

Xerostomia

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ABSTRACT

Introduction: Xerostomia is defined as dry mouth resulting from reduced or absence of saliva flow. Xerostomia is not an ailment, but it may be a symptom of various medical conditions or a consequence of radiation exposure or may be a side effect of medications. However, if left untreated, xerostomia decreases the oral pH and significantly increases the development of dental caries, fungal infections, and various other complications.

Objectives: This review elaborates on various causes, complications, preventive measures, and treatment approaches. Xerostomia is caused mainly due to dehydration, damage to salivary glands, and interference with neural transmission. Preventive measures comprise acting on cause, maintaining salivary function, and prevention of complications. The treatment of xerostomia is divided into four main categories: Palliative or symptomatic, local and systemic stimulation, and prevention of complications.

Conclusion: Xerostomia or dry mouth affects the patient's oral and general health, thereby inhibiting the quality of life. Therefore, the assessment of salivary gland hypofunction, early recognition, and prevention and treatment of xerostomia and its complications will need to be incorporated into everyday clinical dental practice.

Keywords: Artificial saliva, Caries, Complications, Dry mouth, Management, Radiation.

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INTRODUCTION

Saliva is the viscous, clear, watery fluid secreted from the parotid, submaxillary, sublingual, and smaller mucous

glands of the mouth. Saliva contains two major types of protein secretions, a serous secretion containing the digestive enzyme ptyalin and a mucous secretion containing the lubricating aid mucin. The pH of saliva falls between 6 and 7.4.¹ Saliva also contains large amounts of potassium and bicarbonate ions, and to a lesser extent sodium and chloride ions. In addition, saliva contains several antimicrobial constituents, including thiocyanate, lysozyme, immunoglobulins, lactoferrin, and transferrin.^{2,3}

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It is characterized by the following clinical signs:^{4,5}

- Erythematous pebbled oral mucosa or cobble stoned or fissured tongue or atrophy of the filiform papillae.
- On light palpation, the examiner's finger adheres to the mucosal surfaces instead of sliding over.
- After drying the cotton wool, if parotid and submandibular glands are milked, there will be a delay or lack of salivary flow from the duct orifices.

FUNCTIONS OF SALIVA

Saliva performs important functions like mechanical cleansing action, lubrication of the oral cavity, antimicrobial activity, maintaining the integrity of the oral mucosa, control of pH, and remineralization.⁶⁻⁸ The estimated flow rates of saliva are as follows: Parotid (65%~0.26 mL/min), submandibular (20–30% ~0.08 mL/min), sublingual (6%~0.03 mL/min), and minor salivary glands (5%~0.03 mL/min). To assess salivary gland secretion and oral dryness a variety of methods have been used, ranging from self-reported questionnaires (e.g., Xerostomia Inventory),⁹⁻¹¹ visual analog scales, simple functional measures, such as observing if a dental mirror adheres to the buccal mucosa or if a patient can chew and swallow dried biscuits without water to contrast sialography, sialoscintigraphy, sialoultrasonography, biopsy, and sialometry of the minor salivary glands.^{9,12,13} Among these, sialometry is the most objective method to assess salivary function and to determine the quantity of both resting and stimulated whole saliva. Normal daily secretion of saliva is approximately 1 to 1.5 L per day (i.e., 0.5–1 mL/min), although flow rate varies depending on diurnal variation, hydration, food intake, and many other factors.^{14,15}

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ETIOLOGY

The causes of xerostomia may be grouped into three categories.^{16,17}

1. Water or metabolic loss which may be due to dehydration and protein calorie malnutrition. Dehydration may be due to loss of water through skin during fever, burns, excessive sweating, blood loss, emesis, diarrhea, renal water loss either due to polyuria or osmotic diuresis.
2. Damage to the salivary glands, which in turn leads to decreased salivary production. These conditions include: Therapeutic irradiation to the head and neck region, Sjögren’s syndrome, salivary gland diseases, endocrine conditions, such as type I and II diabetes mellitus as well as gestational diabetes, thyroid disease, adrenal conditions, renal or hepatic diseases, infections with hepatitis C virus, human immunodeficiency virus, and human T lymphotropic virus-1.^{18,19}
3. Interference with neural transmission: Certain medications are known to interfere with neural control of salivary glands producing dry mouth as side effect. Cytotoxic drugs, anticholinergic drugs, proton pump inhibitors, psychoactive agents, drugs with sympathomimetic activity, antihypertensives, and diuretics are associated with dry mouth (Table 1).

