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The dental considerations of outpatient inhalation therapy

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ABSTRACT

Inhalation is one of the routes of drug administration used in therapy. Medicines are dispersed via an aerosol spray, mist, powder or vapour that patients breathe into their airways. Depending on the intrapulmonary behaviour of each molecule of the inhaled agent, the prevailing effect obtained may be local or general. Inhaled therapy, due to its local effect, is a cornerstone of obstructive pulmonary diseases like asthma and chronic obstructive pulmonary disease (COPD), while the general effects of vaporised medical cannabis support its use in other indications (e.g. epilepsy, insomnia, spastic pain). Regardless of the purpose of use, an inhaled drug passes through the oropharynx and a major portion of its dose remains there. This paper focuses on the impact of inhaled therapy on the oral cavity, highlighting the issues important for dental practitioners. The most common indications for inhaled therapy are presented together with the devices used for this route of administration and the drugs employed in outpatient care. Particular attention is paid to oral side effects of inhaled medicines and their pathophysiology. The advisable measures for dental care of patients using inhaled therapy are presented.

Keywords: inhaled therapy; asthma; chronic obstructive pulmonary disease (COPD); medical cannabis; oral health.

INTRODUCTION

Humanity has been inhaling substances both for medical and recreational purposes for millennia, notably leading to cultural practices like tobacco and opium smoking. Throughout history, the concepts of pulmonary application in medicine, including inhalation devices and drug formulations, have been continuously developed [1]. The aerosolised administration of medications allows for direct access to the lungs. Depending on the behaviour of each molecule after inhalation, a local pulmonary effect or a systemic action can be achieved; the latter is made possible by the extensive vascular network of the lungs [2].

The most frequent indication for the use of inhalation therapy is the treatment of obstructive pulmonary diseases, especially bronchial asthma and chronic obstructive pulmonary disease (COPD) [3]. The beneficial local effects of inhalation therapy have made it the preferred strategy in these conditions.

In recent years, the systemic effects of cannabis have encouraged the integration of medical marijuana into medical practice. Indications for medical marijuana vary, with the most common including epilepsy, chronic pain, muscle spasticity, sleep problems and appetite issues [4]. Although cannabis-based products for therapeutic use may also be administered orally, the lower bioavailability and delayed onset of action after ingestion support the choice of inhalation [5]. The vaporisation of medical marijuana is the recommended route of administration, while smoking is currently discouraged due to its pronounced side effects and carcinogenicity [6, 7].

Regardless of the indication for use, a significant portion of the inhaled drug remains in the oral cavity and oropharynx, which has implications for oral health [8]. The aim of this paper is to focus on the impact of inhaled therapy on the oral cavity exerted by inhalation therapy when used in outpatient care, with particular attention paid to its oral side effects, pathophysiology, management and prevention.

DEVICES USED IN INHALATION THERAPY

Common to all forms of inhalation therapy and delivery systems is the need to generate an optimal "respirable dose" (<0.5 µm) of a therapeutic agent [3]. Devices used to deliver therapeutic agents as aerosols are based on 1 of 4 platforms: nebulisers, metered-dose inhalers (MDIs, sometimes referred to as "pressurised metered-dose inhalers" – pMDIs), dry powder inhalers (DPIs), and vaporisers [9, 10].

Nebulisers are traditionally used for the acute care of non-ambulatory patients. Solutions and suspensions can be nebulised by ultrasonics or air jet delivery through a mouthpiece, ventilation mask or tracheostomy [3]. In outpatient therapy for pulmonary obstructive diseases, nebulisers are still in use, though not as frequently as other systems. Compared to other systems like MDIs and DPIs, effective drug delivery with conventional pneumatic nebulisers requires less intensive patient training. Moreover, newer nebulisers available are more portable and efficient than traditional jet nebulisers [11]. Devices of a newer class are sometimes referred to as small volume nebulisers, highlighting the difference from older

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types of nebulisers [12]. Nebulisation as a route of administration may be used, for example, in exacerbations of COPD [11].

Metered-dose inhalers are versatile, multi-dose inhalers, where the drug is formulated under pressure in a propellant mix, with the medicine being expelled in a metered volume as the propellant evaporates [3]. Inhalation can be aided by spacers or valved holding chambers attached to the device. A spacer is a tube or extension device placed between the patient and the MDI, while an MDI with a valved holding chamber has a one-way valve at the mouthpiece end to allow inhalation and prevent exhalation into the chamber [9].

