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Effect of asthmatic inhalers on oral health in children: A review

[1]Vinay K, Reader, Department of orthodontics, Dr B R Ambedkar Dental College Bangalore, India.

[2]Deepika. K, PG Student, Department of Pediatric and Preventive Dentistry, V.S Dental College and Hospital, Bangalore, India.

[3]Suma G, Professor, Department of Pediatric and Preventive Dentistry, V.S Dental College and Hospital, Bangalore, India.

Corresponding Author: Suma G, Professor, Department of Pediatric and Preventive Dentistry, V.S Dental College and Hospital, Bangalore, India.

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Abstract

Asthma is a chronic inflammatory condition of the airways characterized by hyper-responsiveness and episodic, reversible symptoms of airflow obstruction. The disease, its severity and the medication are often fluctuating in time and according to the seasons. The start of the asthmatic condition is difficult to assess. Most asthma drugs are inhaled using various forms of inhalers or nebulizers. As the prevalence of asthma is on the rise, the problems caused by asthma medication could result in a significant worldwide dental health problem. Therefore, this review scrutinizes the effects of asthma and its medication on oral health.

Keywords: Asthmatic children, inhalers, oral health.

Introduction

Asthma is a chronic airway disease characterized by inflammation and bronchoconstriction.[1] It is one of the most common chronic medical conditions in childhood and it has steadily increased during the last two decades.[2]

The prevalence of asthma in the world displays large variations. In the mid-1990s, the International Study of Asthma and Allergies in Childhood showed that the highest rates are found in Australia, Peru, New Zealand, Singapore, and the United Kingdom, whereas the lowest are in Albania and Russia. Prevalence rates tend to be highest in economically developed countries with a temperate climate and low in rural subsistence and economically developing communities.[3] Although asthma affects people of all ages, most cases of asthma occur in childhood with peak prevalence between the ages of 6 and 11 years. Until puberty, asthma is more common in boys than in girls, but after puberty the incidence is equal.[4]

In reports from The Swedish Council on Technology Assessment in Health Care (SBU), about 20% of

children under two years of age and about 10% of schoolchildren are affected by asthma (Steinbacher and Glick, 2001). In Western countries, the prevalence of allergic disorders including asthma in children has increased to 41% (Kjellman, 1977; Hattevig et al. 1987; Varjonen et al, 1992). Multiple causative factors including familial, infectious, allergenic, socioeconomic, psychosocial and environmental have been reported. The inflammatory response in the lungs can be triggered by various environmental factors including viral infection, exercise, tobacco smoke, pets, dust, molds and pollen. In susceptible children, these triggers cause swelling and narrowing of the airways characterized by airway hyper-responsiveness, airflow limitation and respiratory symptoms, which are most commonly manifested as coughing or wheezing and chest tightness (Harik et al, 2004).[5]

The treatment of asthma can be divided into two phases: the first is to control the symptoms of the acute phase, such as bronchospasm, with the use of bronchodilator medicines. The second phase is to prevent new acute events through maintenance treatment, by using inhaled or systemic steroids and bronchodilators of long duration [Rang et al., 2003].[6]

Choosing a method of drug administration for children with airway disease is as critical as the choice of medication itself. Inhaled administration of asthma treatments results in higher concentrations of drug at the target organ, the lung, and minimizes systemic adverse events.[7]

Current guidelines recommend the use of inhaled anti-inflammatory agents (corticosteroids and non- steroidal drugs) for the prophylaxis of chronic asthma.[8]

Most asthma drugs are inhaled using various forms of inhalers or nebulizers. Patients should be carefully trained in the use of inhalers for these to be effective. As the prevalence of asthma is on the rise, the problems caused by asthma medication could result in a significant worldwide dental health problem. Therefore, it is necessary to scrutinize the effects of asthma and its medication on oral health.[9]

