

## Original Article

# Occurrence of Oral Candidiasis among Bronchial Asthma Patients on Inhaled Corticosteroids

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## ABSTRACT

**Introduction:** Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation.<sup>1</sup> Since airway inflammation was identified as the major pathologic condition in bronchial asthma, inhaled steroids have played a central role in asthma treatment.<sup>2</sup> The use of steroids facilitates disease control in asthmatic patients, resulting in improved quality of life. The guidelines for the treatment of bronchial asthma worldwide recommend the use of inhaled corticosteroids although highly effective, may be associated with both systemic and local side effects. The most common local adverse effect of ICS is oral candidiasis. The study aimed to ascertain relationship between inhaled corticosteroids and occurrence of oral candidiasis among asthma patients.

**Methodology:** The present study was undertaken among 50 asthmatic patients selected randomly from those admitted in ward & attended OPD of Department of Pulmonary Medicine, C. U. Shah medical college & Hospital, Surendranagar, Gujarat. All patients were subjected to detailed history and throat examination was done at the same time; a quantitative fungal culture was performed by aseptically obtaining a retropharyngeal wall swab from the patients in our study.

**Result:** Among the 50 patients, 32 (64%) were female and 18 (36%) were male. Age is ranged from 16 to 61 years (Mean 40.2 years). In this study a significantly larger amount of *Candida* spp. was detected in 20% asthmatic patients treated with inhaled steroids. The frequency of oral candidiasis was found to be higher in asthmatic patients using rota caps containing budesonide and formoterol via DPI and not rinsing mouth after taking ICS.

**Conclusion:** Occurrence of oral candidiasis is common in patients using inhaled corticosteroids in asthma. Although not life-threatening, these local side effects are clinically significant and stress the need for patient education and inhalation instruction.

**Keywords:** Asthma, inhaled corticosteroids, oral candidiasis.

## INTRODUCTION

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation is defined by history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and intensity together with variable expiratory airflow limitation.<sup>1</sup> Bronchial hyper responsiveness and variable air-flow obstruction in asthma are a consequence of the activity of numerous mediators and inflammatory cells that can cause persistent airway inflammation and remodelling of the airways through fibrosis and smooth muscle cell proliferation<sup>3-4</sup>. Asthma usually begins in childhood or adolescence but can develop at any time in life. It was estimated that more than 339 million people had Asthma globally in 2016. It is a common disease among children. Most asthma-related deaths occur in low- and lower-middle income countries. According to WHO estimates, there were 417,918 deaths due to asthma at the global level and 24.8 million DALYS attributable to Asthma in 2016.<sup>5</sup>

The objectives of therapeutic interventions for asthma include prevention and control of symptoms, reduction of the frequency and severity of asthma exacerbations, and reversal of airflow obstruction<sup>6</sup>.

Glucocorticosteroids are the most potent anti-inflammatory agents currently available for the treatment of asthma. Clinical studies have demonstrated the efficacy of inhaled corticosteroids (ICS) in reducing airway inflammation and hyper responsiveness, as well as in preventing acute exacerbations, improving lung function, and decreasing symptom severity.<sup>7</sup> Because of their proven effectiveness, ICS have gained widespread use in the long-term management of asthma patients.

Unfortunately, ICS can cause both systemic and local side effects; these local side effects can be clinically significant, affect patient's quality of life and compliance with treatment and mask symptoms of more serious disease. Deposition of ICS in the oropharyngeal cavity can cause oropharyngeal candidiasis or thrush.

## METHODOLOGY

The study was carried out at Department of Pulmonary Medicine, C.U. Shah Medical College, Surendranagar after Ethics committee approval with proper informed consent of the patient. 50 asthmatic patients were selected randomly from patients admitted in ward & attended at

OPD. The following parameters were collected: age, gender, type, frequency and duration of inhaler use, type and dosage of medication. Fungal culture was performed by aseptically obtaining a retropharyngeal wall swab from the patients in study.

## RESULTS

We evaluated 50 patients, of whom 32 (64%) were female and 18 (36%) were male. The mean age was  $40.2 \pm 11.28$  years. Majority of patients were of 30-49 years.

In this sample, the mean daily dose of ICS was 400  $\mu$ g and 10 patients (20%) were found to be using budesonide (200mcg) twice a day while 40 patients (80%) were using combination of budesonide (200mcg) and formoterol (6mcg) twice a day. The average duration of treatment with ICS was 14.5 months and median being 4.5 months (range, 1-72 months).

