

# Impact of inhalation therapy on oral health

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## ABSTRACT

Inhalation therapy has been employed as the mainstay of the treatment in chronic respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD). Beta-2 agonists, anticholinergic bronchodilators, inhaled corticosteroids, and sodium cromoglycate are often used alone or in combination in an inhaled form. Studies have shown that inhaled drugs used in the treatment have some adverse effects on the oral health based on their dosage, frequency, and duration of use. Several oral conditions such as xerostomia, dental caries, candidiasis, ulceration, gingivitis, periodontitis, and taste changes have been associated with inhalation therapy. Since the prevalence of chronic respiratory diseases is rising, it is important to provide optimal oral care to the individuals receiving inhalation therapy. This article will review the influence of inhaled drugs on the oral health of individuals and adequate management and prevention of the same.

**KEY WORDS:** Candidiasis, dental caries, gingivitis, inhalation, oral health, xerostomia

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## INTRODUCTION

Inhaled therapy is commonly used treatment in respiratory diseases manifesting with airway obstruction such as asthma and chronic obstructive pulmonary disease (COPD). Asthma is a serious global health problem that usually starts in childhood and many times the patient has to take inhaled therapy lifelong. The prevalence of asthma is rising in many countries of the world.<sup>[1]</sup> COPD usually starts in later years and many patients have severe airway obstruction.<sup>[2]</sup> Such patients continue high dose of inhaled therapy for long duration.

High dosage and long duration of inhalation therapy has been closely linked with several adverse effects on the oral tissues.<sup>[3-6]</sup> In comparison to oral therapy, the dose of inhaled drugs is very low for achieving optimal control of the disease. Since the major proportion of the inhaled drug is retained in the oral cavity and oropharynx, it may

interfere in the normal physiology of oral tissues.

## PATHOPHYSIOLOGY

Prolonged use of beta-2 agonists is associated with the increased frequency of caries. It is explained on basis of effect of beta-2 agonist on salivary secretion. In parotid and other salivary glands, beta-2 receptors are present. It has been suggested that prolonged use of beta-2 agonists is associated with diminished salivary production and secretion.<sup>[3]</sup> There is a reduction in flow rates of whole and parotid saliva by 26% and 36%, respectively.<sup>[7]</sup> As reduced salivary rate is accompanied by a concomitant increase in *lactobacilli* and *Streptococcus mutans* in the oral cavity, it may be one of the major contributing factors in the increase caries rate.<sup>[3,8]</sup> Normal salivary action gets further altered by decreased availability of biologically active components like amylase, calcium ions, secretory IgA, peroxidase, and lysozyme. The decreased output of antibacterial components favors both bacterial colonization and plaque growth. It is reported that higher rate of caries have also been observed, possibly due to inhaled drugs containing fermentable carbohydrates and sugar.<sup>[9-11]</sup>

Low pH is a risk factor for demineralization of the tooth. It has been found that the low pH may be due to the use of the inhaler. There was a significant decrease in the salivary pH to below the critical value of 5.5 for enamel

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demineralization, after 30 mins following their use.<sup>[12]</sup> The beta-2 agonists can cause relaxation of smooth muscles such as the lower esophageal sphincter leading to gastro-esophageal reflux symptoms.<sup>[13]</sup> More consumption of acidic beverages to compensate for reduced salivary flow is common especially among children.<sup>[14]</sup> Both these factors contribute to the further decrease in the salivary pH.

Inhaled corticosteroids are weak organic acids and generally are not metabolized by oral bacteria. They therefore should not pose a pH threat, except when sugar-based inhalers are used.<sup>[15]</sup> The adverse effects may be contributed to the topical effects of these drugs on the oral mucosa, as only 10% to 20% of the dose from an inhaler reaches the lung, rest remains in the oropharynx.<sup>[16]</sup> The local deposition of glucocorticoids is, thus, an important risk factor for oropharyngeal candidiasis. Inhaled drugs can also alter the taste perception due to interaction of drug metabolite and saliva.<sup>[17-20]</sup>