Early manifestation of bronchial asthma at the first year of life can cause dentofacial changes. Therefore, the prompt diagnostic of the illness, as well as the establishment of a proper therapy could improve the symptoms and chronic complications of asthma and also reduce its adverse impact on craniofacial development.[10]

Asthma and dental caries

Dental caries represents a multifactorial disease and it is the single most common chronic disease of childhood. Caries lesion forms through a complex and fermentable carbohydrates on the tooth surface. Caries risk assessment is the determination of the likelihood of the incidence of caries during a certain time period. In 2002, the American Academy of Pediatric Dentistry (AAPD) has developed the caries-risk assessment tool (CAT) based on a set of physical, environmental, and general health factors. One of the components of CAT is children with chronic medical conditions requiring long term medication being at a risk of dental caries as a side effect.[4]

Studies by Ryberg et al. [1987, 1991] [11], Kocata et al.[12], Hanane et al[13], Yadav et al[14], Reddy et al.[15], Ersin et al.[16], Khalilzadeh et al.[17], Wierchola et al[18], Stensson et al.[19], Fang-yi-Wu et al[20], Samec et al[21] and Botelho et al. (2011)[22] found increased caries in asthmatic children compared to non-asthmatic controls.

Studies by Bjerkeborn et al. [1987][23], Eloot et al.[24], Wogelius et al.[25] and Boskabady et al.[26] found no differences in the caries risk in asthmatic and non-asthmatic children.

The role of asthma medications in the prevalence of dental caries has been found to vary by pharmaceutical formulation and frequency and timing of administration: the prevalence of caries was higher in 3- to 18-year-old patients using syrup formulations and according to a survey by mail, when dose frequency exceeded twice daily.[27]

Heidari et al found there was an association between asthma medications and the severity of dental caries and this association was mainly due to the form of medications taken (tablets) rather than different types of drugs or a combination of them.[28]

In 2007, Shashikiran et al, demonstrated that salbutamol inhalers caused a significant increase in caries followed by salbutamol tablets.[25]

It is found that in asthmatic children, a large proportion of inhaled drug is retained in the oropharynx, ranging from 80% with metered dose of inhaler and 60% with dry-powder inhaler with extension tube.[1]

Prolonged use of beta-2 agonists is associated with the increased frequency of caries, which could be explained through the basic effect of beta-2 agonists that are connected to the present beta-2 receptors in the parotid and other salivary glands. The increased susceptibility to dental caries can also be due to the frequent use of dry powder inhaler containing fermentable carbohydrates. The most common is lactose monohydrate and although it is one of the least cariogenic sugars, it can still lead to an increased dental caries risk.

Based on studies, patients undergoing inhalation therapy are subjected to higher risk of dental caries, due to the reduced saliva secretion, decreased pH value, enlarged number of cariogenic bacteria caused by inappropriate oral hygiene. These changes could be related to basic diseases or to the prescribed therapy.

Risk factor for higher caries experience in patients can also be poor hygiene and lack of information about proper maintenance of oral hygiene and preventive measures to preserve dental health.[29]

To reduce the incidence of dental caries in asthmatic children it is suggested to use sugar free medication and fluoridated products to rinse the mouth. Sugary medications and non-regular use of fluoridated rings positively correlate with an increased number of caries. Rinsing and gargling the oral cavity, using spacer devices, and trying to reduce the dosage and frequency of ICS are also recommended.[30]

Asthma and saliva

Salivary flow and composition play a fundamental role in oral health, with a defensive mechanism that can be impaired in the asthmatic condition due to medications used and alimentary habits or lifestyles.[8]

Studies by Ryberg et al.[11], [Shashikiran et al., 2007][28], Paganini et al. [2011], Kocata et al[12] and Mazzoleni et al[30] showed that asthmatic children who medicated with β2 agonists had a decreased saliva secretion rate and increased levels of lactobacilli and mutans streptococci compared with healthy children.

