

Harmful consequences of specific substances on the oral health

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Abstract

Numerous substances may have an adverse influence on the oral region by virtue of their potentially harmful effects. Dental practitioners are often the first to see these effects in the head and neck region. Knowledge of the damaging consequences of agents such as alcohol, tobacco, areca nut, medications, alcohol-containing mouthwashes, dental devices and materials can assist the practitioners in clinical decision-making and accurate diagnosis of associated lesions. More importantly, timely diagnosis and prompt reporting of such harmful effects improve the quality of care. Such knowledge may also help in patient's education for the avoidance of associated adverse effects (AEs). Consequently, a thorough acquaintance of AEs will consolidate the distinct role of medical and oral health practitioners in safeguarding the patients' oral and systemic well-being. This article was planned to review the harmful consequences of specific substances on the oral health. Traditionally, the emphasis of review articles has been on reviewing the harmful effects of a single entity on oral health. This review is unique in the sense that it comprehensively and collectively focussed on the harmful effects on the oral health of addictive and illicit substances (alcohol, betel nut), medications, alcohol-containing mouthwashes, medications and dental materials.

Keywords: Oral health, Adverse effects, Alcohol, Tobacco, Areca (betel) nut, Alcohol-containing mouthwashes, Medications, Dental materials and devices.

Introduction

The adoption of illicit and licit substances has spiralled globally. The consumption of certain substances, such as tobacco and alcohol, has now been regarded as lifestyle habits. The upsurge in the use of alcohol, tobacco and areca nut products is concomitant with an escalation in adverse consequences on the health, society and economy. The consequences are evident in the form of loss of work-related productivity, creativity,

unemployment, associated economic recession, irrational behaviour at home and work due to addiction, life-threatening diseases like cancer and death. The knowledge about the exact mechanism through which various substances affect oral health is still very limited. But it has been proved that the abuse of such substances may have detrimental effects on the oral health.¹

Oral cavity has to bear the direct brunt of the harmful substances, as it serves as a portal of entry for unhealthy stuff such as tobacco, alcohol and other toxic substances.² The most damaging consequence of such substances is cancer of the oral region. But apart from their role in causing oral cancer, using alcohol, tobacco and betel/areca nut also leads to multiple oral and dental implications.³ Substances that are categorised as legal substances, such as prescribed medications and dental materials, also carries the potential of abuse and causing harm to the oral health.⁴

As dental practitioners will be coming across users of both permissible and spurious agents and substances, it is relevant to know about their deleterious effects, as this knowledge may then help determine how an oral healthcare practitioner may advise oral health care recommendations to the patient. Although much has been written about harmful effects of various substances on the general health, less focus is directed on the oral health. Moreover, the emphasis of review articles has been on reviewing the harmful effects of a single entity on oral health. This manuscript has been specific, as it extensively and simultaneously focused on the harmful effects on oral health of multiple entities such as addictive and illicit substances (alcohol, betel nut), medications, alcohol-containing mouthwashes, medications and dental materials.

Alcohol

Today the global presence of alcohol drinkers is exceeding two billion. Alcohol consumption impacts not only the aetiology and onset of diseases and injuries but also adversely influences the clinical behaviour and consequences of disorders, including different types of cancers, heart diseases, liver cirrhosis, diabetes, central obesity, hyperlipidaemias and psychological disorders. Alcohol consumption leads to approximately 3.3 million

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Table-1: Potentially malignant lesions and conditions attributable to the use of alcohol, tobacco and betel nut.

Lesion	Aetiological Factors	Clinical Features	Average Percentage of Malignant Transformation
Erythroplakia	Tobacco/alcohol	Red plaque	Very high (80-90%)
Leukoplakia (nonhomogeneous)	Tobacco/alcohol	Speckled or nodular red and white plaque	High (>30%)
Proliferative verrucous leukoplakia	Tobacco/alcohol	White and red plaque with papillary surface	
Sublingual keratosis	Tobacco/alcohol	White plaque	
Oral submucous fibrosis (OSMF)	Betel nut	Fibrosis and stiffness of oral mucosa	
Leukoplakia (homogeneous)	Tobacco/alcohol	Flat white plaque	Low (<5%)

mortalities annually. Most deaths due to alcohol are heart-related diseases, followed by alcohol-attributable injuries, gastrointestinal diseases (mainly liver cirrhosis) and cancers. Thirty percent of global deaths caused due to oral cavity and pharynx cancers are alcohol attributable.⁵ It is ironical that despite being an established fact that alcohol is responsible for causing an array of diseases, it is considered as a more socially acceptable beverage ingrained in numerous cultures for centuries.¹

