Review
JOURNAL OF UNIVERSITY OF BABYLON
For Pure and Applied Sciences (JUBPAS)
Vol.33 ; No.4 | 2025

Xerostomia And Its Effect On Oral Microbial Growth: An Overview

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Accepted: 24/12/2025 **Published:** 31/12/2025

ABSTRACT:

Dry mouth caused by decreased or absent salivary flow is known as xerostomia. Although xerostomia is not a disease, it can be a sign of several illnesses, a side effect of drugs, or a result of radiation exposure. When xerostomia is untreated, it can lower the pH levels of the mouth and create a favorable environment for the growth of certain microflora, such as Streptococci, Actinomycetes, and Lactobacilli, that can lead to dental cavities, fungal infections, and other problems.

Numerous causes, problems, preventative strategies, and treatment modalities are covered in detail in this analysis. Dehydration, damage to the salivary glands, and disruption of neuronal transmission are the main causes of xerostomia. Acting on the cause, preserving salivary function, and avoiding complications are all examples of preventive approaches. There are four primary approaches to treating xerostomia: symptomatic or palliative, systemic and local stimulation, and preventing complications.

The aim of this investigation is to clarify xerostomia, its causes, its complications, its prevention, treatment, and its effect on oral microbial growth. From this review we conclude that the patient's oral and overall health are impacted by xerostomia, or dry mouth, which lowers their quality of life.

Keyword: Xerostomia, Oral microbiota, Hyposalivation , Dysbiosis, Sjögren's syndrome

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1.INTRODUCTION

One essential element supporting the full operation of the oral tissues is saliva. Hyposalivation and xerostomia are the results of the qualitative and quantitative association between salivary secretion and oral pathology. The subjective complaint of dry mouth is commonly referred to as xerostomia. However, it is more frequent in the general population and rises with age. xerostomia is more common in older adults [1]. It causes discomfort, difficulty speaking, swallowing, and decreased taste perception [2]. While the unstimulated salivary flow rate is roughly 0.3–0.4 mL/min, the usual stimulated salivary flow rate averages 1.5–2.0 mL/min [3]. When the unstimulated salivary flow rate is equal to or less than 0.1 mL/min and the stimulated salivary flow rate is equal or less than 0.5–0.7 mL/min, hyposalivation is analyzed. In patients with obvious hyposalivation, xerostomia is diagnosed. In those patients the rate of saliva flow is lower than the amount of fluid preoccupation across the oral mucosa and above evaporation rate of the fluid from the mouth [4]. Xerostomia is connected with an increased vulnerability to oral health complications, including oral infections, dental caries, and immunological defects, which can damage general oral health [5]. Dry mouth was more common in older adults with diabetes and other chronic conditions who were taking medication continuously. A higher likelihood of self-reported xerostomia was associated with continued use of gastrointestinal tract medicines[6].

In addition to increasing the risk of dental caries, tooth demineralization, tooth sensitivity, and/or mucosal infections, decreased salivary flow can make it harder to taste, chew, swallow, and talk [7]. Hyposalivation-related xerostomia can also cause burning mouth, halitosis, taste alterations, oral fungal infections (like candidiasis), and widespread dental caries [8],[9]. The most popular cause of hyposalivation is the use of specific medications, like: levothyroxine , antihypertensive , antidepressant , hypoglycemic , anticoagulants, antiretrovirals, multivitamins , steroid inhalers , supplements and non-steroidal anti-inflammatory drugs [10]. This is followed by skull and neckline radiation therapy and Sjögren's syndrome. Malnutrition, stress, anxiety, and depression are additional concerns [11]. The population's xerostomia prevalence varies from 5.5% to 46%. According to studies, xerostomia seems to become more common as people age, and incidence varies between the sexes. One explanation could be that older people who take multiple xerogenic medications for chronic illnesses may experience a general decrease in their unstimulated salivary flow rate [8]. Even after obtaining medical or dental advice, xerostomia is still a prevalent ailment that has not been treated, particularly in the elderly population [12]. The aim of this investigation is to clarify Xerostomia, causes, complication, prevention , treatment and its effect on oral microbial growth.

