

Effect of inhalation therapy on oral health in patients with chronic airway disease

Putu Mariati Kaman Dewi ^{1,*} and Made Agustya Darma Putra Wesnawa ²

¹ Department of Conservative Dentistry, Faculty of Medicine, Universitas Udayana, Denpasar, Indonesia.

² Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Udayana, Denpasar, Indonesia.

World Journal of Advanced Research and Reviews, 2024, 23(01), 2502–2508

Publication history: Received on 12 June 2024; revised on 22 July 2024; accepted on 24 July 2024

Article DOI: <https://doi.org/10.30574/wjarr.2024.23.1.2232>

Abstract

The primary treatment for both chronic obstructive pulmonary disease (COPD) and asthma is inhalation therapy. When utilized over an extended period of time, inhalation treatment serves as both a controller and a relief therapy. Oral adverse effects can result from inhaled medications, particularly bronchodilators and corticosteroids that are deposited in the oropharyngeal region. Reduced saliva flow rate, periodontal disease, oral thrush, dental caries, and dental erosion are just a few of the side effects and difficulties associated with using inhaler therapy that are frequently discovered in the oral region. This problem may arise from improper inhaler use, concomitant diseases and conditions of the patient, inadequate education, and inadequate assessment of oral health during inhalation medication. In order to prevent side effects and complications from inhaler therapy, it is essential to comprehend the different types of inhaler drugs and the pathophysiology associated with oral health complications. This will enable clinicians to modify the components of the drug type, the type of inhaler therapy device, and the appropriate method of use based on the unique characteristics of each patient.

Keywords: Inhalation therapy; Oral disease; Asthma; Chronic obstructive pulmonary disease

1. Introduction

The primary and most crucial form of treatment for those with chronic respiratory illnesses, including COPD and asthma, is inhalation therapy. Inhalation therapy is the primary treatment for this chronic airway illness, which is characterized by complaints of shortness of breath, wheezing, chest heaviness, and persistent cough. (1) Long-term inhalation therapy using medication components such as corticosteroids and bronchodilators is necessary for chronic airway disease. Patients with COPD and asthma will undoubtedly utilize inhaler medication more frequently as a result of this worldwide. There are numerous kinds of inhalation therapy devices on the market right now, and each one has unique qualities. Age, length, severity of the condition, type of inhalation therapy, and proper technical application are some variables that affect inhalation therapy's efficacy. (2)

Inhaler therapy's adverse effects, particularly oral and dental diseases, might occur with prolonged use. This frequently happens as a result of improper use of inhaler equipment. (3) Long-term use of inhaler therapy can cause adverse effects on the oral region, including reduced saliva production. Patients with asthma and COPD who take long-term inhaler medication run a higher chance of experiencing these adverse effects if they fail to report their concerns to the physician or if the physician neglects to monitor the state of their mouth and teeth. (4)

Studies have shown a connection between dental and oral health issues and inhalation therapy. Patients with chronic respiratory diseases may have an increase in dental and oral disorders as a result of inhaler therapy side effects, which could lower their quality of life if proper education and intervention are not given. (5) Thus, we will talk about the drawbacks of inhaler therapy in this review and the maintenance of oral and dental health.

* Corresponding author: Putu Mariati Kaman Dewi

2. Inhalation therapy in chronic airway disease

One of the primary treatments for lung and respiratory conditions is inhalation therapy, which works by introducing medication aerosol directly into the airways. (6) Inhalation therapy is useful for both long-term control and as a relief strategy during exacerbations. (7) This inhalation treatment is safe and free of systemic adverse effects, with the goal of delivering rapid action and high effectiveness. The two major medications used to treat COPD and asthma are bronchodilators and corticosteroids, both of which are frequently administered in inhalation forms. Numerous device types are available for use in inhalation therapy; the choice of device is made depending on the specific needs of the patient as well as the drug's properties and preparation.