Oral cancer generally involves lips, tongue, the floor of the mouth, gingivae (gums), palate and buccal mucosa. Oral squamous cell carcinomas (OSCCs) accounts for nearly 90% of all the oral cancers.³ More than half of all oral cancers are presumed to be caused due to the individual and combined effects of alcoholism, smoking/chewing of tobacco and areca nut use.⁶ Exaggerated consumption of alcohol is linked with a threat of the OSCC development.³

Alcohol inflicts damage upon oral mucosa, dentition and salivary glands through the direct action of ethanol and direct/indirect effects of its metabolites such as acetaldehyde, reactive oxygen species (ROS) and fatty acid ethyl esters (FAEEs).⁷

The potential malignant lesions of the oral region are associated with alcohol drinking, tobacco and betel nut are erythroplakia, leukoplakia, proliferative verrucousleukoplakia, etc (Table-1).

Oro-dental health of alcoholics is often neglected and is often associated with specific clinical findings related to the oral region. It includes dental caries, periodontal diseases, dental erosion due to regurgitation of gastric acid, oral pre-malignancies and malignancies.⁸ Moreover, bilateral parotid enlargement due to fat deposition is a common clinical finding in alcoholics. This clinical finding is associated with the alcohol-related complication of alcoholic liver cirrhosis.⁹

Alcohol-containing mouthwashes

A variety of over-the-counter mouthwashes contain alcohol (ethanol) as an ingredient. Incorporation of

alcohol into mouthwashes is for various reasons: it acts as a preservative and enhances flavour, has antiseptic properties, plays a role of solvent for active ingredients and facilitates the penetration of active constituents in the dental plaque biofilm. As ethanol is a cheap constituent and easy to produce, its concentration was found out to be as high as 26% in some of the mouthwashes. Surprisingly, alcohol in mouthwashes imparts negligible supplemental benefits to the efficacy in terms of gingivitis and plaque control.¹⁰ Moreover, the risk of oral carcinoma in smokers who use alcohol-containing mouthwashes is enhanced, as alcohol facilitates the penetration of tobacco-based carcinogens into oral mucosal tissues.¹¹

The prime metabolite of alcohol is acetaldehyde, which is mutagenic as well as carcinogenic. Metabolism of alcohol contained in mouthwashes occurs in the oral cavity and that various oral microbes, particularly plaque bacteria can metabolise alcohol to acetaldehyde.¹⁰ There is a short-term formation of acetaldehyde in the mouth on using alcohol-based mouthwashes, which is detectable in the saliva for up to 10 minutes. Based on the acetaldehyde presence in saliva, there exists a lifetime risk of oral cancer on twice-daily oral rinsing with alcohol-containing mouthwashes.¹²

As alcohol in a mouthwash does more harm than good, the prescription or recommendation of such mouthwashes should be based on consideration of safer alternatives.

Tobacco

Tobacco is generally utilised in the form of smoking and as smokeless tobacco (ST) (Table-2). Tobacco in all forms contains nicotine and has the potential for addiction and damage to the oral and general health. Although there is no tobacco or burning of tobacco involved in e-cigarettes, they are known to contain carcinogens and toxins (such as acetaldehyde and formaldehyde) that are detrimental to the user.¹³

Smoking is prevalent all over the world. According to

Table-2: Main forms of smoked and smokeless tobacco use.