Dry powder inhalers, unlike the previous types of inhalational devices, do not use the drug in the form of a solution or suspension. The compacted powder of a medicine with a carrier, usually lactose, is broken into fine particles by the force of inhalation, a process known as de-agglomeration [13]. Dry powder inhalers typically fall into 2 types: single-dose and multi-dose. Commercially available multi-dose inhalers can be either "passive" or "active". In "passive" DPIs, the energy is provided by the patient, and the powder is dispersed in the stream of inspired air, while in "active" DPIs, the energy comes from the device [3].

Vaporisers are used in inhalation therapy for cannabis administration. These electronic devices heat cannabis formulations (oils, wax, or plant material) without combustion. The process generates an aerosolised mixture of water vapour and compounds derived from the thermal decomposition of marijuana. Heating results in the decarboxylation of the acidic cannabinoids, including Δ-9-tetrahydrocannabinolic acid and cannabichromenic acid, which are converted into Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD), respectively. Since vaping utilizes lower temperatures compared to smoking, this method of administration releases higher concentrations of active ingredients while reducing exposure to carcinogens, making it a recommended approach in therapy [10].

The types of devices used in outpatient inhalation therapy are presented in Table 1.

TABLE 1. Inhalation therapy devices used in outpatient care

Device type	How it works
Nebulisers, SVNs	a drug solution is nebulised in fine vapour by means of ultrasonics or an air jet
MDIs*	a drug solution or suspension is formulated in a propellant mix under pressure, with the medicine being expelled (through a valve) in a metered volume from the volatile mixture as the propellant evaporates
DPIs	the compacted powder of a medicine is broken into fine particles with the force of inhalation in the process called de-agglomeration, which are then inhaled
Vaporisers	formulations such as oil, wax or plant material are heated without combustion, releasing active agents into a vapour that is inhaled by the patient

DPIs – dry powder inhalers; MDIs – metered-dose inhalers; SVNs – small volume nebulisers
* MDIs are also referred to as pressurised pMDIs.

MOST COMMON DRUGS USED IN OUTPATIENT INHALATION THERAPY AND THEIR MECHANISM OF ACTION

Agents used in inhaled therapy, sharing the same route of administration, differ in the mechanism of their therapeutic action. The most popular include β2 adrenoreceptor agonists, muscarinic 3 cholinergic receptor antagonists, corticoids – all exceeding local action desirable in pulmonary obstructive diseases – and general acting cannabinoids.

Beta 2 receptor agonists dilate the airways by stimulating β2-adrenergic receptors. Furthermore, stimulation of the same type of receptors present on mast cells blocks histamine release from mastocytes [14]. According to the time of effect obtained, the drugs of this class can be divided into 3 main groups: short-acting β2-agonists (SABAs), long-acting β2-agonists (LABAs) and ultra long-acting β2-agonists (ultra-LABAs). The use of agents from the first group is beneficial for rapid symptomatic alleviation and bronchospasm prevention, being considered as a rescue medicine. The longer half-life of the second group allows for administration twice a day, while ultra-LABAs require a single inhalation a day. Currently, monotherapy with SABAs, LABAs and ultra-LABAs for asthma is advised against, as it increases the risk of severe medication adverse events. The preferred strategy in asthma therapy is the use of an LABA combined with a corticoid [15].

Muscarinic 3 receptor antagonists dilate the airways and decrease bronchial secretion by inhibiting muscarinic cholinergic receptors [16]. Concerns for potential side effects, mostly associated with the additional blockage of muscarinic 2 receptors, limit the use of higher doses. The use of lower doses, in turn, restricts the bronchodilation obtained [17]. Similar to betamimetics, inhalational cholinolytics can be divided according to the time of their action. Short-acting antimuscarinic agents (SAMAs) may be used in the initial stages of COPD. Long-acting antimuscarinic agents (LAMAs) are used in the therapy of COPD, particularly in combination with LABAs and ultra-LABAs [18]. Due to the amount of time needed for bronchodilation after inhalation (usually exceeding 15 min), neither SAMAs nor LAMAs can be used as rescue agents in case of sudden bronchoconstriction [16].