### Oral manifestations

- **Xerostomia:** Dry mouth or xerostomia is defined as an overall reduction of salivary output. It is an adverse effect observed with use of beta-2 agonists,<sup>[7]</sup> anticholinergic inhalers,<sup>[21]</sup> and inhaled corticosteroids.<sup>[22]</sup> Patients complain of difficulty in talking or swallowing, altered taste, generalized oral discomfort, mouth soreness, burning sensation, and poor retention of artificial dentures. Also seen are generalized erythema of the oral mucosa and a lobulated appearance on the dorsum of the tongue.<sup>[23]</sup> Xerostomia is clinically presented as oral fissuring, ulceration, and epithelial atrophy.
- **Dental caries:** An infectious microbiologic disease of the teeth that results in localized dissolution and destruction of the calcified tissues.<sup>[24]</sup> Under normal conditions, the tooth is continually bathed in saliva. Saliva is supersaturated with calcium and phosphate ions and capable of remineralizing the very early stages of caries formation, particularly when the fluoride ion is present.<sup>[25]</sup> Fluoride slows down the progression of caries. When salivary flow is diminished or absent, there is increased food retention. Since salivary buffering capacity has been lost, an acidic environment is encouraged and persists longer. This in turn encourages aciduric bacteria which relish the acid conditions and continue to metabolize carbohydrate in the low pH environment. The stage is set for uncontrolled carious attack. Dental caries is thus caused due to imbalance between saliva, plaque, tooth, microflora, and dietary substrate over a certain period of time. It has been found that higher risk of caries is seen in the more developed mixed or permanent dentition of the individuals on the inhalation therapy.<sup>[26,27]</sup> The initial lesion is a reversible incipient caries seen as chalky white appearance on the tooth surface. This can progress rapidly into a grayish or blackish discoloration finally leading to cavitated caries. It is seen frequently on the labial surfaces of the anterior teeth and on the occlusal surfaces of the posterior teeth.
- **Oral mucosal changes:** With the use of inhaled corticosteroids, oropharyngeal candidiasis<sup>[28]</sup> occurs as a potential adverse effect. Most commonly, seen as pseudomembraneous lesion (thrush), it clinically presents as white, soft plaques that leaves a painful erythematous, eroded, or ulcerated surface. The common sites are buccal mucosa, oropharynx, and lateral aspects of tongue. Patients may complain of tenderness, burning, and dysphagia once the pseudomembrane gets disrupted. The use of inhaled corticosteroids can also result in throat irritation, dysphonia, cough,<sup>[5]</sup> dryness of oral cavity and rarely, tongue enlargement.<sup>[29]</sup>
- **Ulceration:** Ulceration of the oral mucosa is seen mainly due to xerostomia and immunosuppression caused by inhaled drugs.<sup>[30,31]</sup> Before the appearance of an ulcer, the involved area produces burning or tingling sensation. A lesion is surrounded by an erythematous halo and is covered by a yellowish fibrinous membrane. They develop over the movable mucosa of the oral cavity.
- **Taste disturbances:** Oral mucosal diseases including candidiasis, prophylactic drugs such as nedocromil, and anticholinergics<sup>[16]</sup> are important etiologic factors. Xerostomia produces taste changes secondary to incomplete food solubilization and by diminished transport of tastant molecules to taste buds.
- **Halitosis:** Bad breath could be due to oral infections and xerostomia.<sup>[32]</sup>
- **Gingivitis and periodontitis:** Increased level of gingivitis is observed with the use of inhaled corticosteroids.<sup>[33,34]</sup> Mouth breathing habit in these patients further increases gingivitis due to dehydration of the alveolar mucosa. Higher prevalence of periodontal diseases has been reported possibly due to the pathological activation of the immune system, inhaled drugs, or an interaction between them.<sup>[30]</sup> Saliva plays an important role in restricting the periodontal disease, thus any drug affecting the salivary secretion remarkably affects the severity of the periodontal disease.<sup>[3,35]</sup>
- **Others:** Adrenal insufficiency and growth impairment<sup>[36]</sup> are possible adverse effects of inhaled corticosteroids. Acute adrenal insufficiency has been significantly reported in individuals on inhaled corticosteroid therapy.<sup>[37]</sup> It may lead to severe hypotension, nausea, and shock.

Gastro-esophageal reflux due to beta-2 agonists increases the chances of dental erosions.

### DIAGNOSIS

The diagnosis of oral candidiasis is usually based on clinical appearance but should be confirmed by laboratory tests. These tests include cytologic smears with potassium hydroxide, biopsy for periodic acid-Schiff and Gram staining for tissue infiltration by spores and hyphae, or culture. The diagnosis of dental caries is based upon careful clinical and radiographic examination. Stimulated saliva specimens can be tested to access flow rate, pH, and

buffer capacity. The saliva sample can also be tested for the presence of *Streptococcus mutans* and *Lactobacillus* using chair-side immunoassays.