Forms	Description
Smoked	
Cigarette	Combination of cured and finely cut tobacco, reconstituted tobacco and other additives stuffed into a paper wrapped cylinder. Many cigarettes have a filter on one end
Cigar	Larger than cigarettes with no filter and made up of a single type of air-cured or dried tobacco
Pipe	Consist of a chamber or bowl, stem and mouthpiece. Tobacco is placed into the bowl and lit. The smoke is then drawn through the stem and mouthpiece and inhaled
Bidi	Small, thin hand-rolled cigarettes wrapped in leaf
Kreteks	Also known as clove cigarettes. Contain a mixture of tobacco, cloves and other additives
Electronic cigarettes	Battery-powered device that contains a cartridge filled with nicotine, flavour and other chemicals. It turns the nicotine and other chemicals into a vapor that is then inhaled by the user
Hookah/ Sisha (water pipe)	Tobacco with fruit or vegetable heated & smoke filtered through water
Smokeless	
Chewing tobacco (may come in flavors)	
Loose leaf	Cured (aged) tobacco, typically sweetened and packaged in pouches
Plug	Cured tobacco leaves pressed together into a cake or "plug" form
Twist or roll	Cured tobacco leaves twisted together like a rope
Snuff	
Moist	Cured (aged) and fermented tobacco processed into fine particles
Dry	Fire-cured tobacco in powder form
Snuff	Moist snuff packaged in ready-to-use pouches resembling small tea bags
Dissolvables (slowly dissolve in the mouth)	
Lozenges	Resembles tablets
Sticks	Have a toothpick-like appearance
Strips	Thin sheets that work like dissolvable breath or medication strips

World Health Organisation's (WHO) estimates, globally there are around 1,100 million smokers. They represent about one-third of world population aged over 15 years.⁹ For smoking, various practices are prevalent around the world, such as smoking cigarettes, cigars, pipe, bidi and reverse smoking. Bidi is a form of unfiltered cigarettes that contains a small amount of flaked tobacco, commonly used in South Asia. Reverse smoking is a practice of holding the lit end of a cigarette in the mouth, seen in India, Philippines, Taiwan and Latin America. Cigarette smoking is responsible for diseases of heart and lungs and various cancers. On an annual basis, tobacco use is responsible for causing around six million mortalities.¹⁴ Tobacco use in all forms carries a significant risk of development of OSCC, leukoplakia and erythroplakia. In contrast to the ST users, smokers are five times more prone to be affected by the cancers of the oral region. Forty different types of carcinogens were found to be present in tobacco smoke, including benzopyrene, nicotine, benzene, carbon monoxide (CO), propylene glycol, cadmium, tar, acetone, lead, formaldehyde, etc.³

Smokers also remain highly susceptible to periodontitis and dental caries. Plaque samples from smokers were found to contain higher proportion of bacteria responsible for causing periodontitis, such as *Peptostreptococcus micros*, *Porphyromonas gingivalis*, *Campylobacter rectus* and *Tannerella forsythia*. In smokers, a greater incidence of dental caries compared to non-smokers was attributed to enhanced colonisation of *Streptococcus mutans* in oral biofilms.¹⁵

ST is a form of tobacco that is not ignited. Based on its main forms, there is a great assortment of ST products and diversity in patterns of ST use across the globe. ST is usually placed in the buccal vestibule to suck on or masticate it. Admixture of tobacco and saliva that is produced may be spit out or swallowed. Dry type of snuff can be sniffed or inhaled into the nose. In South Asia, ST and related products are consumed in high amounts. In India and Pakistan, tobacco mixed with other ingredients is chewed in a variety of forms such as gudakhu (tobacco powder, molasses and other ingredients), gutka (betel nut, tobacco, slaked lime and flavours), khaini (tobacco, lime paste and areca nut), kiwam (tobacco, slaked lime

and spices), mawa/ kiwam (tobacco, slaked lime and areca nut), mishri (roasted tobacco in powdered form applied to teeth), paan (areca nut plus tobacco products wrapped in betel leaf), paan masala (tobacco, areca nut, slaked lime, betel leaf and flavours, sometimes chewed after meals) and zarda (tobacco leaf boiled with spices and lime until evaporation). In Pakistan and Afghanistan, nass or niswar — a mixture of tobacco, slaked lime, menthol, ash, cotton or sesame oil and other ingredients — is commonly used.^{3,16} ST contains more than 20 known carcinogens. Tobacco-specific N-nitrosamines (TSNA) is an abounding carcinogen present in un-ignited tobacco. TSNA owes its formation to the processes of drying and fermentation of tobacco.^{7,16} There have been reports of cancerous growth and other oral mucosal lesions affecting the intraoral region coming into contact with the ST products.^{3,16,17}