We performed a thorough literature search in PubMed and Google Scholar. To narrow the search and find pertinent papers, we used a variety of topic-related keywords, such as "xerostomia," "dry mouth, "oral microbiome," and "treatment." In order to find more relevant papers, we also looked through the reference lists of the articles that were found. Original research articles, systematic reviews, and meta-analyses were all included in the inclusion criteria.

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2. CAUSES

There are notable similarities between the difference of xerostomia and hyposalivation. Dry mouth is typically caused by a decrease in saliva creation to roughly 50% of the unstimulated level [13]. Xerostomia may also be caused by changes in the content of saliva This symptom is extremely prevalent and frequently observed as a side effect of various medications. It is more prevalent in elderly adults and those who breathe with their mouths (mostly due to the fact that these persons are more prone to take many drugs). Reduced salivation (hyposalivation), or a change in saliva consistency and consequently a complaint of xerostomia, can be brought on by dehydration, radiation therapy that affects the salivary glands, chemotherapy, and a number of disorders. There may occasionally be a psychogenic rationale for the complaint and no discernible cause [14].

A summary of the main causes of xerostomia can be seen in Table1 [15].

Systemic diseases	**Sjogren's syndrome, diabetes mellitus, Parkinson's disease, encephalitis, brain tumors, Plummer Vinson disease, hypertension, HIV infection, systemic rheumatic diseases, sarcoidosis, Alzheimer's disease, cystic fibrosis, aplasia, chronic tuberculosis, primary biliary cirrhosis, hemolytic anemia, malignant lymphoma, systemic lupus erythematosus, scleroderma, dermatomyositis, pernicious anemia, hypothyroidism, amyloidosis**
Other causes of xerostomia (no drugs or systemic diseases)	**Radiotherapy and chemotherapy, infections, inflammation, tumors and sialolithiasis in salivary glands, salivary gland excision, vitamin A deficiency, menopause, stress, anxiety, dehydration, neurological disorders, senility, oral sensory dysfunction, iron deficiency, folic acid deficiency, uremia, polyuria, diarrhea, mouth breathing, bone marrow transplantation, endocrine disorders, pancreatic insufficiency**

2.1. The role of Oral Microbiota in Xerostomia

The numerous distinctive niches in the oral cavity , that resides numerous microbial species, are an essential character of the oral microbiome ,which is an essential element of the human microbiome. This habitat includes a diverse spectrum of microbes, such as bacteria, viruses, fungus, protozoa, and archaea which together provide a complex environmental system vital for both oral and systemic health. The predominant oral disorders, including periodontal infections and tooth caries, are significantly related to microbiota. As a reaction to the increasing comprehension of the oral ecosystem, numerous novel strategies designed to adjust the microbiome for the protection and restoration of a healthy mouth environment have been established. Within the ecosystem of the mouth cavity saliva plays a necessary part at protecting a varied and a healthy microorganism community. It offers important nutrients, enables the clearing of diet remains and microbes. It includes as well antimicrobial elements that aid the directing of the development and the structure of the inhabitant microorganisms [16].

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The oral ecosystem becomes exposed to important microbial shifts when salivary production is declined, just as that which is seen in xerostomia. By performing vital tasks like mechanical clearing, antimicrobial defense, and oral microbiome management, saliva plays a critical role in preserving the delicate balance of the oral microbial ecology. The equilibrium of the oral microbiome can be severely impacted by xerostomia, a condition marked by a progressive decline in salivary gland function and changes in salivary composition, which can result in dysbiosis. In this ecosystem, some oral microbial populations are linked to systemic disorders in addition to oral health problems. As a result, this complex and varied oral microbial environment is essential for maintaining and promoting oral health, and any changes to it could raise the risk of pathogenicity [14].

The colonization of nonoral bacteria, such as *Staphylococcus aureus* and coliforms, is a major part of the changes in bacterial composition linked to xerostomia. Additionally, both the incidence of *Candida* infections and the prevalence of *Candida* species have significantly increased. The colonization of nonoral bacteria is probably a result of reduced immune function delivery, which is usually made easier by saliva. However, the few community profiling studies that have been done to compare the bacterial makeup of oral communities in individuals with hyposalivation with control groups have produced inconsistent results and either no significant differences or very slight alterations [17].