2.1. Pharmacokinetics of inhalation therapy

The amount of medication that is deposited in the lungs during inhalation therapy is between 15% and 20%, which has therapeutic effects. The oropharyngeal tract is where the majority (80%) of medications that are breathed end up before being swallowed and entering the digestive system. Aerosol drug deposition is caused by three processes: diffusion, sedimentation, and inertial impaction. Compared to oral medications, less medication from inhalation enters the bloodstream. One benefit of using inhaled medications to treat chronic airway illnesses is that they have fewer systemic adverse effects and direct pharmacological action on the airways. The pharmacokinetics of inhaled medications require careful consideration since, in the event of overuse, the majority of the inhaled drug will settle in the oral cavity and throat, potentially resulting in local side effects. Therefore, pulmonologists and dentists must provide regular supervision and evaluation when employing inhalation therapy.(1)

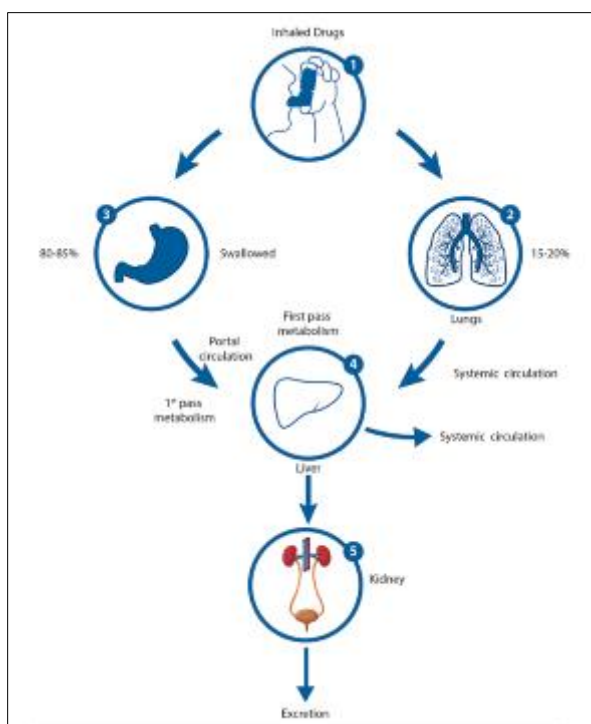


Figure 1 Pharmacokinetics of inhaled drugs(1)

2.2. Types of inhalation therapy

The many and diverse kinds of inhalation therapy devices are available, and they can be customized to the patient's preferences and needs. Pressurized metered-dose inhalers (pMDI), dry powder inhalers (DPI), soft mist inhalers (SMI), and nebulizers are among the commonly accessible inhaler devices nowadays. Each type of inhaler device has pros and cons. Inhaled corticosteroid (ICS), long-acting antimuscarinic agent (LAMA), short-acting antimuscarinic agent (SAMA), long-acting beta 2 agonist (LABA), and combinations such as LABA-LAMA and LABA ICS as well as the triple LABA-LAMA-ICS combination are among the drug components that are involved in inhalation therapy. (7)

Patients who meet all cognitive, coordination, and manual power requirements may benefit from pressurized metered-dose inhalers. Patients with mild to moderate deficits in these variables may benefit from the use of add-on devices such

as spacers, face masks, and valved holding chambers, or from breath-actuated metered-dose inhalers or soft-mist inhalers. In these situations, metered-dose inhaler medication should be permitted by using the personal assistance resources that knowledgeable family members or caregivers can provide. Patients with good cognitive and physical abilities and a sufficient peak inspiratory flow may be eligible for dry powder inhalers. For those who are incapable or reluctant to utilize handheld inhalers, nebulizers may be recommended. To minimize adverse effects, close observation is necessary following the start of a particular inhalation therapy. (8)

3. Risk factors for side effects of inhaler therapy

One of the most often mentioned obstacles to adherence is the abuse of inhalers. Because they may increase the chance of adverse effects and problems in the teeth and oral cavity, a number of factors that affect how inhaled medications deposit in the mouth and nose must be taken into account. These factors include:

3.1. Type of inhaler

The restrictions of any inhalation device must be considered as they may raise the possibility of adverse consequences. (2,3) The use of pMDI necessitates good synchronization between inhalation and expiration, and it has constraints linked to significant oropharyngeal deposition. Children and the elderly with inadequate inspiratory abilities cannot utilize DPI because it demands a sufficient inspiratory flow ability. (6)

3.2. Drug formulation

Because it has to do with aerosol deposition in the airways, the kind of medication component used in inhalation therapy must be taken into account. Particularly for muscarinic antagonist activity, which is frequently detected in small airways, muscarinic receptors are present in numerous medium and large airways. Both beta-adrenoreceptors and corticosteroid receptors are dispersed throughout the respiratory tract. Smaller-sized pharmaceuticals will be deposited in the small and distal airways, while larger-sized drug components will be deposited through impaction in the oropharynx and conducting airway. The optimal inhalation medication is between 1 and 5 μm in size because it can effectively target small airway targets and produce therapeutic effects. (6)

3.3. Patient factor

Patient factors include the geometric structure of the airways, lung and airway conditions, and the patient's inhaler-using capacity. The shape of the airways affects the pattern of drug deposition in the lungs as well. Larger particles tend to stay in the upper airways, whereas smaller particles drift with the airflow and deposit in the lower airways because of the bronchi's bifurcation and the airways' curvature. In conditions like asthma and COPD, the airways become inflamed and obstructed. As a result, there is less medication left in the airways and the airflow is altered. Mucus plugging and narrower airways in severe disease cause more turbulence in the airways, which lowers medication deposition. (1)

4. Side effects of inhaler drugs in the oral cavity and pathogenesis

When using inhalation therapy, oral symptoms are highly common and are closely related to the amount, frequency, length of time, and use of the inhaler. Regardless of age or gender, the oral findings linked to inhaler users were the same. On the other hand, significant manifestations were noted in relation to the medicine dosage as well as the kind, frequency, and length of inhalers. (3) Reduced saliva flow rate related to the function of saliva and the relationship between the inhaler's components and the cells in the salivary glands, periodontal disease, oral thrush, dental caries related to the relationship with saliva flow rate, and dental erosion are among the side effects of inhalation therapy that are related to the mouth and teeth. (9–11)

4.1. Xerostomia

The primary line of treatment for COPD and asthma is inhalers. A deficient inhaling technique affects over 30% of adults with asthma, causing 80% of the medication to be deposited in the oropharynx. This significantly alters the efficacy of treatment and increases the risk of local or systemic side effects. (10) Because only 10–20% of the dose enters the lung and the remaining is kept in the oropharynx and oral cavity, it interferes with normal oral tissues and produces inhalation treatment side effects that, if left untreated, could have detrimental effects on oral tissues. The effects of the medications used in inhalers, as well as the kind, frequency, and length of use, all affect the severity and frequency of oral disorders that affect users of inhalers. (3)

Through a variety of mechanisms, inhalational treatments can influence salivary secretion and exacerbate xerostomia. (12) Burning feeling, altered taste, and sore mouth are further symptoms of xerostomia. (3) Cholinergic and adrenergic transmission work together to precisely control salivary secretion in a physiological setting. One well-known adverse effect of medications with cholinolytic qualities is dry mouth. This observation holds much more true in the case of M3 receptor antagonists, since stimulation of the aforementioned receptor type is accountable for salivary production in addition to mucous secretion and bronchial constriction. As a result, it has been shown that even localized inhalation of these substances reduces saliva production.