Areca (betel) nut and betel quid ('paan')

The areca or betel nut is the fruit of the areca palm (*Areca catechu*). The areca nut is cultivated mainly in India, Sri Lanka, Bangladesh, the Philippines, South China, the East Indies and parts of Africa. The nut may be used fresh or after curing the dried nut by roasting or boiling.¹⁸

A 'betel quid' (consistent with 'pan' or 'paan' in Urdu and Hindi) is a folded leaf package. Mainly it is composed of betel leaf, betel nut, tobacco and slaked lime. Based on the individual taste preferences, aromatic spices and condiments such as cloves, fennel seeds, cardamom, saffron, saccharin-containing sweeteners and flavourings are also included. The buccal vestibule is the preferred area for placement of betel quid, where it is chewed slowly to squeeze out its juice.^{18,19}

Consuming areca nut and betel quid on a regular basis have potentially damaging consequences on the oral health ranging from subtle to life-threatening. These consequences can be split off into two distinct categories: those influencing the oral hard structures that include teeth (dental attrition and areca staining), their supporting periodontium (periodontitis) and the oral soft tissues, that include oral mucosa and gingivae (oral/ pharyngeal cancers, oral submucosal fibrosis, lichenoid lesions and gingival disease). Moreover, chewing of areca leads to the generation of unusual masticatory forces. The temporomandibular joint (TMJ) has to bear the brunt of these forces, consequently resulting in degenerative changes in the TMJ. These changes ultimately lead to clinical manifestations of pain and limited mouth opening.^{9,20}

Oral submucous fibrosis (OSMF) is a premalignant disease affecting the oropharyngeal region. In the past numerous causes were presumed to have a role in its development,

such as iron deficiency, immoderate use of chillies and autoimmune reaction. However, based on epidemiological data now it has been established that areca nut is the sole aetiological agent of OSMF.²⁰ Alkaloids are the most important of all the chemical compounds present in *Areca catechu*. The four alkaloid compounds identified through biochemical testing are arecoline, arecaidine, guavacoline and guavacine. These agents are identified to have a potential role in OSMF by stimulating the fibrosis of oral mucosal tissues.¹⁹

Numerous dental practitioners are oblivious to the habitual consumption of areca nut with tobacco in their patients of Asian descent. The knowledge and identification of the role of such agents in causation of oral premalignant and malignant lesions is of utmost significance for raising the awareness through education to limit the use of areca nut and betel quid.²¹

Medications

Adverse effects (AEs) to medications are a frequent occurrence.²² Every part of the oral mucosa may be affected by AEs of medications with topical or systemic administration.²³ The medications most commonly associated with AEs in the oral region are nonsteroidal anti-inflammatory drugs (NSAIDs), receptor blockers, phenytoin, calcium channel blockers, etc. (Table-3). The common clinical manifestations of medication-induced adverse reaction affecting the oral region may include orofacial swelling, dryness in the mouth, altered taste, oral malodour, non-specific ulcers, vesiculobullous eruptions, oral mucosal pigmentation and discoloration of teeth. Certain medications are associated with characteristic oral drug reactions, as is the case of gingival hyperplasia associated with use of cyclosporine and phenytoin. Still, some of the AEs may often resemble clinical features of clinical entities such as lichen planus, erythema multiforme (EM), or pemphigus. Such cases should increase the clinician's index of suspicion for making the correct diagnosis.²⁴ A wide array of medications — especially NSAIDs, tetracyclines, estrogens, phenothiazines and sulphonamides — may give rise to EM. The development of simultaneous oral and cutaneous lesions of pemphigus may occasionally be associated with the administration of medications with active thiol groups, such as NSAIDs (diclofenac, piroxicam), rifampicin, penicillamine and angiotensin-converting-enzyme (ACE) inhibitors. Lichen planus (LP) is a chronic inflammatory condition affecting the cutaneous and oral regions. Oral LP presents as bilateral white reticulations or papules in combination with soreness, ulcerations and erosions affecting the intraoral region. Such eruptions are often difficult to be differentiated

Table-3: Medications most commonly associated with AEs in the oral region.