RADIATION-INDUCED XEROSTOMIA

Xerostomia is one of the most common complications during high-dose radiation therapy (RT) for head and neck cancer (HNC) and has a significant impact on quality of life, requiring careful planning of long-term dental and oral care.²⁰⁻²² Standard RT for advanced HNC involves

fractionated doses of 10 Gy weekly (2 Gy daily on 5 consecutive days) over 5 to 7 weeks to a total dose of 50 to 70 Gy. Parotid glands exposed to doses of greater than 60 Gy sustain permanent damage with no recovery in salivary hypofunction with time.^{23,24} Radiation-induced xerostomia starts in the first week of RT during which salivary flow decreases for 50 to 60% and after 7 weeks of RT diminishes to approximately 20%.

MEASUREMENT OF DRY MOUTH

Xerostomia can be measured by directly subjecting the individuals to prevalidated questionnaire and analyzing the response. There are two methods applied²⁵⁻²⁸:

1. Single-item approach in which a single valid question is used to find the symptoms of dry mouth.
2. Multi-item approach involves a set of questions with same response options for each question. The participants should respond to each question with Yes/No response, and the number of positive responses are counted and used as index score either as a single count or after recording the count into ordinal categories.

COMPLICATIONS

Patients with xerostomia may be asymptomatic without complaints and, rarely, complain of dry mouth and develop various complications²⁴ (Table 2). Patients usually experience difficulties while speaking, chewing, swallowing, and wearing dentures. Oral mucosa is dry and sensitive; prone to injuries, fungal infection, and inflammation; painful with burning sensations; taste is altered; and halitosis is present. In patients with Sjögren’s syndrome in which exocrine glands and the connective tissue are affected, patients complain about the dryness of the eyes.^{29,30}

Table 1: Drugs associated with dry mouth

Drugs that directly damage salivary glands	Cytotoxic drugs
Drugs with anticholinergic activity	Anticholinergic agents: Atropine and hyoscine Antireflux agents: Proton-pump inhibitors (e.g., omeprazole)
Central-acting psychoactive agents	Antidepressants, including tricyclic compounds Phenothiazines, Benzodiazepines Antihistamines Bupropion
Opioids	
Drugs acting on sympathetic system	Drugs with sympathomimetic activity (e.g., ephedrine) Antihypertensives: Alpha-1 antagonists (e.g., terazosin and prazosin); alpha-2 agonists (e.g., clonidine); beta blockers (e.g., atenolol, propranolol)
Drugs that deplete fluid	Diuretics

Table 2: Consequences and complications of xerostomia

1	Dry mouth
2	Thirst
3	Difficulties in oral function
4	Dysphagia
5	Taste disturbances
6	Altered speech
7	Difficulties wearing dentures
8	Mucosal changes
9	Injuries of oral mucosa
10	Oropharyngeal burning
11	Mucus accumulation
12	Food retention in the mouth
13	Plaque accumulation
14	Hyposalivation-associated caries
15	Changes in oral microbial flora
16	Oropharyngeal infections
17	Fungal infections
18	Nocturnal oral discomfort

Various treatment modalities have been suggested to overcome the problem of xerostomia in complete denture patients. Incorporating reservoirs containing salivary substitutes into dentures is one of these treatment modalities (Table 2).

TREATMENT

Treatment of xerostomia depends on the cause and the degree of damage of the salivary glands, thus it comprises of etiologic, stimulative, symptomatic, or palliative approach. Current therapies include saliva substitutes, saliva stimulants (sialagogues), and nonpharmacological approaches.³¹

Local Stimulation

The combination of chewing and acidic taste, as provided by chewing gums or solid food or fruits, preferentially acidic (apple, pineapple, carrots, etc.), can be very effective in stimulating saliva flow for patients who have remaining salivary function. Electrical stimulation has also been used as a therapy for salivary hypofunction but has been inadequately investigated clinically.¹³

Systemic Stimulation

Any agent that has the ability to influence salivary glands to increase production of saliva is termed a secretagogue.³² Among many examined agents, only four sialagogues have been examined extensively in controlled clinical trials; these are bromhexine, anetholetrithione, pilocarpine hydrochloride (HCl), and cevimeline HCl. Among these, pilocarpine HCl is the best studied sialagogue. After the administration of pilocarpine, salivary output increases rapidly, usually reaching a maximum within 1 hour. The best-tolerated doses are those of 5.0 to 7.5 mg, given three or four times daily. The duration of action is approximately 2 to 3 hours.¹⁵

Symptomatic Approach

A number of saliva substitutes have been developed for the palliative care of patients with salivary hypofunction. They are usually in the form of liquid, spray, or gel and have moistening and lubricating properties to provide prolonged wetness to the oral mucosa. Commercial artificial saliva should resemble normal saliva in its properties.³³ Mucin-based salivary substitutes are known to have the best wetting properties on denture base as well as on oral mucosa.