Kargul et al stated a decrease in pH in medicated asthmatics.[31] In 2013, Alaki et al. demonstrated higher lactobacilli levels among children with asthma than that in children without asthma.[32]

The use of asthma medications such as beta 2 agonists influences the salivary secretory rate. The children with asthma had a lower secretion rate of whole saliva and lower parotid saliva secretion rate compared with children without asthma. Furthermore, children with asthma treated with beta 2 agonists had a significant decrease in the concentrations of total protein and amylase in the saliva and Streptococcus mutans values

were higher in these children than in children without asthma.

Ersin et al, showed that the type of asthma medication had no effect on salivary flow, pH or the buffering capacity of the saliva.[15]

Stimulation of salivary secretion rate normally decreases the concentration of both sIg A and BAGP in saliva (Brandtzaeg, 1971; Ericson et al., 1975; Shannon and Suddick, 1975). However, Ryberg at al found the lower secretion rate in the asthmatic group was not associated with a higher concentration of these two substances. This could indicate that the drug or the disease has interfered with the biosynthesis or the release of proteins. Auto-antibodies against the beta 2-adrenoceptor have been found in asthmatic patients (Szentivanyi, 1980; Venter et al., 1980, 1981).[11]

Lenander-Lumikari et al. stated that the mean stimulated salivary flow rate was lower in the asthmatic group than the control group, but no differences in microbial counts were found in their study.[33]

Chakiri et al[13] revealed the presence of a dry mouth in asthmatic against controls. Hegde et al. in 2012 found that levels of salivary antioxidants reduced in asthmatic children.[13]

Therefore, the asthmatic children should be encouraged to rinse their mouth after the use of the inhaler. The use of sugar-free chewing gum to stimulate salivary flow and buffer oral acids should also be encouraged.

Asthma and gingivitis

McDerra et al. found that 4-year-old to 10-year-old children with asthma had more plaque, gingivitis, and calculus compared with healthy controls. Higher prevalence of calculus in asthmatic children is thought to be due to an increase in the levels of calcium and phosphorous in submaxillary and parotid saliva. This can also contribute to an increase in periodontal problems in asthmatics.[34]

An increase in the dental plaque index on the buccal surfaces of the teeth was observed, possibly because lingual surfaces are protected by the cleaning effect of tongue movements.

Tuula et al showed the group of children who received beclomethasone for treatment had more gingival inflammation than those children with disodium cromogly gate treatment. Both drugs are administered by inhalation through the mouth, and neither of them affects the salivary glands. The peroxidase activity in asthmatic children did not differ from their healthy controls, although they showed increased gingivitis. This indicates that in asthma the peroxidase defense mechanism is not altered. There was a slight increase in the arginine aminopeptidase activities, an enzyme group involved in inflammatory reactions.[35]

Yadav et al[14], Hanane et al[13], Shulman et al. in 2009[36], Laurikanen and Kuusisto in 1998[33], McDerra et al. in 1998[34] and Hyyppa et al. in 1984 demonstrated that asthma patients suffered more from gingivitis than the control groups, while Bjerkeborn et al. in 1987[23], Sowmya et al.[14] encountered no differences in the gingival index. McDerra et al. and Hyyppa et al. did not detect any differences in the index of plaque. Hence, there is a need to educate this group of patients about their increased risk and the importance of proper plaque control.

Various explanations have been put forward for why children and adolescents with asthma have significantly more severe gingivitis than controls. Firstly, it could be the result of an altered immune response. In fact, the concentration of immunoglobulin E in gingival tissue was found to be elevated in asthmatic patients, which caused gingival destruction. Additionally, an enzyme

group involved in inflammation (the arginine aminopeptidases) was found to be slightly elevated in the gingival fluid of asthmatic children, indicating that gingival inflammation was increased in asthma. Moreover, the tendency to breathe through the mouth could cause the dehydration of alveolar mucosa, resulting in a worsening of the oral condition. Finally, the use of inhaled steroids has been linked to increased levels of gingivitis. [13]

Recent evidence has shown that poor periodontal condition is a potential risk factor for systemic inflammatory diseases, including allergic disease. The study also demonstrated a positive correlation between poor oral health and asthma, AR, atopic dermatitis in Korean adolescents.[37]

A study by Kargul et al. showed that chewing sugar-free gum for at least one minute after using an inhaler can neutralize the interdental plaque pH.[31] Proper tooth brushing habits and lifestyle modification should be implemented for each asthmatic child to counteract and prevent gingival inflammation.