Additionally, two studies [18,19] found that patients with Sjögren's syndrome had a higher percentage of *Streptococci* in their tongue microbiome, whereas another study found that the same patient population had a lower salivary microbiota. In particular, *Porphyromonas*, *Fusobacterium*, and *Treponema* were more prevalent in the oral microbiota of individuals with xerostomia after radioiodine therapy (RAI) for differentiated thyroid cancer (DTC).

The *Porphyromonas* genus may be a major community driver in the development of xerostomia, according to subsequent investigations. A pro-inflammatory milieu may be fostered by these changes in microbiota composition and related functional changes. The dysregulation of inflammatory and antioxidant metabolic pathways, along with the observed dysbiosis in the oral microbiota, may worsen the course of xerostomia [20].

2.2. Physiological

Sleep reduces salivary flow rate, which might cause a brief feeling of dry mouth when you wake up. This is sometimes referred to as "morning breath" when it is linked to halitosis. Another typical symptom of anxiety is dry mouth, which is most likely caused by an increased sympathetic drive [21]. Stress causes our bodies to go into a "fight or flight" mode, which will obstruct the flow of saliva in the mouth [22]. Hyposalivation, which is the body's attempt to preserve fluid, is known to occur when dehydration occurs [14]. The augmented occurrence of xerostomia in elder adults may be partially explained by physiological period-associated changes in salivary gland tissues, which can result in a little decrease in salivary production

However, it is believed that polypharmacy is the primary culprit in this population, as aging alone is unlikely to result in any appreciable drops in salivary flow rate [23],[24].

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2.3. Drug induced xerostomia

Medication side effects are the most frequent cause of xerostomia, aside from physiological factors [14]. One name for a drug that is known to induce xerostomia is xerogenic [24]. There are more than 400 drugs linked to xerostomia. The disorders for which these drugs are administered are often chronic, even though drug-induced xerostomia is usually reversible. Regardless of whether the individual prescriptions are xerogenic or not, the chance of developing xerostomia rises with the number of medications consumed The dryness usually begins soon after the problematic medicine is started or when the dosage is increased, Drugs that are diuretic, sympathomimetic, or anticholinergic are typically to blame [22].

2.4. Sjögren's syndrome

Autoimmune diseases that harm cells that produce saliva may be the cause of xerostomia. One such condition is Sjögren's syndrome, which manifests as arthralgia, myalgia, and fatigue. The condition is characterized by incendiary alterations in the glands that create humidity throughout the body, which results in decreased discharges from glands that yield tears, saliva, and other excretions. The combination of xerostomia and dry eyes is known as primary Sjögren's syndrome. Similar to the primary form, secondary Sjögren's syndrome also includes a number of other connective tissue conditions, such as rheumatoid arthritis or systemic lupus erythematosus[13].

2.5. Celiac disease

A small intestine enteropathy is celiac disease. It is brought on by consuming gluten in the diet of those who are vulnerable. It is a genetically determined susceptibility. The only cure for the chronic illness at the moment is to permanently cut out gluten from one's diet [25].

2.6. Radiation therapy

Another significant cause of xerostomia is radiation therapy for head and neck cancers (including brachytherapy for thyroid tumors) in which the salivary glands are near or inside the region that is exposed to radiation. 52 Gy of radiation is enough to seriously impair salivary function. Up to 70 Gy of radiation are typically used in radiotherapy for oral malignancies, which is frequently administered in conjunction with chemotherapy, which may also negatively impact salivary flow. Radiation damage to the parasympathetic nervous system is the cause of this adverse effect [13].

2.7. Sicca syndrome

" The word "sicca" simply means "dry." Although there are different definitions and no particular diagnosis, Sicca syndrome can refer to dryness of the mouth and eyes that is not brought on by autoimmune diseases (e.g., Sjögren syndrome).

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2.8. Other causes

Mouth breathing can also result in oral dryness [24]. which is typically brought on by a partial blockage of the upper respiratory tract. Fever, diarrhea, vomiting, and bleeding are a few examples [25].