While the release of salivary proteins is caused by β -adrenoreceptor stimulation, asthmatic patients who utilize β -2-mimetics inhalations on a regular basis experience alterations in both the amount and quality of saliva secreted. (12) Beta-2 agonist-containing asthma drugs may lower salivary flow rates, which may hinder saliva's ability to exit the mouth and lessen its buffering power. (5) In asthmatic patients, xerostomia was also linked to inhaled corticoids. The precise mechanism is still unknown, though, and there is ongoing debate on the influence of additional variables, such as the illness itself. In addition to being a bothersome condition that lowers the quality of life for the patient, xerostomia may exacerbate other illnesses and encourage their growth. (12)

4.2. Dental Caries and Dental Erosion

The biochemical interaction of acidogenic bacteria, fermentable carbohydrates, and host factors, including teeth and saliva, led to the development of dental caries. When physiological circumstances are met, saliva production in the right amounts and composition helps to prevent tooth cavities. Through its ability to act as a buffer and self-cleaning agent on the tooth surface, saliva lowers the cariogenic potential of dental plaque. Reduced salivary flow rate from inhalation therapy can lead to decreased salivary and plaque pH, an increase in lactobacilli and *Streptococcus mutans* counts, and increased food retention on teeth.

Drugs inhaled are often acidic and can lower salivary pH below the crucial point of 5.5 for as long as 30 minutes, demineralizing enamel and accelerating the progression of dental caries and erosion, particularly in situations when salivary flow and buffering capacity are inadequate. By stimulating β 2 adrenoreceptors, inhaled β -mimetics may also contribute to erosive lesions of teeth through a separate mechanism, resulting in lower oesophageal sphincter relaxation. (3) Drugs ingested can reduce salivary flow rate and buffering capacity, which accelerates the degradation of teeth. (3) Compared to other inhalers that do not contain such sugars, inhalation medications in the form of dry powder frequently contain extra lactose, which can significantly lower salivary pH levels. It has been proposed that this could have a significant role in the demineralization of enamel and the growth of cariogenic bacteria. Nonetheless, several authors discovered that there was no meaningful correlation between the occurrence of caries and lactose in inhalation medications. (13)

4.3. Candidiasis

The widespread immunosuppressive and anti-inflammatory effects of steroids, which result in decreased salivary flow rate and increased salivary glucose concentration, are thought to be the cause of the high prevalence of candidiasis among inhaler users. (3,9) When using DPIs and larger dosages of a medication, the risk is greatest. There is uncertainty regarding the precise mechanism by which ICS facilitates the advancement of oral candidiasis. Since only 10–20% of a dose is delivered, depending on whether the device reaches the lungs, local corticoid effects on the oral mucosa are thought to be most likely. The local immune response to *Candida* spp. in the oral cavity may be hampered by corticoids' immunosuppressive and anti-inflammatory qualities. Another explanation could be the observed alterations in saliva, such as an increase in glucose and a contemporaneous decrease in immunoglobulin A excretion. When lactose is employed as a carrier in DPIs, it can indirectly promote fungal growth by increasing salivary glucose excretion and corticoid uptake in the oropharyngeal area. (12)

4.4. Gingivitis and Periodontitis

Periodontium was affected in severe cases like gingivitis/gingival enlargement/ periodontitis, which was due to a decrease in salivary protection owing to the reduction in salivary flow and concentration of secretory immunoglobulin A (IgA) or dehydration of alveolar mucosa due to mouth breathing that causes alteration of immune response and increase concentration of immunoglobulin E (IgE) in the gingival tissue, which leads to higher incidence of calculus due to increased levels of calcium and phosphorus in the saliva and also causes decrease in bone mineral density associated with inhaled corticosteroids. (3) Corticosteroids were proven to enhance bone resorption and, in this way, can promote periodontitis in asthmatic patients, and these results were reported to be most pronounced in the case of chronic and general administration.

5. Management

5.1. Communication and education on the correct use of inhalers

Efforts are needed to prevent oral diseases in COPD patients, especially for those who regularly use inhalers to treat COPD. Health workers, especially pediatricians, pulmonologists, and dentists, must be more aware of COPD patients' dental and oral health conditions. (14) Proper knowledge and understanding of the relationship between COPD and oral disease is also required. Education that can be given to COPD patients includes education on the dangers of smoking and their relationship with oral health, promotion of dental health, routine dental and oral care for COPD patients, education on the correct selection and use of inhalers, sugar-restricted diet patterns, and regular oral pH measurements. (15)

