Many systemic diseases directly or indirectly increase the risk for tooth decay. The impact of different diseases, drugs for their treatment, diet and fermentable carbohydrates in the etiology of dental caries cannot be seen outside the living conditions of subjects, their socioepidemiologic status, age, habits, oral hygiene, use of fluoride etc.

CONFLICT OF INTEREST: NONE DECLARED.

REFERENCES

1. Shashikiran ND, Reddy VVS, Krishnam RP. Effect of antiasthmatic medication on dental disease: Dental caries and periodontal disease. J Indian Soc Pedod Prev Dent. 2007 Apr-Jun; 25(2): 65-68.
2. 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 Jul-Aug; 35(4): 240-246.
3. 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(3): 207-211.
4. Meldrum AM, Thomson WM, Drummond BK, Sears MR. Is asthma a risk factor for dental caries? Finding from a cohort study. Caries Res. 2001; 35(4): 235-239.
5. Steinbacher DM, Glick M. The Dental Patient with Asthma. An Update and Oral Health Considerations. J Am Dent Assoc. 2001 Sep; 132(9): 1229-1239.
6. Reddy DK, Hegde AM, Munshi AK. Dental Caries Status of Children with Bronchial Asthma. J Clin Pediatr Dent. 2003 Spring; 27(3): 293-295.
7. Meldrum AM, Thomson WM, Drummond BK, Sears MR. Is asthma a risk factor for dental caries? Finding from a cohort study. Caries Res. 2001; 35(4): 235-239.
8. O'Sullivan EA, Curzon MEJ. Drug treatments for asthma may cause erosive tooth damage BMJ. 1998 Sep 19; 317(7161): 820.
9. Kargul B1, Tanboga I, Ergeneli S, Karakoc F, Dagli E Inhaler medicament effects on saliva and plaque pH in asthmatic children. J Clin Pediatr Dent. 1998 Winter; 22(2): 137-140.
10. Dubus JC1, Marguet C, Deschildre A, Mely L, Le Roux P, Brouard J, Huiart L. Réseau de Recherche Clinique en Pneumonologie Pédiatrique.Local side-effects of inhaled corticosteroids in asthmatic children: influence of drug, dose, age, and device. Allergy. 2001 Oct; 56(10): 944-948.
11. Kharitonov SA, Yates D, Robbins RA, Logan-Sinclair R, Shinebourne EA, Barnes PJ. Increased nitric oxide in exhaled air of asthmatic patients. Lancet. 1994 Jan 15; 343(8890): 133-135.
12. Ryberg M, Moller C, Ericson T. Saliva composition and caries development in asthmatic patients treated with β2 adrenoceptor agonists: A 4 year follow up study. Scand J Dent Res. 1991; 99(3): 212-218.
13. Bjerkeborn K, Dahllo¨FG, Hedlin G, Lindell M, Mode´er T. Effect of disease severity and pharmacotherapy of asthma on oral health in asthmatic children. Scand J Dent Res. 1987; 95(2): 159-164.
14. 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(4): 240-246.
15. Meldrum AM, Thomson WM, Drummond BK, Sears MR. Is asthma a risk factor for dental caries? Finding from a cohort study. Caries Res. 2001; 35(4): 235-239.
16. Eloot AK, Vanobbergen JN, De Baets F, Martens LC. Oral health and habits in children with asthma related to severity and duration of condition. Eur J Paediatr Dent. 2004; 5(4): 210-215.
17. Locker D. Measuring social inequality in dental health services research: Individual, household and community based measures. Community Dent Health. 1993; 10(2): 139-150.
18. Zukanovic A. Efikasnost „Cariogram" modela u evaluaciji rizikofaktora karijesa kod dvanaestogodišnjaka (The efficacy of „Cariogram" model in evaluation of cavity risk factors in twelve-year old children). Magistarski rad, Sarajevo, 2005.
19. 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 Jul-Aug; 35(4): 240-246.
20. Tanaka K, Miyake Y, Arakawa M, Sasaki S, Ohya Y. Dental caries and allergic disorders in Japanese children: the Ryukyus Child Health Study. J Asthma. 2008 Nov; 45(9): 795-799.
21. Stensson M, Wendt LK, Koch G, Oldaeus G, Birkhed D. Oral health in preschool children with asthma. Int J Paediatr Dent. 2008 Jul; 18(4): 243-250.
22. Lachapelle D, Couture C, Brodeur JM, Sévigny J. The effects of nutritional quality and frequency of consumption of sugary foods on dental caries increment. Can J Public Health. 1990 Sep-Oct; 81(5): 370-375.
23. Rugg-Gunn AJ, Edgar WM. Sugar and dental caries: a review of the evidence. Community Dent Health. 1984 Jul; 1(2): 85-92.
24. Duggal MS1, van Loveren C. Dental considerations for dietary counselling. Int Dent J. 2001; 51(6 Suppl 1): 408-412.