Glucocorticoids exhibit potent anti-inflammatory action. These agents block the first enzyme in the prostaglandin and leukotriene synthesis pathways and also hamper proinflammatory cytokine production and release. Although inhaled corticoids (ICS) are not endowed with broncho-dilatating properties, they enhance the action of betamimetics and are used in compound formulations [16]. Especially, the combination of LABA/ICS is more efficient in decreasing the risk of asthma exacerbations and the need for systemic steroids [15].

If there is such an indication, drugs from all 3 groups mentioned above may be administered together – an example of such a strategy is the combined formulation of a LAMA glycopyrronium bromide, an ultra-LABA indacaterol, and the synthetic steroid mometasone furoate, which can be used in asthma as a once-a-day inhalation [19]. Although LABA/LAMA

combined therapy is the strategy of choice in COPD treatment, triple therapy may be prescribed for patients with significant eosinophilia or frequent exacerbations of the disease [20].

Cannabis-based products for medicinal use in inhalation therapy contain cannabinoids derived from the cannabis plant. In order to distinguish plant-derived cannabinoids from synthetic cannabinoids and endogenous counterparts (endocannabinoids) the term 'phyto-cannabinoids' is generally used [21]. The most important ones are THC and CBD, and in clinical practice, the combination of both agents is usually employed [6]. Δ9-tetrahydrocannabinol and CBD have contrasting mechanisms of action on the endocannabinoid system, which is widely expressed in the mammalian central and peripheral nervous systems. These actions may account for their complex therapeutic effects [6].

The most common drugs used in outpatient inhalation therapy currently available in Poland, along with their characteristics, are summarised in Table 2.

ORAL SIDE EFFECTS OF INHALATIONAL THERAPY – INSIGHTS INTO PATHOPHYSIOLOGY

Regardless of the indication for use, a major portion of the inhaled dose of the drug remains in the oral cavity and oropharynx. Active agents may influence regulatory mechanisms important for oral cavity homeostasis. Properties of formulations, together with non-active ingredients, are also not indifferent to oral health. Oral side effects of outpatient inhalation therapy:

- xerostomia (dry mouth),
- dental caries,
- erosions,
- fungal infections (most often oral candidiasis),
- taste disturbances,
- halitosis (bad breath),
- gingivitis and periodontitis,
- oral mucosal lesions.

Xerostomia

Inhalational therapeutics can affect salivary secretion, contributing to xerostomia through different mechanisms [8]. Under physiological conditions, salivary secretion is a finely orchestrated process regulated by both cholinergic and adrenergic transmission [22]. Dry mouth is a well-known side effect of drugs with cholinolytic properties. In the case of M3 receptor antagonists, this observation is even more valid, as stimulation of the mentioned receptor type is responsible not only for bronchial constriction and mucous secretion but also for salivary production [23]. Therefore, even local use of these agents via inhalation was reported to decrease salivary production [24].

TABLE 2. The most common drugs used in outpatient inhalation therapy currently available in Poland

Therapeutic effect obtained (local/general)	Mechanism and place of therapeutic action	Drug class	Drugs available in Poland	Formulation
Local	β-2-adrenoreceptor stimulation in airways	SABAs	fenoterol hydrobromide,	aerosol
			salbutamol (albuterol) sulphate	aerosol, dry powder, nebulisation solution
		LABAs	formoterol (eformoterol) fumarate dihydrate	aerosol, dry powder
			salmeterol	aerosol, dry powder
		ultra-LABAs	indacaterol, ondacaterol, vilanterol	currently only in compound formulations
	M3 cholinergic receptor antagonism in airways	SAMAs	ipratropium bromide	aerosol, nebulisation solution
		LAMAs	glycopyrronium (glycopyrrolate) bromide	aerosol, dry powder
			tiotropium bromide	aerosol, dry powder
			umeclidinium bromide	dry powder
	anti-inflammatory action in airways	ICS	beclometasone dipropiate	aerosol
			budesonide	dry powder, nebulisation solution
			fluticasone	currently only in compound formulations
			ciclesonide*	aerosol
			mometasone furoate	currently only in compound formulations

TABLE 2. The most common drugs used in outpatient inhalation therapy currently available in Poland

