The effect of inhaled corticosteroid on oral conditions among asthmatic children

Meena O. Abdul Wadood B.D.S. (1)
Zainab A.A. Al-Dahan, B.D.S., M.Sc. (2)

ABSTRACT

**Background:** Inhalation therapy has been employed as the mainstay of the treatment in chronic respiratory diseases such as asthma. Patients taking asthma medication may be at risk of oral candidiasis (1). The purpose of this study was to assess the local effect of ICS on oral tissue by measuring Candida albicans count colonies in saliva among 12 years old asthmatic children who were collected from AL- Zahra Center Advisory for Allergy and Asthma, and compares them with non asthmatic children of the same age and gender.

**Material and Methods:** The total sample involved sixty children of 12 years old, thirty asthmatic children who received medium dose of ICS/day (200-400 microgram/day) for 2 years and 30 non-asthmatic children. The unstimulated saliva was collected under standard condition and then analyzed for Candida albicans colony counts assessment.

**Results:** The mean rank of the colony counts were found to be higher among asthmatic than non-asthmatic children with statistically significant difference (P<0.05). Concerning each gender, the results illustrated that the difference for boys was statistically non significant (P>0.05), while for girls the difference was statistically significant (P<0.05). Concerning gender differences, data analysis showed that the mean rank of Colony counts were found to be higher among girls than boys in both groups with statistically non-significant difference (P>0.05)

**Conclusions:** The findings of the present study showed that the asthmatic disease and ICS treatment play an important role in elevation of the candida prevalence in oral cavity.

Keywords: asthma, candida, inhaled corticosteroid. (J Bagh Coll Dentistry 2015; 27(1):169-174).

INTRODUCTION

Inhaled corticosteroid (ICS) therapy is commonly used for treatment of allergic phenomenon such as asthma (1). Patients taking asthma medication may be at risk of oral candidiasis (2). The local mode of action of ICS lead to local adverse effects of ICS on oral tissue (3, 4), the one most common local adverse effect of ICS is oral candidiasis (5). Previous studies which regarding the incidence of *Candida* in inhaled corticosteroid treated patients reported divergent results. Dubus et al. (6), Ellepola and Samarayake (7), Fukushima et al. (8) and Fukushima et al. (9), suggested that the inhaled corticosteroids in addition to other host factors could potentially increase the risk of oral candidiasis.

On the other hand, Komiyama et al. (10), reported that the percentage of *Candida* were 43.33% in thirty asthmatic children of 4 -12 years old who treated with corticosteroids for period range between 2-48 months and were 30% in thirty control children with no significant difference between them and no correlation was observed between the number of colony-forming units of *Candida* per ml of saliva (CFU/ml), dose of medication and time of treatment. While Adams et al. (11) Rachelefsky et al. (12), and van Boven et al. (13), had been conducted the association between ICS and the occurrence of oral candidiasis regardless of the dose.

Söderling et al. (14), and Cortelli et al. (15), reported that females tended to have higher *Candida* prevalence than males. While Lotti et al. (16), and Reynaud et al. (17), found no relationship between the *Candida* counts and age or gender.

Saliva is a diagnostic and monitoring method for many infectious diseases (18), saliva contain a large numbers of proteins that participate in protection of oral tissue in addition to several peptides with fungal killing activity that had been identified (19), in this way saliva determined the composition of the oral micro flora and controlled oral health (20), by maintaining the integrity of the oral hard tissues and soft tissues through the salivary immune and non-immune defense proteins (21-23).

This study was performed to provide greater visibility to the harmful effects of beclamethasone inhaler on oral pictures among asthmatic children aged 12 years in comparison to control group to evaluate the association between ICS, asthma and oral health which include salivary *Candida* prevalence.

MATERIALS AND METHODS

In the present investigation, the study group included 30 asthmatic children aged 12 years old who received medium dose of ICS/day (200-400 microgram/day) for 2 years, they were examined in AL- Zahra Center Advisory for Allergy and Asthma during the period from 20 December 2013 till the end of March 2013. The control group included 30 non asthmatic children who possess as much as similarity as possible to the
study group with regard to age, gender, social structure and geographic position except in asthmatic condition. Both groups should not possess any systemic disease that could effect on salivary analysis.

The collection of unstimulated saliva was performed under standard condition according to the instructions cited by Navazesh and Kumer \(^{(24)}\) and immediately placed it in ice box until reach the microbiological laboratory. At the Ministry of Science and Technology fungal laboratory, each salivary sample of control and study group was dispersed using vortex mixer for 1 minute and then tenfold dilutions were performed by transferring 0.1 ml of each suspension from each tube of the control and study to 0.9 ml of sterile phosphate buffer saline (pH 7.0), then from dilution \(10^{-2}, 10^{-3}, 10^{-4}\) salivary samples, 0.1 ml was taken and spread on the Sabourauds dextrose agar (SDA), the plates were incubated aerobically for 48 hr at 37°C, then the colony–forming unit per milliliter was counted (CFU/ ml) for all the plates.

The Identification of Candida albicans (C.albicans) can be done through: (A) Colony morphology: Colonies of C. albicans appeared smooth, creamy in color with yeast odor and typically medium sized (1.5-2 mm) diameter which later develop into high convex, off-white large colonies after 2 days \(^{(25,26)}\). (B) Gram stain: A small inoculum from a discrete, singly isolated colony was picked up from SDA plates separately under sterilized conditions and subjected to gram's stain according to Koneman et al. \(^{(27)}\). (C) Germ tubes formation: Under light microscope (100 x magnification), the presence of germ tubes were the characteristic of C.albicans. Figure (3)

The differences in C.albicans \(x10^{2}\) quantities (CFU /ml) between asthmatic and non-asthmatic children are demonstrated in Table (2). Results reported that the mean rank of the colony counts were found to be higher among asthmatic than non-asthmatic children with statistically significant difference (Mann Whitney=311.5, Z= -2.180, P=0.029). Concerning each gender, the results revealed that the difference for boys was statistically non significant (Mann Whitney=99, Z= -1.130, P=0.259), while for girls the difference was statistically significant (Mann Whitney=58, Z= -2.087, P=0.037).