Asthma and growth

Since growth retardation in childhood asthma was first described by Cohen et al in 1940 there have been many conflicting views concerning its occurrence. Some workers have noted growth retardation only in those children treated with corticosteroids, while others have related it to the severity of asthma. The observation that bone age was retarded to the same extent as height suggested that the short stature was associated with developmental delay and led to the prediction that these children would ultimately grow to normal heights. This was supported by Ferguson et al, who also noted that short stature was three times more prevalent in children with allergic respiratory disease than the general population.[38]

Several factors affect growth such as chronic disease, genetic background, suppression of the HPA axis and onset of puberty and therefore it is difficult to fully assess the effects of steroids on growth.[39] Severe asthma therefore may confound the results of several studies which aim to determine whether ICS suppress growth. The limitations in studies exploring this field are: a short study duration which would not include final height and the measure of growth such as knemometry whereby the length between the knee and heel is measured.[40]

Long term studies in this field are rare. However, they have shown that although ICS such as high dose beclomethasone result in delayed puberty and slower growth velocity, catch up growth allows them to reach their growth potential (predicted adult height).[38] Another long-term study comparing asthmatics and non-asthmatics found that after accounting for mid-parental height, predicted height for asthmatics was comparable to healthy controls and that ICS had no effect on growth.[41]

A recent study assessed the effects of inhaled steroids on bone density and growth. The authors found that children on budesonide and beclomethasone dipropionate had reduced linear growth and this did persist for up to two years from treatment commencement.[42]

A recent Cochrane review found that regular ICS use even at low to medium doses was associated with a 0.48 cm/year reduction in linear growth in children with mild to moderate asthma. They found that the effect decreased after the first year however there was limited long-term data and therefore could not ascertain whether ICS affected long-term growth.[43]

Several studies indicated an effect on growth using low to moderate doses of inhaled steroids.[39,44] The duration of growth suppression, however, seems limited to the

initial phase of treatment and of small magnitude.[45] In the long-term follow-up of the CAMP study, growth reduction by inhaled steroids was only approximately 1 cm over 4–6 years treatment compared with nedocromil and placebo.[46] In another study following up children into adult life, there were no differences between measured adult height and targeted adult height in asthmatic patients treated with inhaled steroids, healthy controls and siblings of asthmatics.[47]

Another concern is possible systemic effect of high doses inhaled steroids initially reported by Priftis et al.,[48,49] and the more recently reported cases of symptomatic hypoglycemia by Drake et al.[50] and others[51,52,53]. Pituitary–adrenal suppression was reported in preterm very low-birth weight infants treated with fluticasone[54], and Kannisto et al.[55] reported mild adrenal suppression in children on moderate doses of budesonide and fluticasone. These studies demonstrate the need to individually assess all children treated with inhaled steroids, and in children with need of medium to high doses a stimulation test of the adrenals should be done. [45]

When Martin et al reviewed all McNicol and Williams cases at the age of 21 years, they noted that complete catchup growth had occurred.[56]

Hauspie et al in their mixed longitudinal study also stated that height growth retardation was related to the degree of severity of asthma.[57] They considered that the retarding effect on growth caused the delay in the onset of puberty, with the subsequent catchup growth apparently overcoming all previous effects of the disease. They speculated that the growth retardation could have been due to various factors suggested in the past: respiratory insufficiency with hypoxia, inadequate nutrition, chronic or recurrent infections, long term stress, and suppression of normal activity.