Alcohol may contribute to liver illness, dehydration, or disorders of the salivary glands [24]. There is also the potential cause of smoking [22].Other recreational substances including heroin, hallucinogens, cannabis, methamphetamine, and others may be involved. Due to dehydration, hormonal conditions like poorly managed diabetes, chronic graft against host disease, or insufficient water consumption in patients receiving hemodialysis for renal damage can, moreover, cause xerostomia . Oral dehydration may be produced by nerve injury. The nerves connected to salivary flow may be impacted by injury to the skull and neck caused by facial injuries or surgery [13].

Hepatitis C virus (HCV) infection may result in xerostomia, and sarcoidosis is an uncommon cause of dysfunctional salivary glands. A similar salivary gland illness, can result from an infection with the Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (AIDS), like Diffuse Infiltrative Lymphocytosis Syndrome (DILS) [13].

Xerostomia is one of the most common and enduring oral symptoms linked to COVID-19, much like taste dysfunction. In contrast to ageusia, dysgeusia, and hypogeusia, xerostomia, dry mouth, and hyposalivation are often disregarded in COVID-19 patients and survivors, despite their intimate relationship with the virus [26].

3. COMPLICATION

Xerostomia patients can have no symptoms at all or, in rare cases, experience dry mouth and other consequences. Patients typically have trouble swallowing, chewing, speaking, and wearing dentures in addition the oral mucous membrane is sensitive and dry; it is disposed to inflammation, fungal infections, and injuries; it hurts and burns; its taste is changed; and it has halitosis. Patients who suffer from Sjögren's syndrome, which affects the connective tissue and exocrine glands, often complain of dry eyes [27].

To address the issue of xerostomia in individuals with complete dentures, a number of therapy approaches have been proposed. Including salivary replacement reservoirs in dentures is one of these methods of treatment [28]. Table 2.

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Table 2: Consequences and complications of xerostomia [29].

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

4. PREVENTION OF RADIATION XEROSTOMIA

To prevent radiation-induced salivary dysfunction without sacrificing oncologic treatment, a number of techniques have been developed, such as surgical salivary gland transfer, cytoprotectants, and parotid gland sparing radiation therapy [30].

• **Parotid gland-sparing radiotherapy**: In order to prevent needless radiation exposure of the nearby salivary gland, this therapeutic strategy directs the radiation beams toward the target tumor tissue. The use of intensity-modulated RT and 3-dimensional conformal RT techniques in clinical practice made this possible.

• **Cytoprotectants:** The most researched of these drugs is radioprotector amifostine, which has been designed to shield normal tissue from the harmful effects of radiation therapy and/or chemotherapy. In its active form, it enters cells and nuclei and functions as a scavenger of free radicals, preventing deoxyribonucleic acid from being damaged by radiation.

• **Salivary gland transfer**: This method suggests surgically moving the submandibular gland to the sub mental region, away from the radiation's path. This operation is limited if the patient declines surgery, if postoperative radiotherapy is not scheduled for the patient, and if the tumor involves the sub mental space.

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5. COMPLICATION

All patients with dry mouth undergo complications prevention, which tries to stop the onset of stomatitis, dental cavities, and oral fungal infections [30],[31] .

Dental cavities, which can be avoided by using a 1.1% sodium fluoride dentifrice or gel daily, should be closely watched for in patients with severe xerostomia. The degree of caries development, the underlying illness or cause that caused the dry mouth, and the severity of gland dysfunction should all be taken into consideration while using fluoride [32].

6. FUNGAL INFECTIONS (CANDIDOSIS)

At the start of treatment, topical antifungal drugs such as nystatin and amphotericin B were effective for oral candidosis. In patients with dentures and denture stomatitis, a combination of antifungal medications and surface application was reported [30].

7. DENTURE DISCOMFORT

Soaking dentures before putting them in the mouth and misting prostheses with artificial saliva before using denture adhesives12 can assist patients who wear dentures to feel less uncomfortable. Mastication and swallowing will be facilitated by wetting dentures before meals and by consuming more liquids throughout the meal. Discomfort will be reduced with the use of modified denture fabrication, such as flexible complete denture and the split denture technique[31].

