

FREQUENCY OF ORAL CANDIDIASIS IN ASTHMA PATIENTS USING INHALED CORTICOSTEROIDS BY DIFFERENT INHALER DEVICES

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ABSTRACT

Objective: In this study, we aimed to compare the frequency of oral candidiasis in asthma patients using inhaled corticosteroids by metered dose inhalers via spacer and Rota caps via Revolizer.

Methods: Asthma patients using inhaled corticosteroids by MDI via a spacer device or Rota caps via Revolizer for at least 2 months presenting to consultant chest clinics were divided into two groups. Group A were patients that used inhaled steroids by MDI via spacer and Group B had patients who used Rota cps via Revolizer. The throat was checked for any oral candidiasis by attending physician in all patients and detailed examination of throat performed by ENT consultant in patients who reported discomfort in throat or dysphonia.

Results: Out of total 150 patients (group A: 66 and group B: 84) included in the study, 82 (55 %) were females and 68 (45%) were males. Age ranged from 13 to 78 years (Mean 44.58). 106 patients (71 %) included in the study had moderate asthma while 54 patients (29%) had severe asthma. Only 39 patients (26%) reported any discomfort in the throat while 111 patients (74%) had no such complaints. Frequency of oral candidiasis was 14 (16.7%) in Group B patients using Rotacaps containing Budesonide 400 mcg and Formoterol Fumerate 6 mcg via Revolizer and it was 4 (6.1%) in Group A patients who used MDI containing Fluticasone propionate 250 mcg + Salmeterol xinafoate 25 with spacer device. It was higher in Group B patients as compared to Group A ($p < 0.05$). The frequency of oral candidiasis was also higher in patients > 50 years of age as compared to patients less than 50 years of age.

Conclusion: This study showed a higher rate of oral candidiasis in patients using Rota caps containing Budesonide and formoterol by Revolizer as compared to MDI with spacer.

Key words: Asthma; Oral Candidiasis; Inhaled Corticosteroids

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INTRODUCTION

Being chronic inflammatory disorder of the airways, inhaled corticosteroids is the most effective first line treatment for the control of asthma. Guidelines recommend inhaled corticosteroids in all the stages of asthma in all age groups as a treatment of first choice.¹ Small doses of inhaled steroid may suffice for mild persistent asthma whereas larger doses are needed for control of moderate to severe persistent asthma.

Still uncontrolled, it may need addition of long acting beta₂ agonist such as salmeterol or formoterol which is available in combination with inhaled steroids in a

single device and both can be released together in a single puff. It not only enhances its efficacy as both molecules reaching the airways together might have synergistic effect but also improve compliance of the patient to treatment.² Addition of leukotriene inhibitors such as Montelukast to the inhaled steroids is another option.³ Unfortunately the frequent use of inhaled corticosteroids, especially at higher doses is associated with both systemic and local side effects. The systemic side effects are well known and serious and are usually dose dependent as up to 80% of the dose delivered by a conventional metered-dose inhaler (MDI) is swallowed.⁴ They include osteoporosis,⁵ adrenocortical suppression,⁶ bruising and thinning of

the skin,⁷ cataracts formation and glaucoma.⁸ On the other hand local side effects are few and minor such as oro-pharyngeal candidiasis, dysphonia and hoarseness of voice but they are important clinically as they are more common, develop quickly during therapy and easily reported by the patient. Moreover they may hamper the compliance of patients to inhalers. The exact prevalence of the local side effects is not known but different studies report prevalence ranging from 5 to 10% up to 58 to 60% depending upon type of studies, length of observations, and methods for recording side effects (questionnaire or inspection).^{9,10}

The inhaled corticosteroids used in Pakistan are largely in the form of MDIs. Some patients cannot use them efficiently despite repeated instructions. This problem can be overcome and efficacy of inhaler improved to some extent with the use of large volume spacers that also reduces the side effects.¹¹ But the problem with large volume spacers is that they are inconvenient to carry and therefore have negative effect on patient's compliance or virtually confines the treatment compliant patients to their homes. Worldwide, a variety of dry powder inhalers, breath actuated metered dose inhalers and Rota caps used via Revolizer are available for patients unable to take metered dose inhalers. Of them the use of Rota caps via Revolizer has the potential to be the device of choice for both patient as well as the physician as it is easy to operate and handle, portable and comfortable device.¹² DPI in the form of rota cap is now available in Pakistan for some time.

Physicians prescribing these different inhaler devices notice differences in the frequency of oro-pharyngeal deposition and candidiasis with these preparations. A common observation is that the use of Rota halers is more commonly associated with oro-pharyngeal discomfort and candidiasis than the MDIs. A study by Fahrettin Talay et al showed that the frequency of oral candidiasis was higher in asthma patients taking

Miflonide (budesonide 400 mcg) + Foradil (formoterol 12 mcg) via an aerolizer than those of other asthma patients using DPI ($p < 0.05$).¹³ No such data is available in our setup for the Rota caps via Revolizer that are available in Pakistan.

The objective of this study is to see the frequency of oro-pharyngeal candidiasis with use of inhaled corticosteroids using MDI and Rota halers.