Therapeutic effect obtained (local/ general)	Mechanism and place of therapeutic action	Drug class	Drugs available in Poland	Formulation
Local	mixed compound formulations – in airways	LABA/ICS	beclomethasone + formoterol	aerosol, dry powder
			budesonide + formoterol	aerosol, dry powder
			fluticasone propionate + salmeterol	aerosol, dry powder
		ultra-LABA/ICS	indacaterol + mometasone furoate	dry powder
		SABA/SAMA	fenoterol hydrobromide + ipratiopium bromide	aerosol, nebulisation solution
			ipratropium bromide + salbutamol sulphate	nebulisation solution
		ultra-LABA/LAMA	glycopyrronium (glycopyrrolate) bromide + indacaterol	dry powder
			tiotropium bromide + olodaterol	aerosol, dry powder
			umeclidinium bromide + vilanterol	dry powder
			budesonide + formoterol fumarate dihydrate + glycopyrronium (glycopyrrolate) bromide	aerosol
		LAMA/ultra-LABA/ICS	glycopyrronium (glycopyrrolate) bromide + indacaterol + mometasone furoate	dry powder
			umeclidinium bromide + vilanterol + fluticasone furoate	dry powder
General	cannabinoid receptors stimulation within central and peripheral nervous system	phyto-cannabinoids	medical marijuana (the most important active ingredients Δ-9-THC and CBD)	plant material – dried female inflorescence of a *Cannabis sativa* L.

Δ-9-THC – delta-9-tetrahydrocannabinol; CBD – cannabidiol; ICS – inhaled corticoids; LABAs – long-acting beta 2 agonists; LAMAs – long-acting muscarinic antagonists; SABAs – short-acting beta 2 agonists; SAMAs – short-acting muscarinic antagonists; ultra-LABAs – ultralong-acting beta 2 agonists
* Ciclesonide is a pro-drug that is converted into an active product by the lung esterase enzymes.

Although β-adrenoreceptor stimulation is responsible for salivary proteins secretion, Ryberg et al. were first to observe that chronic use of β-2-mimetics inhalations brought both quantitative and qualitative changes in saliva secretion in asthmatic patients [22, 25].

Inhaled corticoids were also associated with xerostomia in asthmatic patients [8]. However, the exact mechanism remains obscure, and the question of the impact of other factors, including the disease itself, is still raised [26].

Cannabis abuse was reported to pose a detrimental influence on oral health [27]. Side effects of marijuana affecting the oral cavity were described well in literature; however, one should bear in mind, that on average, most of the findings reported concern people using it for recreational purposes, usually smoking in high amounts exceeding therapeutic doses [21]. Nevertheless, vaping for medical indications may still result in xerostomia. Both types of cannabinoid receptors – CB1 and CB2 – are present in the peripheral acinar cells, ductal system, and nerve endings in salivary glands and their stimulation limits saliva production [28].

Xerostomia is not only a troublesome condition, lowering the patient's quality of life, but it may contribute further to other ailments, fostering their development.

Dental caries

Dental caries is the most prevalent chronic disease worldwide. It develops through gradual complex biological interactions between acidogenic bacteria, fermentable carbohydrates and host factors such as teeth and saliva [29]. In physiological conditions, saliva excreted in the proper amount and composition plays an important role in preventing dental caries [22]. Saliva reduces the cariogenic potential of dental plaque by self-cleaning the tooth surface, regulating the pH value through its buffering capacity and controlling oral microflora [29]. Decreased salivary flow increases susceptibility to dental caries. Especially in patients receiving inhaled β-mimetics, salivary output was reduced along with protein components, responsible, among others, for the antimicrobial properties of saliva [30]. Subsequent to xerostomia, changes in the oral microbiota reported in patients on inhaled therapy, include an increase in *Streptococcus mutans* and *Lactobacillus* spp., significantly contributing to dental caries development and progression [8, 31]. The bitter taste of medicines used in inhaled therapy of asthma and COPD is the reason for adding fermentable carbohydrates, which are substrates for cariogenic bacteria [32]. Cannabis use has been often connected with dental caries [21, 27]. While in the case of recreational use and abuse, poor oral hygiene is an important factor contributing to dental caries in cannabis

smokers, the risk of dental caries still exists in patients using medical marijuana due to decreased salivation and well-known orexigenic effects of cannabinoids, frequently manifesting in carbohydrate craving [33].