A study by Lynn et al suggested the effect was primarily on the mechanism responsible for the 'switching on' of puberty itself. The regulation of height growth has been shown to be normal in all children followed up. The only deviation from the established centile pattern has been the preadolescent deceleration in growth velocity seen in the children with delayed puberty, and this is physiological.[39] Tanner has described this period as having the 'lowest growth velocity ever experienced' and talks about the immediate pre-adolescent velocity being so low that parents sometimes allege, mistakenly, that the child has actually stopped growing altogether for a year or more'.[58]

It is imperative that clinicians are aware of these effects to ensure that they can be minimized and patients can be monitored effectively and promptly. [40]

Asthma and malocclusion

Epidemiological studies showed that nearly 74% to 81% of asthmatic patients have also allergic rhinitis. It is important to point out that patients with allergic rhinitis or asthma as well as patients with nasal septum deviation, enlarged adenoids or nasal polyp generally present mouth breathing which is often related to malocclusion etiology. [59]

Barros et al, in a cross-sectional study, observed a positive correlation between allergic rhinitis and mouth breathing.[60] Venetikidou also reported a higher prevalence of mouth breathing in asthmatic patients.[54] On the other hand, no association between asthma and impaired nasal breathing was observed in the study by Kumar et al, but as the severity increases, the frequency of normal/ minor malocclusion cases also significantly increases.[59]

Wenzel et al reported that inhaled budesonide can reduce nasal obstruction in allergic children and, therefore,

normalize possible changes in cranio-cervical angulations observed.[61]

Tanaka LS et al, Bivariate and multivariate analysis showed higher prevalence of malocclusion and consequent facial changes in asthmatic children and adolescents when compared to control ones. These changes in occlusal features (increased maxillary over jet and open bite) are more common in patients with an early disease onset, when the disease started at the first year of age, especially in mixed dentition group. [62]

Faria et al also reported an association between asthma onset and dentofacial changes observed in adults. Facial growth is most prominent during childhood under 15 years of age and the authors verified that crossbite and crowding are often observed in asthmatic adults in whom the disease begun before 14 years of age.[63] However, Venetikidou showed no statistically differences among overbite and overjet prevalence in asthma group when compared to control one. [64]

The results of Gautam et al are in contrast with Faria et al who found no association between asthma severity and malocclusion in adults, despite other study have previously reported this correlation in children. [59]

Bresolin et al. studied the association between allergic rhinitis and frequency of dentofacial deformities. They observed that children with rhinitis had a longer anterior face, increased overjet, a deeper palate, and significantly narrower intermolar distances in the upper arch.[63]

A statistically significant relationship found between the frequency of crossbites and the frequency of mouth breathing. Additionally, a statistically significant relationship was found between the frequency of crossbites and the facial type in the experimental group. The frequency of crossbites appears to be related to abnormal facial types.[64]

Special oral health attention should be provided to asthmatic children and adolescents to intercept malocclusions at early stages.[59]

Asthma and dental erosion

In the study by Kocata et al, although the salivary pH was statistically lower in asthmatics than non-asthmatics, it was not below the 'critical pH' (5.5) which resulted with the enamel demineralization.[12]

A decrease of the salivary and plaque pH has been detected in asthmatic children after the use of aerosol metered-dose inhalers.[65] Inhalant powders, as the powdered form of Flixotide (Fluticasone) and Serevent (Salmeterol), contain lactose as a carrier for the active substance of the medicine. The pH values of most inhalant powders are less than 5.5.[66] This low pH value of the inhaled drug, associated with a reduced salivary flow rate, may make asthmatics more susceptible to erosion.[67,68]