PATIENTS AND METHODS

All the asthmatic patients using inhaled corticosteroids by metered dose inhaler with a spacer or Rota Caps by Revolizer for at least 2 months, presenting to outpatient chest consultant clinics in Peshawar were included in the study irrespective of their age and sex. Written informed consent was taken from all the participants. The patients were divided into 2 groups. Group A consisted of patients using inhaled corticosteroids by metered dose inhalers containing Salmeterol xinafoate 25 mcg + Fluticasone propionate 250 mcg, 2 puffs twice daily, with spacer device. Group B had patients using ICS Rotacaps containing Budesonide 400 mcg + Formeterol Fumerate 6 mcg used twice daily via Revolizer device. After documenting the personal and clinical data and examination of the chest, the throat was examined for the presence or absence of any abnormality in the oral and pharyngeal mucosa and patients who reported change in the voice or dysphonia were referred to consultant ENT specialist for further detailed examination of the Vocal cords and larynx using indirect laryngoscopy. All the findings were recorded in a proforma and results analyzed at the end.

RESULTS

Out of total 150 (group A: 66 and group B: 84) patients included in the study, 82 (55%) were females and 68 (45%) were males. Age ranged from 18 to 78 years (Mean 44.58). The demographic characteristics of

Table 1: Characteristics of Asthma Patients

	Group A (n= 66)	Group B (n=84)
Male	32 (47%)	36 (53%)
Female	34 (42%)	48 (58%)
Age	Mean 44.58 years	45.39 years
Mean duration of asthma medicine used	8.38 months	6.54 months
Severity of asthma: Moderate	48 (72%)	58 (69%)
Severe	18 (28%)	26 (31%)

Table 2: Oral and Laryngeal Findings in Patients Using ICS by Different Devices

Group of patients	Total number of patients	Oral Candidiasis n (%)
Group A	66	4 (6.1%)
Group B	84	14 (16.7%)
Age < 50	90	6 (6.66%)
Age > 50	60	12 (20%)
Dysphonia:		
Present	39	6 (15.38%)
Absent	111	12 (10.81%)

patients are given in table 1. Only 39 patients (26%) reported any discomfort in the throat while 111 patients (74%) had no such complaints. Frequency of oral candidiasis was 14 (16.7%) in Group B patients using Rotacaps containing Budesonide 400 mcg and Formeterol Fumerate 6 mcg via Revolizer and it 4 (6.1%) in Group A patients who used MDI containing Fluticasone propionate 250 mcg + Salmeterol xinafoate 25 with spacer device. It was higher in Group B patients as compared to Group A ($p < 0.05$). The frequency of oral candidiasis was also higher in patients > 50 years of age as compared to patients less than 50 years of age (Table 2).

DISCUSSION

In this study the frequency of oral candidiasis was found to be higher in asthmatic patients using Rota caps containing budesonide + formoterol via a Revolizer (group A) as compared to the patients using metered dose inhalers having Fluticasone + Salmeterol via spacer device (group B). This difference may partly be due to the difference in the corticosteroid molecules used as it was not the same in both the groups i.e. Fluticasone in group A and Budesonide in group B. Although all the inhaled steroids work by binding to a common glucocorticoid receptor so that same clinical effect can be achieved with all inhaled steroids, although not always at the same dose. Similarly there are differences in the side effects profile of different inhaled steroids given in doses to achieve an equal clinical effect, although its importance is debatable. The other cause of difference in the frequency of this side effect may be due to the difference in delivery mechanism of the steroid molecule. The dry powdered inhalers use lactose as bulking agent that aid in powder uptake from the device during inhalation. High lactose content in the dry powder inhaler and Rotahaler may be enabling higher uptake of steroid in oral and laryngeal regions, leading to development of oral candidiasis. A meta-analysis of 23 different studies had shown signifi-

cantly increased risk of oral candidiasis, dysphonia, and pharyngitis with MDI and DPIs at all doses vs placebo.¹⁴

In our study, frequency of oral candidiasis was found to be higher in asthma patients above the age of 50 years as compared to below 50 years of age irrespective of the type of inhaler delivery device they were using. Oral candidiasis is commonly seen in the elderly. Tanida et al.¹⁵ revealed that the decreases of salivary flow rates and salivary anti-candidal factors, suppression of salivary neutrophil function and the increase of candida adhesion sites on keratinocytes predispose elderly individuals to oral candidiasis. In the present study, frequency of oral candidiasis was more in asthma patients who complained of dysphonia. Cesar A and colleague¹⁶ demonstrated that there is a positive correlation between voice problems and inhalation of corticosteroids.

A meta-analysis of randomized controlled trials demonstrated that budesonide was associated with the highest risk of dysphonia when compared with beclomethasone and fluticasone. When comparing ICSs at high dosages, budesonide was associated with the greater risk of dysphonia as compared to fluticasone.¹⁷ The results of our study indicate that oral and pharyngeal disorders may arise in majority of asthma patients using inhaled steroids via MDIs and DPIs. Meticulous examination by ENT specialist is required to pick this condition early as patients may only complain when they have severe discomfort and dysphonia.

Our study had many limitations. One of it was that we had not strictly excluded those patients who were at higher risk of oral and pharyngeal candidiasis any way like diabetics, immune-compromised patients, those taking certain medications like antibiotics or steroids or undergoing chemotherapy or radiation treatment for cancer and patients wearing dentures and having conditions that cause dryness of mouth. The other drawback was that the randomization into groups was

not very accurate. The input of ENT specialist in thorough and systematic examinations needed to be more to see for problems in the vocal cords and larynx.

CONCLUSION

In conclusion, this study showed a higher rate of oral candidiasis in patients using Rota caps containing Budesonide and formoterol by Revolizer as compared to MDI with spacer. Further studies including a more robust study design and more comprehensive oral and laryngeal examinations before and after treatment may provide more detailed information on this subject.

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