Erosions

Inhaled drugs are usually acidic and can decrease salivary pH below the critical value of 5.5 for up to half an hour, resulting in enamel demineralisation, contributing to both dental caries and erosion progression, especially when salivary flow and buffering capacity are deficient [34]. The effect was most pronounced in the case of DPIs [35]. Inhaled β-mimetics may contribute to erosive lesions of teeth in a different mechanism too, causing lower oesophageal sphincter relaxation by stimulating β2 adrenoreceptors [36]. Oral dryness may encourage patients to quench the first with fizzy drinks, many of which are acidic and can contribute to further enamel damage [32].

Fungal infections

Oral candidiasis is a well-known side effect of inhaled corticoid therapy [16]. The risk is most pronounced with higher doses of a drug and DPIs use [37]. The exact mechanism by which ICS aid oral candidiasis progress has not been clearly established. As, depending on the device, only 10–20% of a dose administered reaches the lungs, local corticoid effects on oral mucosa are suspected to be most probable. Immunosuppressive and anti-inflammatory properties of corticoids may hamper the local immune response towards *Candida* spp. in the oral cavity [38]. Observed changes in saliva, including glucose increase with concurrent decrease of excreted immunoglobulin A, form another possible explanation [39]. Last but not least, lactose used as a carrier in DPIs can indirectly favour fungal growth, enhancing corticoid uptake in the oropharyngeal region as well as intensifying salivary glucose excretion [38].

Other inhaled drugs used in pulmonary obstructive diseases can contribute to the progress of this opportunistic oral infection, especially if they decrease saliva excretion and contain carbohydrates [8]. Also, cannabis use was associated with the risk of oral candidiasis, by providing favourable conditions for fungal growth in the oral cavity due to lowering saliva excretion, increasing carbohydrate intake and elevating the level of carbon dioxide [27].

Taste disturbances

Xerostomia contributes to changes in taste through incomplete food solubilization and hampering the transport of taste molecules to the taste buds [8]. Research conducted by Arias-Guillen et al. found that asthmatic children using inhaled β-mimetics and corticoids required higher concentrations of substances to perceive sweet and bitter tastes compared to their healthy counterparts [40]. The contribution of corticoids to taste disorders has been reported in the literature, and a suggested mechanism is the direct interaction of the drugs and their metabolites with oral mucosa [41]. Inhaled medications may also indirectly favour taste disturbance by fostering the development of oral candidiasis [42].

Cannabinoid receptors are present in the human tongue, including epithelial cells adjacent to taste buds [21]. Cannabinoid receptor 1 stimulation was reported to selectively enhance sweet taste sensitivity [43].

Halitosis

Bad breath (halitosis) usually is secondary to the aforementioned side effects, especially xerostomia, oral candidiasis and gastro-oesophageal reflux [44]. Observed changes in the microflora of oral cavity following inhalation therapy can also contribute to oral odour [8].

Gingivitis and periodontitis

The risk of gingivitis and periodontitis may be elevated in patients using inhalational therapy [45]. The first condition is reversible and, in most cases, results from plaque accumulation, while the second is an irreversible disease characterised by pathologic loss of the periodontal ligament and alveolar bone [46]. Proposed mechanisms linking inhalational therapy with gingivitis and subsequent periodontitis focus on changes in saliva, namely, decreasing its flow and reducing the protein component [8]. Corticoids 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 [47]. Inhaled corticoids, although used locally, are also related to a decrease in alveolar bone mineral density [48].

Despite high doses of phyto-cannabinoids being reported to suppress the growth of *Porphyromonas gingivalis* and *Filifactor alocis*, which are 2 periopathogens important in periodontitis development and progress, chronic cannabis use was suggested to be a potential risk factor for periodontal disease [49, 50]. The question of whether medical cannabis vaporisation poses a similar threat to the periodontal health of patients remains open and is still being discussed, but such a side effect cannot be excluded [21, 51].