Table (3) shows comparison between genders in asthmatic and non-asthmatic children, the mean rank of colony counts were found to be higher among girls than boys with statistically non-significant difference (P>0.05).

**RESULTS**

The description of the samples is illustrated in Table (1). The C. albicans carrier group of asthmatic children was represented by 60%, while the C. albicans carrier group of non-asthmatic children was represented by 33.33%. The asthmatic children without C. albicans were represented by 40%, while the non-asthmatic children without C. albicans were represented by 66.67%.

![Table 1: Description of the experimental samples](image)
Table 2: Difference in salivary \textit{C. albicans} x 10^2 quantities (CFU/ml) between the asthmatic and non-asthmatic children

<table>
<thead>
<tr>
<th>Variables</th>
<th>Genders</th>
<th>Asthmatic</th>
<th>Non-asthmatic</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Median</td>
<td>Mean± S.D.</td>
<td>Mean rank</td>
</tr>
<tr>
<td>\textit{C. albicans} x10^2 (CFU/ml)</td>
<td>Boys</td>
<td>16</td>
<td>24.25±69.07</td>
<td>18.31</td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>14</td>
<td>15.21±29.97</td>
<td>17.36</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>20.03±53.77</td>
<td>35.12</td>
<td>30</td>
</tr>
</tbody>
</table>

(Non Sig. at P>0.05; *S: Sig. at P<0.05 between asthmatic and non-asthmatic children)

Table 3: Genders difference for asthmatic and non-asthmatic children

<table>
<thead>
<tr>
<th>Variables</th>
<th>Genders</th>
<th>Asthmatic</th>
<th>Non-asthmatic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Median</td>
<td>Mean± S.D.</td>
</tr>
<tr>
<td>\textit{C. albicans} x10^2 (CFU)</td>
<td>Boys</td>
<td>10</td>
<td>10.5</td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>8</td>
<td>11.5</td>
</tr>
</tbody>
</table>

(Non Sig. at P>0.05 between asthmatic and non-asthmatic children)

Figure 1: \textit{C. albicans} colonies on SDA (15x magnification)

Figure 2: Gram’s stain of \textit{C. albicans} colonies showing gram positive stains (100x magnification).
DISCUSSION

Data analysis of the current study concluded that the percentage of C. albicans in carrier group of asthmatic children were higher than non-asthmatic children and the mean rank of the colonies counts were found to be higher among asthmatic than non-asthmatic children with statistically significant difference. These finding were in agreement with Dubus et al. (6), Ellepola and Samaranayake (7), Fukushima et al. (8), Adams et al. (11), Fukushima et al. (9), Rachelefsky et al. (12), and van Boven et al. (13), and in disagreement with Komiyama et al. (10), generally it is difficult to compare the prevalence of C. albicans (CFU/ml) reported by different studies in literature with that of the present study, this might be due to variability in the type and dose of ICS used, frequency of the use of medication, patient compliance with instructions for administration, duration of drug therapy and the mode of delivery (direct or with spacer) or due to the hospital-based population of children with moderate asthma or due to methodologic issues such as study design, sample size, age, gender and length of observations. The findings of the current study can be explained by the fact that the mechanisms by which ICS cause local adverse effects have appear to be related to the deposition of the active ICS into the oral cavity, since the major proportion of the inhaled drug is retained in the oral cavity and oropharynx and only 10-20% reach to the lung during drug administration (29), so it might interfere with normal physiology of oral tissues (3), and it might interferes with the cell-mediated immunity and involve the inhibition of normal host defense functions of neutrophils, macrophages and T lymphocytes at the oral mucosal surface and the esophagus that cause local immunosuppressant in oral cavity (7,30), the decreased efficiency of the immune system may in turn allow an opportunistic infection of Candida (31), or ICS might cause an increase in salivary glucose levels, which stimulate growth, proliferation and adhesion of Candida to oral mucosa (32) and these events accompanied by acid production and a significant concomitant reduction in pH to very low levels (33,34).

However, the reduced pH levels may potentiate Candida virulence by enhancing acidic proteases and phospholipases enzymes of the yeast (35). In addition the results of the this study might be due to the presence of some predisposing factors in asthmatic children who treated with ICS that influence Candida carriage more than the non-asthmatics which include the lack of salivary flushing action and absence of antifungal salivary constituents such as lactoferrin and lysozyme which was attributed to underlying disease and medication intake, the deficiency of salivary IgA which caused by ICS (36,9), the significant alterations in the microbial flora which occur with ICS, the intake of medication at night before going to bed due to poor patient awareness, no oral hygiene measures after medication, the diminution of salivation and lack of masticatory movements during the night might increased C. albicans prevalence which predisposed to candidosis (37).

Furthermore this study showed that the prevalence of colonies counts was higher among girls as compared with boys among asthmatic and non-asthmatic children with non-significant difference, these results were in agreement with Söderling et al. (14), and Cortelli et al. (15) and in disagreement with Lotti et al. (16) and Reynaud et al. (17), the disagreement with these studies could be due to ethnic differences, sample size and...
In conclusion, this study found clinically relevant increased *Candida* prevalence in asthmatic patients who received ICS treatment. This study stresses the need for patient education and inhalation instruction, in order to avoid this local adverse effect, thereby increasing therapy effectiveness and patients' quality of life.

REFERENCES

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