For patients who use inhalers, education can be provided in the form of side effects of inhalation therapy on the oral cavity, education about checking dental health every six months, education about how to maintain oral health at home with proper tooth-brushing techniques and the use of dental floss once daily or more. Additionally, instructions should include rinse mouth with water or neutral-pH mouthwash containing 0.05% sodium fluoride after using inhaler, especially before bed. Using an antimicrobial mouthwash, such as mouth rinses with 0.2% chlorhexidine, is also advised. Dietary changes that are advised include consuming more foods high in fiber, cutting back on refined carbs, and consuming less snacks or beverages that contain sugar in between main meals. Nuts, cheese, fruit, and vegetables are examples of foods with low cariogenic potential. Artificial sweeteners can be made with sugar replacements such as sorbitol, aspartame, saccharin, and xylitol. In addition, patients are counseled to drink extra water. Applying fluoride gels, varnishes, and pit and fissure sealants can help prevent dental cavities. (3)

5.2. Avoid risk factors

In managing oral diseases in COPD, efforts are needed for early diagnosis of oral disorders, specific dental therapy, and comprehensive management of COPD. Early diagnosis through routine oral dental examinations is required in all COPD patients. A clinical pathway is needed in COPD primary care that is integrated with dental and oral health, which includes efforts to prevent oral disease in COPD, early diagnosis, and comprehensive management.

5.3. Management of chronic airway diseases and systemic diseases

The treatment of COPD and asthma involves both pharmaceutical and non-pharmacological components. Early identification and treatment of coexisting ailments, such as diabetes, heart issues, and mental health issues. This is significant since it may impact how COPD and asthma develop as well as raise the risk of oral and dental illnesses.

5.4. Maintain Oral Health

For patients using inhaler therapy, local preventive dental care techniques and collaboration between pulmonologists and dentists may significantly enhance oral health. Due to the high expense of therapies that may not be required if sufficient preventive measures were followed, prevention, early diagnosis of various disorders, and routine maintenance of oral health are also crucial. Programs for dental health care and prevention can lead to improvements. (13,15)

Dental caries prophylaxis includes topical fluoride application, pit and fissure sealants, and dietary change. It may be advantageous for patients receiving inhalation therapy. Fluoride formulations are offered in two forms: toothpaste and mouth rinse for patients and gels and varnishes for use in offices. The quality of the mineralized tooth tissues is enhanced by fluoride. It takes on the roles of the hydroxyl ions in the hydroxyapatite crystal lattice structure of dental enamel. Because of its increased acid resistance, the resultant chemical, fluorapatite, can be used to prevent tooth erosion and caries. Regular dental checkups should be performed at intervals of no more than six months. Restricting refined carbs and sugary foods is the recommended dietary intervention. It's crucial to rinse patients mouth out with water after inhaling before going to bed. Xerostomia may develop if there is a growing subjective perception of dry mouth. The first suggested actions in such a case are to minimize ethanol beverages and strong flavors, add a moist, sugar-free diet, and sip still, non-carbonated water frequently. The use of pharmaceutical medications that increase salivation and artificial saliva replacements (sprays, lozenges, and mouth rinses) may be required if the issue is not remedied. (12)

6. Conclusion

Inhalation therapy is the main therapy in the management of chronic airway diseases, especially asthma and COPD. In terms of the pharmacokinetics of inhalation therapy, only 15-20% of inhaled drugs enter the respiratory tract; the remaining 80% will be deposited in the oral cavity, which can increase the risk of side effects in the oral cavity. This risk will be higher if education and intervention are not carried out regarding the appropriate use of inhalation therapy and assessment and routine oral health care for asthma and COPD sufferers who regularly use inhalation therapy. Health workers, especially pulmonologists and dentists, have an important role in educating and managing asthma and COPD sufferers regarding dental and oral health due to the use of inhaler therapy to reduce the risk of side effects and improve the patient's quality of life.

Compliance with ethical standards

Acknowledgments

The author would like to express gratitude to Faculty of Medicine Universitas Udayana.