## CLINICAL MANAGEMENT OF ORAL EFFECTS

Early recognition and management of xerostomia is important to prevent its deleterious dental effects. The palliative care includes frequent sipping of water, intake of moist sugar-free diet, and avoiding products containing alcohol or strong flavorings.<sup>[23]</sup> The next step constitutes the use of salivary stimulants and salivary substitutes as an essential oral health measure. Sucking on grape or lemon and use of small and frequent meals increase salivary flow. Sugar-free chewing gums, containing casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), xylitol, or chlorhexidine, will increase the salivary flow rate.<sup>[38]</sup> CPP-ACP is preferred due to its remineralizing action.<sup>[39]</sup> Xylitol is a naturally occurring sweetener that cannot be fermented by cariogenic bacteria.<sup>[40]</sup> Prolonged use of xylitol reduces *Streptococcus mutans* counts in the plaque and saliva, and the acidogenic potential of the plaque, whilst increasing its mineral content. Experimentally, chewing gum for at least 1 min after using an inhaler neutralizes the plaque pH.<sup>[12]</sup> The systemic use of drugs such as pilocarpine (15 mg tid) and cevimeline (30 mg tid) has proved successful in stimulating saliva. Saliva substitutes containing carboxymethylcellulose in the form of sprays, lozenges, or mouth rinses may also be added. The sprays should be directed towards the inside of the cheeks and not down the throat.<sup>[41]</sup>

The majority of candidal infections may be simply treated with topical anti-fungal agents. Nystatin ointment (100,000 units/g) can be applied directly to the affected site on gauze pads. Sugar-free antifungal vaginal suppositories, dissolved in the mouth, are recommended to avoid dental caries.<sup>[42]</sup>

Pain relief of erythematous and ulcerated lesion can be obtained with use of a topical anesthetic agent such as lidocaine or topical diclofenac.<sup>[43]</sup> In mild cases, use of protective emollient is sufficient. Oral rinses such as diphenhydramine elixir 12.5 mg/5 ml, dyclonine HCl 1%, and sucralfate 10% may be necessary.<sup>[44]</sup> In more severe cases, topical steroids, such as fluocinonide gel 0.05% or clobetasol propionate gel 0.05%, can be applied directly over the lesion after meals and at bed time two to three times a day, or mixed with an emollient.<sup>[45]</sup> Proper fluid intake and nutritional supplements must be recommended.

The management of gingivitis and periodontitis require direct intervention steps that include eradication of local irritants by professional cleaning, measures to prevent xerostomic effects especially in mouth-breathers, use of antimicrobial mouth rinses such as chlorhexidine mouth rinse, and topical antibacterial preparations such as metronidazole gel. Halitosis and bad taste gets resolved to some extent along with the management of xerostomia and dental infections. Patients usually get relieved when informed about the cause

behind the altered taste being the inhaled drugs. Use of herbs and spices that will augment taste perception can be suggested. Gastric regurgitation must be treated with the use of proton pump inhibitors like omeprazole (20 mg per day).

Adrenal insufficiency may develop during major dental procedures or general anesthesia. Oral corticosteroid such as prednisone (5 mg) must be administered within 2 h before a procedure to prevent stress-induced complications.

The management of the dental caries is generally focused to restore the functional integrity and esthetics of the dental tissues depending on the severity of the condition. A preventive approach is followed by definitive treatment that includes restorations, treatment of dento-alveolar abscesses, and tooth extractions.

## Preventive strategies

Special prophylactic attention must be given to the individuals on inhalation therapy.

- Educate the patients about the possible adverse effects of the inhalation therapy.
- Insist on the use of inhalers with a spacer device to reduce the medication deposits in the oral cavity and oropharynx. The time lag in delivery permits more of the particles to evaporate; hence, more particles are inhaled into the lung.
- Encourage regular dental check-ups at least every 6 months.
- Promote oral hygiene practices that include proper tooth brushing after every meal and use of dental floss at least once a day.
- Instruct the patients to adequately rinse the mouth with neutral pH or basic mouth rinses (milk, water, sodium fluoride 0.05% mouth rinses) immediately after using an inhaler especially before bedtime. This is to counteract the acidic pH of the dry powder inhalers.
- Immediate brushing of the teeth after using inhaler should be avoided as it may damage the already weakened enamel due to acidic pH.
- Recommend the use of anti-microbial mouth rinses such as chlorhexidine mouth rinses (0.2%).
- Institute dietary modification that includes restriction of sugary foods or drinks between meals, avoiding refined carbohydrates, and consuming food rich in starch and fiber. Foods like fruits, vegetables, cheese, peanuts have low cariogenic potential. Sugar substitutes such as aspartame, saccharin, xylitol, and sorbitol can be used as sweeteners. Prescribe nutritional supplements and advice more fluid intake.
- Recommend pit and fissure sealants, and fluoride varnishes and gels (1% sodium fluoride or 0.4% stannous fluoride).

## CONCLUSION

Adverse effects of the inhalation therapy can lead to deleterious consequences in the absence of intervention.

Since a large number of populations are affected by chronic respiratory diseases across all ages, gender, and racial groups, the resulting oral health is a major concern worldwide. Development of novel vehicles for the delivery of medications may prevent the adverse oral effects. Education, research, and evidence-based practice are the foundations for success in creating positive outcomes in such individuals. It is thus imperative to identify, manage, and prevent the adverse impacts of inhalation therapy to improve the quality of life.

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