Lenander-Lumikari et al. [2000] examined the effect of three different steroids on plaque pH. The dry powder inhalers containing lactose caused a decrease in plaque pH, but all values remained above the critical level of pH 5.5. The use of a Turbohaler (no lactose carrier) did not affect plaque pH.[69] A study of Tootla et al. [2004][65] evaluated the acidogenic potential of asthma inhalers, metered dose inhaler and dry powder inhaler formulations. Although none of the inhalers were able to demonstrate an acidogenic response below the "critical" pH, the substantial pH drops observed with the lactose-based dry powder inhalers may be an important consideration for enamel demineralization. With exception of the study of Kargul et al. [1998] thus far no other published report could prove a significant oral pH reducing effect of inhalers to or below the critical level of pH 5.5.[24]

Wee et al showed asthmatic children presented significantly higher dental caries and dental erosive lesions than their matching controls.[37]

Conflicting results concerning the association between asthma and tooth erosion were published[67]. Dugmore and Rock[70] in a representative random sample of adolescents in the UK found no association between asthma and tooth erosion. They also reported that 88% of drugs prescribed for asthma had a pH above 5.5. However, some drugs inhaled to combat asthma have a pH low enough to cause erosion, particularly when they come in frequent and/or sustained contact with teeth. When asthma medication is taken from an inhaler, the lips form a seal around the nozzle of the inhaler, covering and protecting the labial surfaces of the incisors and canine teeth.

Drugs used as bronchodilators act to relax smooth muscle. This may affect the esophageal sphincter in addition to the bronchus and thereby potentiate the gastroesophageal reflux, which is a recognized etiological factor in tooth erosion. The patients might increase their consumption of acidic drinks in an attempt to compensate for reduced saliva flow, increased dry mouth and the taste of drugs. The authors concluded that it is difficult to support an association between such drugs and the erosion on the population level.

They also stated that most asthma inhalation medicaments are not acidic and pose no threat to the dentition. There seems to be no clear evidence of an association between decreased salivary flow rate due to asthma medication and tooth erosion. The proportion of drugs used that may promote gastroesophageal reflux is low and unlikely to have a significant influence on tooth erosion prevalence, and they could not approve the thesis that asthmatic children consume more potentially erosive drinks than non-asthmatics.[71]

Sivasithamparam et al. [72] found that gastroesophageal reflux does not appear to contribute in a side-specific manner to erosion in asthmatics. Al-Dlaigan et al.[68] observed that the higher prevalence of erosion in their sample of asthmatic patients was associated with reflux. This is interesting, because the systematic review by Tolia and Vandenplas[73] showed that the prevalence of gastroesophageal reflux disease in asthmatic children (pooled weighted average prevalence of 23.4%) is greater than in healthy controls. This is also true in adults, where the prevalence of gastroesophageal reflux disease in those suffering from asthma is as high as 59.2%. Although it is still not known whether there is an actual causality association between both conditions, dentists should consider the likelihood of erosive lesions in asthmatic patients to be related with a possible reflux disease.[71]

Conclusion

Oral health status of asthmatic children are comparatively poor with high dental caries experience, poor gingival health, dental erosion, malocclusion and compromised oral hygiene status. The prevalence of increased dental caries, gingivitis and compromised oral hygiene status had a positive association with the medication taken.

Asthmatic children need to be put on preventive schedule to counter the ill effect of asthma and its medication. Constant monitoring by pediatric dentist and general pediatrician may help in declining the effect of disease. The asthmatic children should receive oral health education and proper technique of using inhaler.

The prompt diagnosis of asthma, as well as the correct pharmacological treatment, could improve not only its symptoms and chronic complications, but also it could reduce its impact on craniofacial development. Special oral health attention should be provided to asthmatic

children and adolescents as well as it can be recommended that dentists should be included at the multidisciplinary team involved in asthma assistance. The pedodontist along with Pulmonologist, Otolaryngologist and Orthodontist together can help a suffering child have a happy, healthy and active childhood.

In conclusion, asthmatic patients especially in the younger age should receive intensive preventive care, including oral hygiene instruction, dietary advice and regular topical fluoride treatments.

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