8. FINDING OF XEROSTOMIA

The goal of the diagnosis is to minimize adverse effects in xerostomia patients by starting treatment as soon as possible. To ascertain the possible etiological problems and investigate the causes of xerostomia in order to create an analysis, a medical history is necessary. The history of radiation therapy, medication, and the existence of systemic illnesses are therefore three orders of factors that must be understood. The patient is asked a number of questions, such as whether he has xerostomia, whether he has to rinse his mouth, whether he can eat a cracker without drinking water, whether his tongue parts food and adheres to his teeth, and how much water he drinks every day. To ascertain the possible etiological problems and investigate the causes of xerostomia in order to create an analysis, a medical history is necessary. The history of radiation therapy, medication, and the existence of systemic illnesses are therefore three orders of factors that must be understood. The patient is asked a number of questions, such as whether he has dry mouth, whether he has to rinse his mouth, whether he can eat a cracker without drinking water, whether his tongue parts food and adheres to his teeth, and how much water he drinks every day[33].

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Clinical signs like salivary gland palpation, oral mucosa and hydration observation, salivary content under the tongue, cracked lips, saliva entrance and surface, caries detection, candidiasis, burning sensation, and others are used to make the qualitative clinical diagnosis of xerostomia. A number of techniques have been developed to assess the degree of dry mouth, with the most commonly utilized being computed tomography, ultrasonography, magnetic resonance, salivary gland biopsy, sialochemistry, sialometry, and scintigraphy [34].

In command to explore salivary glands anatomy define, sialography is an imaging procedure that requires injecting a backward form of radiopaque substantial into the salivary duct system. Although this test is crucial for demonstrating the existence of nodules or sialectasis, it has drawbacks, including the technique's complexity because it is intrusive and the patient may respond to the contrast material either abruptly or over time.

When the major or minor salivary glands are biopsied, inflammatory infiltrations, acinar destruction, thick mucus-filled salivary channel dilatation, and occasionally fibrosis can be found [35].

Tests like computed tomography, magnetic resonance imaging, and ultrasound can also help diagnose disorders of the salivary glands, determine the cause of symptoms, or assess potential malfunction of the salivary glands [36].

Calculating the rate of salivary flow. To estimate the participation of the salivary glands in patients with dry mouth, complementary procedures such as vitalometry and scintigraphy—an imaging diagnostic technique of nuclear medicine that enables the study of the physiology of the many organs—must be conducted. Sialometry, which includes determining palatal secretion (PAL), unstimulated salivary flow rate (u-SFR), stimulated salivary flow rate (s-SFR) and parotid secretion (PAR), is a rather common procedure in routine scientific repetition [37].

The most straightforward techniques for assessing salivary glandular function are these measures. Measuring salivary flow, or the volume of saliva generated in a given amount of time, is crucial. Hyposalivation is characterized as very low unstimulated and stimulated salivary flow rates of less than 0.1 and 0.7 mL/min, respectively [38].

At rest, the submandibular and sublingual glands produce the majority of the secretion, which varies from 0.25 to 0.35 mL/min. The parotids make up half of the salivary volume when stimulated. The process of measuring how much saliva a person produces at a specific moment is called "stimulated and unstimulated salivary flow." Typically, five minutes are spent measuring the stimulated salivary flow and fifteen minutes are spent measuring the unstimulated salivary flow [39].

This type of measurement has the advantages of being simple to use, inexpensive, and potentially accessible to the majority of the residents at risk. The analysis of the dysfunction of salivary gland is made using information obtained from the patient's symptoms, clinical examination that confirms the clinical signs, then measurement of stimulated salivary flow [32].

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9. TREATMENT

Treating xerostomia successfully is challenging and frequently ineffective [23]. This entails identifying any reason that can be fixed and eliminating it if at all possible; nevertheless, in many situations, the xerostomia itself cannot be fixed, therefore therapy is indicative and also emphases on avoiding tooth decay by enhancing oral hygiene. When xerostomia is brought on by hyposalivation as a result of an underlying chronic illness, it may be permanent or even progressive [24].Saliva stimulants and/or replacements may be used to treat malfunctioning of the salivary glands:

Saliva substitutes are viscous items in the form of mouth rinses , mouth washes , gels , viscous liquids , sprays, oils, and pastilles that are applied to the oral mucosa [13].Water, mucin-based and carboxymethylcellulose-founded artificial salivas, and other materials (milk, vegetable oil) are included in this:

Mucin Spray: Four studies have been conducted to examine the benefits of Mucin Spray on xerostomia; nevertheless, there isn't much proof that Mucin Spray works better than a placebo at easing dry mouth symptoms [13]. Mucin Lozenge: The efficacy of mucin lozenges has only been the subject of one trial [40]. It demonstrated that Mucin Lozenges were unsuccessful as soon as related to a placebo, despite being rated as having a high risk of bias. A mucoadhesive disk is a disk that adheres to the palate and contains flavoring, lubricating, and antibacterial ingredients. They were tested against a placebo disk in one trial. Curiously, patients who received the real disk and those who received a placebo reported feeling more wet in their mouths. There were no negative consequences noted. Before any judgments be made, more research in this area is required [13].