Disclosure of conflict of interest

The author declares no conflicts of interest.

References

- [1] Salvi S, Shevade M, Hadda V, Aggarwal A, Apte K, Barne M, et al. A Practical Guide on the Use of Inhaler Devices for Asthma and COPD [Internet]. Journal of The Association of Physicians of India ■ Published on 1 st of Every Month. 2021. Available from: <https://www.researchgate.net/publication/350088942>
- [2] Suthar J, Patel ZA, Shelat B. Assessment of Inhalation Techniques in COPD and Asthma Patients using Metered Dose Inhaler and Rota-haler. Indian Journal of Pharmacy Practice. 2019 Sep 19;12(4):217–24.
- [3] Ayinampudi B, Gannepalli A, Pacha V, Kumar J, Khaled S, Naveed M. Association between oral manifestations and inhaler use in asthmatic and chronic obstructive pulmonary disease patients. J Dr NTR Univ Health Sci. 2016;5(1):17.
- [4] Gupta V, Gupta A, Kudiyar N. Original Research Assessment of association between oral manifestations and inhaler use in asthmatic and chronic obstructive pulmonary disease patients. Journal of Advanced Medical and Dental Sciences Research [Vol 10]Issue [Internet]. 2022;5. Available from: www.jamdsr.com
- [5] Sim KY, Jang YS, Yoon NY, Park EC. Association between Asthma and Oral Health Symptoms in Adolescents. Int J Environ Res Public Health. 2023 Feb 1;20(4).
- [6] Pleasants RA, Hess DR. Aerosol delivery devices for obstructive lung diseases. Respir Care. 2018 Jun 1;63(6):708–33.
- [7] Pepper AN, Cooke A, Livingston L, Lockey RF. Asthma and chronic obstructive pulmonary disease inhalers: Techniques for proper use. Allergy Asthma Proc. 2016 Jul 1;37(4):279–90.
- [8] Hagemeyer L, van Koningsbruggen-Rietschel S, Matthes S, Rietschel E, Randerath W. From the infant to the geriatric patient—Strategies for inhalation therapy in asthma and chronic obstructive pulmonary disease. Vol. 17, Clinical Respiratory Journal. John Wiley and Sons Inc; 2023. p. 487–98.
- [9] Chhabra K, Sood S, Sharma N, Singh A, Nigam S. Dental management of pediatric patients with bronchial asthma. Vol. 14, International Journal of Clinical Pediatric Dentistry. Jaypee Brothers Medical Publishers (P) Ltd; 2021. p. 715–8.
- [10] Pacheco-Quito EM, Jaramillo J, Sarmiento-Ordoñez J, Cuenca-León K. Drugs Prescribed for Asthma and Their Adverse Effects on Dental Health. Vol. 11, Dentistry Journal. MDPI; 2023.
- [11] Gani F, Caminati M, Bellavia F, Baroso A, Faccioni P, Pancera P, et al. Oral health in asthmatic patients: a review: Asthma and its therapy may impact on oral health. Vol. 18, Clinical and Molecular Allergy. BioMed Central Ltd; 2020.
- [12] Pasternak M. The dental considerations of outpatient inhalation therapy. Pomeranian J Life Sci. 2023;69(3):52–9.

- [13] Bozejac BV, Stojšin I, Đurić M, Zvezdin B, Brkanić T, Budišin E, et al. Impact of inhalation therapy on the incidence of carious lesions in patients with asthma and COPD. *Journal of Applied Oral Science*. 2017 Sep 1;25(5):506–14.
- [14] Usmani OS.

Choosing the right inhaler for your asthma or COPD patient

. *Ther Clin Risk Manag*. 2019 Mar;Volume 15:461–72.
- [15] Raj R, Manu MK, Prakash PY, Singhal DK, Acharya S. The effect of 6 months or longer duration of chronic obstructive respiratory disease medication on the oral health parameters of adults. *Special Care in Dentistry*. 2018 May 1;38(3):133–8