Nonpharmacological Approaches

- *Acupuncture*: Acupuncture is a non-allopathic alternative treatment method that claims to increase the salivary flow in healthy individuals, patients with

Sjögren's syndrome, and those with radiation-induced salivary gland damage. A needle is inserted at L1–2 point of the nondominant hand on the radial side of the second digit, in the depression anterior to the metacarpophalangeal joint and is purported to cause salivary stimulation.³⁴

- *Neuroelectrostimulation*: Most efficient method of relieving xerostomia is by sending low-intensity electric pulses for the stimulation of nerves associated with stimulation of salivary secretion. Three generations of intraoral electrostimulating devices were developed:
 1. First-generation device (Salitron, USA) – consists of a mouth piece with stainless steel electrodes and console with battery and electronic signal-generating power source. The mouthpiece was applied to the intraoral mucosal surfaces between the dorsum of the tongue and palate, which improves salivary secretion.
 2. Second-generation device (Saliwell GenNarino, Germany) – mainly consists of three components: A miniaturized electronic stimulator that has a signal generator, power source, and conducting circuit. The frequency and duration of usage depend on severity of xerostomia.
 3. Dental implant-based third-generation intraoral device (Saliwell crown, Germany) was developed to generate continuous stimuli without interfering with normal function.³⁵
- *Laser phototherapy (LPT)*: Studies have shown the efficiency of low-intensity infrared laser in stimulating cell proliferation in the salivary glands. The efficiency of LPT is based on its capacity to modulate various metabolic processes, such as adenosine triphosphate production, nitric oxide release, and formation of reactive oxygen species.

PREVENTION OF RADIATION XEROSTOMIA

Several strategies have been developed which include parotid gland sparing RT, cytoprotectants, and surgical salivary gland transfer to avoid radiation-induced salivary dysfunction without compromising oncologic treatment.³⁶

- *Parotid gland-sparing radiotherapy*: This therapeutic approach focuses the radiation beams to the target tumor tissue with the aim to avoid unnecessary radiation of surrounding salivary gland. This was enabled by the implementation of 3-dimensional conformal RT and intensity-modulated RT techniques in clinical practice.
- *Cytoprotectants*: Several agents have been developed to protect normal tissue against cytotoxic effects of RT and/or chemotherapy among which the most

investigated is radioprotector amifostine. In active form, it enters the cells and nuclei where it acts as a scavenger against free radicals, thus preventing radiation damage of deoxyribonucleic acid.

- *Salivary gland transfer*: This technique proposes surgical transfer of submandibular gland to the submental space outside the path of radiation. This procedure has limitations: If patient refuses surgical treatment; if patient is not planned to receive postoperative RT; and if submental space is involved with tumor.

PREVENTION OF XEROSTOMIA COMPLICATIONS

Prevention of complications is carried out in all patients with dry mouth, and aims to prevent development of caries, oral fungal infection, and stomatitis.^{37,38}

Caries

Patients with significant xerostomia should be closely monitored for the development of dental caries, which may be prevented by the daily use of 1.1% sodium fluoride dentifrice or gel. Application of fluoride should be adjusted accordingly to the severity of the gland dysfunction, the degree of development of caries, and the underlying disease or the cause that led to the dryness of the mouth.³⁵

Fungal Infections (Candidosis)

Treatment of oral candidosis with topical antifungal medications, such as nystatin and amphotericin B proved to be successful at the beginning of the therapy. A combination of antifungal drugs and application on the surface of dentures was described in patients with dentures and denture stomatitis.³⁹

Denture Discomfort

In denture-wearing patients, wetting dentures before placing them into the mouth and spraying prostheses with artificial saliva before applying denture adhesives¹² will help in reducing the discomfort. Wetting dentures before meals and taking more fluids during meal time will aid in mastication and swallowing. Adapted denture fabrication (split denture technique and flexible complete denture construction) will help in alleviating discomfort.³⁵⁻³⁸

CONCLUSION

Oral health and function depend on salivary function. Although xerostomia is common in elderly patients, it is frequently not assessed and managed on time. Due to serious complications of dry mouth that affect oral and general health, the quality of life of these patients is

decreased. Therefore, the assessment of salivary gland hypofunction, early recognition, prevention, and treatment of xerostomia and its complications will need to be incorporated into everyday clinical dental practice.

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