Adverse effect	Medication
Oral ulcerations	NSAIDs (aspirin, piroxicam & naproxen), angiotensin receptor blockers (captopril & losartan)
Gingival enlargement	Phenytoin, calcium channel blockers (nifedipine & amlodipine)
Discoloration of teeth	Fluoride, iron supplements, tetracyclines, chlorhexidine
Oral dryness	Amphetamine, anticholinergic drugs (atropine), antidepressants (amitriptyline), antiemetics (metoclopramide), bronchodilators (albuterol), antihistamines (loratadine & chlorpheniramine), anxiolytics (alprazolam), decongestants (pseudoephedrine & phenylephrine), diuretics (hydrochlorothiazide), narcotic analgesics (morphine), skeletal muscle relaxants (orphenadrine)
Pseudomembranous candidiasis (Thrush)	Inhaled corticosteroid aerosols (fluticasone & beclomethasone), broad-spectrum antimicrobials
Taste alteration	Metronidazole, griseofulvin
Oral mucosal/gingival pigmentation	Antimalarials, phenothiazine, phenytoin, minocycline

NSAIDs: Nonsteroidal anti-inflammatory drugs.

clinically and histologically from the lesions of idiopathic mucocutaneous LP. Antihypertensive agents (ACE inhibitors, β -blockers and diuretics) and NSAIDs are known to be classically associated with induction of oral LP-like eruptions in susceptible individuals.^{24,25}

"Aphthous-like" ulcers are the clinical form of oral ulceration that occurs due to a variety of causes. Medications with active thiol groups, including piroxicam (NSAIDs) and captopril (β -blocker) are also implicated in the aetiopathogenesis of these ulcers. Oral mucositis is a common complication of chemotherapy. The oral mucosa undergoes atrophy and breakdown leading to ulcers and severe pain. It begins 5-10 days after the initiation of chemotherapy and lasts 7-14 days. Chemotherapeutic drugs, such as cisplatin, 5-fluorouracil, methotrexate, doxorubicin, cyclophosphamide and hydroxyurea are stomatotoxic and can induce ulcerative mucositis.²⁵

A range of oral opportunistic infections may occur as a result of long-term immunosuppressive therapy. Immunosuppressed patients remain at a risk of developing pseudomembranous candidiasis and viral infections. Kaposi's sarcoma and non-Hodgkin's lymphoma may be the rare complications of drug-related immunosuppression.²⁴

Salivary glands are also sensitive to the AEs of medications. Numerous medications induce the AEs of hyposalivation and xerostomia. Clinical manifestation of oral dryness can occur as an adverse effect of over 500 medications.²⁶ Individuals with severe long-standing oral

dryness remain at risk of developing infections, such as dental caries, candidiasis and bacterial sialadenitis. From the perspective of oral rehabilitation, xerogenic medications in elderly denture-wearing individuals can hamper the retention of prosthesis. Such medications adversely affect the salivary wetting mechanics that are crucial for an effective retention of dentures.^{25,27}

Hard tissues of the oral region can also be affected by AEs of certain medications. Some medications by interfering with odontogenesis cause intrinsic discolouration of teeth. Such discolouration is permanent.²⁴ Agents responsible for permanent discolouration of dentition include tetracyclines (yellow $\rightarrow$ brown/grey discoloration), minocycline (green-gray/blue-grey), ciprofloxacin (greenish) and fluorides (white/brown). Medications that cause extrinsic (superficial) discoloration include chlorhexidine (yellow/brown discoloration), iron salts (black) and essential oils (yellow/black).²⁸ Tooth erosion may be caused by medications (anticholinergics, calcium channel blockers, progesterone and theophylline) that carry the risk of causing gastroesophageal reflux disease (GERD). The disease results in regurgitation of gastric acid into the oral cavity. Medications with a low potential of hydrogen (pH) such as aspirin, anti-asthmatic drugs and some mouthwashes may also lead to dental erosion.²⁹