Biotin Oral Balance Gel and toothpaste: The efficiency of Biotin Oral Balance toothpastes and gel has been the subject of one trial. Biotin products were "more effective than control and reduced dry mouth on waking," according to the results [41].

Saliva stimulants include parasympathomimetic medications (choline esters, such as pilocarpine hydrochloride and cholinesterase inhibitors), chewing gum, organic acids (vitamin C or ascorbic acid, malic acid), and other compounds (nicotinamide, sugar-free mints). Historically, oral tablets have been used to provide medications that increase saliva production, which the patient then swallows. Despite this, toothpastes also include some saliva stimulants. Lozenges, which are swallowed after being held in the mouth, are gaining popularity[13].

Pilocarpine: When pilocarpine lozenges were administered, a 2006 study by Taweechaisupapong found no "statistically significant improvement in xerostomia and saliva production compared to placebo [13].

Physostigmine Gel: A study by Knosravini in 2009, revealed that after taking physostigmine, saliva increased five times and mouth dryness decreased. Although chewing gum promotes saliva production, there isn't much proof that it alleviates the symptoms of dry mouth [42].

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"There is insufficient evidence to determine whether pilocarpine or physostigmine are effective treatments for Xerostomia," the Cochrane oral health committee stated. Further investigation is required [13].

While saliva substitutes can help with xerostomia, they usually don't help with the other issues related to malfunctioning salivary glands. Although there is little evidence to support treating radiation-induced xerostomia, parasympathomimetic medications (saliva stimulants) like pilocarpine may alleviate xerostomia signs and extra issues related to salivary gland dysfunction [32]. To a certain degree, stimulants and replacements both alleviate symptoms. Only those who still have some observable salivary function are likely to benefit from salivary stimulants [24]. There was insufficient evidence to support the effectiveness of any particular topical medication, according to a comprehensive analysis that included 36 randomized controlled trials for the treatment of xerostomia. According to this review, topical treatments are only likely to have transient, reversible effects[13].

There was little evidence, according to the review, although sugar-free chewing gum produces more saliva, that oxygenated glycerol triester spray worked well than electrolyte sprays, and there isn't any solid evidence that it alleviates symptoms [13]. Furthermore, there is insufficient data to determine if mastication gum is a more or less successful treatment. Although there was insufficient evidence, there is a possibility that integrated mouthcare systems and intraoral devices may be useful in symptom reduction , There was little indication to provision the administration of pilocarpine in the conduct of radiation-tempted salivary gland dysfunction, according to an organized evaluation of the control of radiotherapy-tempted dry mouth with parasympathomimetic medications. It was recommended that the aforementioned group be given a trial of the medication, unless there are any contraindications (at a dosage of five milligrams three times per day to diminish lateral effects) [43].

It may take up to 12 weeks to see improvements. Pilocarpine, however, does not always work to alleviate the symptoms of xerostomia. The evaluation also found that the use of additional parasympathomimetics in this group was not well supported by the available data [44]. According to a different systematic review, there is some weak evidence that amifostine can prevent dehydrated mouth or lower the threat of reasonable to severe dry mouth in patients undergoing head and neck radiation therapy (with or without chemotherapy) in the short- to medium-term (three months after radiation) period. However, it is unclear if this impact lasts for a full year after radiation treatment [45].

The patient's oral and overall health are impacted by xerostomia, or dry mouth, which lowers their quality of life. Therefore, it will be necessary to integrate the evaluation of salivary gland hypofunction, early detection, prevention, and treatment of dry mouth and associated sequelae into routine clinical dentistry practice.

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Conflict of interests.

There is no conflict of interests.

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