Oral mucosa lesions

Mucosal lesions are another oral side effect that can trouble patients receiving inhalational treatment [8]. Usually, lesions are located in the dorsal part of the tongue, palatal and buccal mucosa – areas exposed to the medication given [8, 52]. Findings differ in severity and may present as areas of hyperaemia, plaque-like changes or even ulcerations [52, 53]. The mechanism for the formation of the lesions is complex. Oral mucosa is affected directly both by agents inhaled and the process of administration itself, with a crucial role of negative pressure formed by inhalational devices [52]. Among factors indirectly aiding the development of mucosal lesions, salivary output reduction plays an important role as it is related to all drugs discussed [8, 27].

The vasodilatation due to β2 adrenoreceptor stimulation is a possible explanation of hyperaemia [53]. Corticoids are also known to hamper collagen synthesis and suppress the immune response which furthermore hampers oral wound healing and fosters the development of the aforementioned

lesions [52, 54]. Defective collagen, in addition, results in blood vessel fragility [54].

DENTAL CARE OF PATIENTS USING INHALATION THERAPY

Preventive strategies play a pivotal role in the dental management of patients using inhaled therapeutics [8]. The advisable measures for the use of dental care in patients using inhaled therapy are presented in Table 3.

Dental practitioners should educate patients about the potential side effects of inhalation therapy. Contact with the attending physician is, as always, advisable and allows for addressing the oral health issues of this special group of patients in the best way possible. Both general and dental considerations are important in the choice of a device used [55]. Devices with a spacer or valved chamber, due to a lag time in delivery, reduce the amount of medicine left in the oral cavity and oropharynx; therefore, they are recommended [8]. In the case of medical cannabis, prescribed plant formulations should be vaporised, not smoked [6, 7].

The simplest measure that should be employed is rinsing the mouth with water adequately after inhalation, especially before bedtime. Oral hygiene practices, including proper teeth brushing after every meal and dental flossing at least once a day, need to be implemented. However, patients should be instructed not to brush their teeth immediately after inhalation due to a pronounced risk of enamel damage [32]. This consideration is notably important in the case of DPIs, which have the most acidic properties among inhalation formulations [35]. Mouth rinses are also valuable; however, patients should choose ethanol-free formulations [8]. Another simple measure that ought to be employed is tongue scraping. Tongue scraping is a key element of oral hygiene that also prevents the development of halitosis. Tongue cleaning should be carried out using a tongue scraper applied gently with low force, at least once a day, after toothbrushing. The use of a regular toothbrush for tongue hygiene is advised against as it can be injurious, damaging the tongue surface. The same applies even more to power toothbrushes [56].

Dental caries prophylaxis, which may be beneficial for patients on inhalation therapy, includes pit and fissure sealants, topical fluoride administration and dietary modification. Fluoride formulations are available in both forms applicable for in-office use (gels and varnishes) and for patient use (toothpaste, mouth rinse) [32]. Fluoride improves the quality of mineralised tooth tissues. It replaces and assumes the positions of the hydroxyl ions in the crystal lattice structure of hydroxyapatite in tooth enamel. The resulting compound, fluorapatite, is more resistant to acidic conditions, making it useful in the prophylaxis of dental caries and erosion [57]. Regular dental check-ups with intervals no longer than 6 months are recommended. The advised dietary intervention consists of restricting sugary foods and snacks between meals, limiting refined carbohydrates and choosing foods with

TABLE 3. Dental care of patients using inhaled therapeutics

Choice of a device	• choice of devices with spacers or valved chambers is advised whenever possible (for pulmonary indications), • prescribed plant material should be vaporised with the use of a dedicated device, not smoked (medical cannabis therapy)
Oral hygiene	• mouth rinsing with water after inhalation (especially important before bedtime), • teeth brushing with fluoridated toothpaste after every meal but not immediately after inhalation (crucial in the case of acidic formulations – DPIs), • dental flossing at least once a day, • tongue scraping (mechanical tongue cleaning) with a manual scraper, • mouth rinses without ethanol
Dietary intervention	• restriction of sugary foods and snacks between meals, • limitation of refined carbohydrates, • choice of food with lower cariogenic potential, • alcoholic, sugary and acidic beverages are advised against
Professional dental prophylaxis	• regular check-ups (intervals no longer than 6 months), • pit and fissure sealants, • fluoride prophylaxis – gels, varnishes
In-office dental care	• xerostomia – first step: frequent sipping of a still, non-carbonated water, moist diet with strong flavourings limitation; second step: artificial saliva substitutes; third step: sialagogues after attending physician consultation (attention: the use of pilocarpine and cevimeline require risk assessment in patients with pulmonary obstructive diseases), • dental caries – as in other patients*, • erosions – as in other patients; in patients using beta-mimetics, the risk of GORD is present – consultation with the attending physician and referral to a gastroenterologist, • oral candidiasis – antifungal therapy based on mycological identification, dietary intervention, mouth rinse with sodium bicarbonate, PDT, • gingivitis – oral hygiene regimen, professional plaque control (SRP), • periodontitis – professional periodontal care