Based on the potential of medications to cause AEs, it is imperative that dentists must pay particular attention to the medications that their patients receive. Furthermore, the active and prompt involvement of dentists in evaluating and reporting medication-related AEs in the

head and neck regions is of utmost importance. As active involvement is crucial to protecting the health and well-being of patients.²²

Dental Materials and Devices

In addition to medications, the practice of dentistry also involves the use of devices, biomaterials, disinfecting and anaesthetic agents. All these may potentially cause AEs in patients and members of the dental team. AEs related to dental materials range from contact allergy to lethal anaphylaxis. The dental materials suspected to cause allergic reactions in the oral cavity are composites, local anaesthetic agents, impression materials, endodontic materials and metals. The clinical features of contact allergy of the oral region range from dryness, pain and burning of oral mucosa to cheilitis and non-specific stomatitis.³⁰

Less than one percent of people may be allergic to the mercury and other metals from dental amalgam. Allergy to mercury in dental amalgam fillings is manifested in the form of a swollen lip, perioral inflammation, lichenoid reactions and intraoral soreness. In patients suspected of amalgam contact hypersensitivity lesions, removal of dental amalgam is followed by considerable improvement.³¹

Dental sensitivity is a frequent AE of tooth bleaching agents such as hydrogen peroxide or carbamide peroxide. This sensitivity usually continues to affect until 3-4 days after completion of the bleaching treatment. However, sometimes it may get prolonged for up to a month.²⁹

A variety of dental materials such as filling materials, endodontic sealers, impression materials, dental cements, dry socket dressings and periodontal dressing materials contain eugenol as a major constituent. Eugenol at high concentrations can produce both local irritative and cytotoxic effects, as well as hypersensitivity reactions. Moreover, pulp may undergo considerable damage on direct application of eugenol to it. For avoiding AEs associated with eugenol, eugenol-containing materials need to be used according to manufacturer's instructions and in appropriate amounts. For patients who are allergic to eugenol, eugenol-free alternatives are available.³²

Certain components in toothpaste that act as calculus inhibitors, such as zinc citrate and tetrasodium pyrophosphate, can cause superficial shedding of the oral mucosa in some consumers. This reaction is assumed to be caused by oral irritation rather than an allergic reaction. Cinnamon-flavoured products (toothpaste, chewing gum, food, candy and mouthwash) have the

potential to initiate allergic reactions in sensitive individuals. This allergy is manifested in the form of stomatitis known as cinnamon contact stomatitis (CCS).³³

The main purpose of local anaesthetics (LA) injection is to alleviate pain and other discomfort associated with dental procedures. Generally, it is a safe manoeuvre and sensory perception comes back to normal within few hours. Prolonged and permanent loss of sensation can be the most serious AE to LA injection. This usually affects the mandibular or lingual nerves, or both. If it's temporary, the sensation usually returns after a few days, weeks or months. Infiltration of the maxillary nerves rarely leads to a prolonged loss of sensation.³⁴

Last but not least, dental personnel are also prone to the occupational AEs associated with various dental materials and equipment. Latex gloves are the main culprits for inducing allergic AEs in susceptible dental staff (dentists, dental nurses, hygienists and a receptionist), whereas in dental technicians the main offender for induction of allergic AEs remains the acrylic resin. Allergies due to these agents rarely cause any oral manifestations in the susceptible dental personnel. The AEs include sneezing, runny nose, watery eyes, facial swelling and breathing problems. Moreover, AEs of latex and acrylic resin may affect hand and wrist regions with manifestations such as swelling and itching.^{30,35}

Conclusion

Given the countless harmful effects of the alcohol, tobacco and betel nut on the oral and general health, the general public should be informed about the associated risks of these substances through awareness campaigns and activities. Oral health practitioners can play a crucial role in counselling their patients for the cessation of smoking, drinking and betel nut chewing. Ideally, the medications and dental materials should not be detrimental to the oral and general health of the patients and dental personnel. Because of increased incidence of AEs to medications and dental materials, it is important that hypersensitive individuals are identified at the onset of any treatment. Doing so will be helpful for avoiding adverse manifestations in the clinics. It is also imperative that the oral health practitioners should have a good knowledge of the AEs that can be induced by medications and materials. On encountering such AEs, this knowledge can be helpful in providing information and referral for treatment if indicated.

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