Of the sample as a whole, 35 (70%) reported performing oral hygiene after ICS use. The frequency of oral candidiasis in asthmatic patients using rota caps containing budesonide and formoterol via DPI was 18 % compared to those using MDI (2%).

**Table 1: The Demographic characteristics of the bronchial asthma patients on inhaled steroids**

Variables	Patients (N=50)
<b>Sex</b>	
Male	18
Female	32
<b>Age Group</b>	
<18 years	5
18-29 years	5
30-49 years	33
>50 years	7
<b>Mean age (years)-</b>	<b>40.2<math>\pm</math>11.2</b>

**Table 2: General Characteristics of patients with Br. Asthma using inhaled corticosteroids (n=50)**

Characteristics	Cases (%)
<b>Treatment</b>	
Budesonide (200 $\mu$ g) Bd	10 (20)
Budesonide (200 $\mu$ g) + Formoterol (6 $\mu$ g) Bd	40 (80)
<b>Duration</b>	
<6 months	27 (54)
>6 months	23 (46)

**Table 3: Frequency of Oral Candidiasis**

Variables	Total Cases (n=50) (%)	Oral Candidiasis (%)
<b>Type of Device</b>		
DPI	40 (80)	9 (18)
MDI	10 (20)	1 (2)
<b>Mouth Rinse after taking ICS</b>		
Regularly	35 (70)	4 (8)
None	15 (30)	6 (12)

(n=Frequency; DPI=Dry Powder Inhaler; MDI=Metered dose inhaler; ICS= Inhaled corticosteroids)

## DISCUSSION

In the present study, we evaluated the oral adverse effects of inhaled steroids in association with the *Candida* spp. in the retropharyngeal wall as detected by fungal culture. It has been suggested that oropharyngeal candidiasis occurs because of the decreased local immunity involving inhibition of normal host defence functions of neutrophils, macrophages, and T lymphocytes at the oral mucosal surface and esophagus<sup>8</sup> or because of an increase in salivary glucose levels, which stimulate growth of *Candida albicans*.<sup>9</sup> Oropharyngeal candidiasis is a condition commonly associated with the use of nebulized corticosteroids.<sup>10</sup> This side effect may be attributed to the topical effects of these medications on the oral mucosa, as only 10 to 20% of the dose from an inhaler actually reaches the lungs, while the rest remains in the oropharynx. The incidence of oral candidiasis can vary from 1 to 77% with ICS treatment, probably because of the difference in methods used to detect it.<sup>11</sup>

In this study the frequency of oral candidiasis was found to be higher in asthmatic patients using Rota caps containing budesonide + formoterol via DPI as compared to the patients using metered dose inhalers. Generalized immunosuppressive and anti-inflammatory effects of steroids are thought to play major role in pathogenesis of candidiasis.<sup>7</sup>

A study by Fukushima et al<sup>12</sup> suggested that ICS can decrease salivary IgA. This host factor can contribute to the development of oral candidiasis. Knight and Fletcher<sup>13</sup> reported that patients who are treated with corticosteroids show a higher level of salivary glucose than the control group. Also, many of the dry powder inhalers contained lactose monohydrate as the carrier vehicle in proportion of 10–25 mg per dose.<sup>14</sup> This higher glucose concentration can also promote growth, proliferation and adhesion of *Candida* to the oral mucosal cells.<sup>15</sup> As mentioned earlier, asthmatics that are medicated with  $\beta_2$  agonist show a decreased salivary flow rate. This decreased salivary flow rate can be associated with higher oral *Candida* counts.<sup>16</sup> Increased risk of oropharyngeal candidiasis in patients taking ICS has also been associated with concomitant use of oral steroids, antibiotics, or diabetes medications.<sup>17</sup>

The common, clinically significant local side effects associated with ICS for the treatment of persistent asthma can affect patient quality of life, can hinder compliance with therapy, and can also mask symptoms of more serious disease. Therefore, there is an existing need for an ICS with relatively low oropharyngeal exposure and efficacy that is at least comparable with current therapies. To reduce the occurrence of local side effects, an ICS should possess characteristics such as low oropharyngeal deposition and activation, solution formulation, small particle size, and activation in the lung.<sup>18</sup>

## CONCLUSION

In conclusion, occurrence of oral candidiasis is common in patients using inhaled corticosteroids in asthma. Proper inhalation techniques and use of MDI with spacer devices, as well as rinsing the mouth after ICS inhalation, are effective in lowering oropharyngeal ICS deposition, and thereby may reduce the occurrence of oral candidiasis. Mainly,

this study stresses the need for patient education and inhalation instruction.

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