DPIs – dry powder inhalers; GORD – gastro-oesophageal reflux disease; PDT – photodynamic therapy; SRP – scaling and root planing
* Rubber dam use in patients with COPD is not preferred. If a rubber dam is essential in the procedure, supplementation with oxygen in low concentrations through a nasal tube is advisable.

lower cariogenic potential. The choice of drinks is also important, requiring attention, particularly considering the ability of all agents described to lower saliva excretion. Furthermore, the habit of mouth breathing, observed in patients with obstructive pulmonary diseases, is also a factor contributing to mouth dryness, in addition to pharmacotherapy [58]. Patients should be encouraged to quench their thirst with water, avoiding sugary, acidic and alcoholic beverages. Carbonated drinks, in particular, pose a high risk to the oral health of patients using inhaled therapy due to the doubly damaging effects of both low pH and often high sugar content [32]. If the subjective impression of dry mouth is increasing, there is a risk of developing xerostomia. Frequent sipping of still, non-carbonated water, adding a moist, sugar-free diet, and limiting ethanol beverages and strong flavourings are the first recommended steps in such a situation. In cases where the problem is not resolved, the use of artificial saliva substitutes (sprays, lozenges, mouth rinses) and pharmacological agents that improve salivation may be needed [59]. Implementation of the latter, usually pilocarpine or the more selective cevimeline, requires attending physician consultation, particularly in patients with obstructive pulmonary diseases. The mechanism of action of the 2 mentioned sialagogues (agents that enhance salivation) is a result of stimulation of the M3 receptor in salivary glands. The same process, however, is highly undesirable in the airways; therefore, risk assessment, the choice of a dose and formulation, or consideration of a different strategy are needed [60]. Other oral health conditions that may arise in patients using inhaled therapeutics similarly require prompt action. Dental caries management, in general, is the same as in other populations. However, the use of a rubber dam in procedures may be unacceptable in patients with COPD. This is not related to the medication used but to the disease itself, as the rubber dam further compromises the airways. If a rubber dam is absolutely necessary (e.g. root canal treatment), administration of low concentrations of supplemental oxygen via a nasal cannula is a prudent solution [61]. Erosions in patients using beta-mimetics can be a symptom of a gastro-oesophageal reflux disease resulting from lower oesophageal sphincter relaxation due to β2 receptor stimulation. In such a situation, consultation with the attending physician and referral of the patients to a gastroenterologist is recommended [8]. In the case of oral candidiasis, management is based on a correct diagnosis, where clinical findings are supported with antifungal pharmacotherapy based on mycological isolation and identification of drug sensitivity [62]. Additional strategies in candidiasis treatment include dietary intervention – restriction of carbohydrate intake, use of sodium bicarbonate rinse, photodynamic therapy and probiotics [63, 64]. As dental plaque accumulation plays a crucial role in gingivitis, the management of this entity requires an oral hygiene regimen together with scaling and root planing, a professional in-office procedure for removing dental calculus accumulation [65]. Developing periodontitis demands from a dental practitioner prompt diagnosis. In this irreversible condition, measures used in gingivitis management are insufficient, and patients need to be referred to professional care from a periodontologist [46].

SUMMARY

Dental practitioners must consider both the medications used and the method of administration when reviewing patients' medical histories. Inhaled drugs, in particular, can have a significant impact on oral health as a substantial portion of the dose remains in the oropharynx. It is crucial for dental practitioners to be knowledgeable about the potential side effects of inhaled therapy in outpatient care and address them correctly through proactive prophylaxis and prompt management when these side effects occur.

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