Review

Dry mouth: A critical topic for older adult patients

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A B S T R A C T

Purpose: Diminished salivary flow, or dry mouth impacts the oral health of many older adults, dentate and edentulous. As a result typical oral conditions can prove more challenging to both the patient’s comfort and home care and the treatment selected by the clinician. This paper will review issues of dry mouth from a clinical and symptomatic perspective and will include the condition’s causes, treatment and prevention.

Study selection: We performed a review of PubMed using the words: older adults, dry mouth, xerostomia, radiation-induced xerostomia, and salivary gland hypofunction. We selected 90 articles with a clinical application perspective.

Results: When it comes to treatment of dry mouth conditions, either objective or subjective, there are no easy answers as to the best course of action for a specific individual. While most of the cited studies have examined the most difficult cases of dry mouth (e.g. Sjögren’s syndrome, and that seen during and post head and neck cancer treatments), there are many older adults who demonstrate dry mouth from the use of multiple medications. This paper presents a summary of the etiology, diagnosis, prevention, and pharmacological and non-pharmacological treatment of dry mouth (salivary hypofunction and xerostomia in older adults).

Conclusions: It is important to understand the causes of dry mouth and to educate our patients. Starting a prevention program as early as possible considering the most practical, cost effective and efficient treatments with the best risk-benefit ratio will help to diminish dry mouth symptoms and sequelae.

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1. Overview of older adults and oral conditions

The proportion of older adult people in developed countries has increased considerably during the last few decades and is expected to increase further in the next years. This is a result of what has been called the “demographic transition,” a term used to describe the increasing life expectancy and concurrent fall in the birth rate occurring in industrialized nations [1]. Japan has led the way in this shift with people aged 65 years or more currently comprising 23% of the Japanese population and projected to increase to 38% of the population by 2050 [2]. Although this growth in the percentage of elderly in the population may not be as marked in other developed countries, the same trends are evident. In China, the equivalent estimates are 8% currently with 23% being projected for 2050; in Europe, the equivalent proportions are 16% and 27%; in North America, 13% and 22% and in New Zealand, 14% and 25%. This demographic shift to greater percentages of older adults will have important implications for health care services. Larger populations of elderly often mean greater numbers of the oldest of the old: that is, people 80 years of age and older, who frequently are frailer and face more morbidity and disabilities. Consequently, an increasing proportion of health care services will be required for these individuals than is routinely needed for younger elderly, the 65–79 year olds [3].

Advances in oral health care and treatment during the past few decades have resulted in a reduced number of edentulous with the proportion of adults who retain their teeth until late in life increasing substantially [2,4]. The numbers of older people with oral related problems, including those who are dentate has also increased. The complexity of oral health status, numerous co-existing systemic diseases and the use of multiple medications make older people more vulnerable to oral problems when compared to younger groups. This is even truer for those elders who are cognitively impaired [5,6]. Recent literature has described the relevant medical characteristics of old age, including the multi-morbidity, poly-pharmacy, frailty, disability and care dependency as the “geriatric syndrome” [7]. Van der Putten and de Baat suggested that weakened oral health has the potential to become a component of the geriatric syndrome [8].

The oral health of older people has warranted considerable research attention in the last two to three decades. In discussing the epidemiology of oral conditions among this group, Murray included the following listing of findings: tooth loss, dental caries, periodontitis, dry mouth, oral pre-cancerous or cancerous lesions and oral health related quality of life [9]. Van der Putten and de Baat added to this list the findings of substantial tooth wear, oral implants and sophisticated tooth and implant supported removable dentures and/or fixed dental prostheses [8], concluding that older adults are in continuous need of preventive and curative oral health care.
Mulligan and Vanderlinde suggested a model to follow in order to cover the interactions of the medical, behavioral, dental/oral and psychosocial factors of older adults [10]. All of these topics in any detail would result in a lengthy treatise beyond the scope of most periodicals. Therefore, this paper will limit itself to a discussion of just one of the clinical conditions frequently seen in older adults: dry mouth. We feel this topic to be particularly relevant as a geriatric dentistry foundation topic, for in caring for elders, practitioners soon discover the interrelationship of many of the oral conditions previously mentioned with dry mouth. Therefore this review article will focus on diminished salivary flow, or dry mouth sensations from a clinical and symptomatic perspective. Causes, treatment and prevention will be considered.

2. Saliva, its function and benefits

Saliva provides important protection to the teeth and the tissues of the mouth due to its cleansing, lubricating and antimicrobial properties [11,12]; promotion of remineralization of the teeth; transport of digestive enzymes; and assistance in speech, mastication and deglutition [13–15]. When the term “dry mouth” is invoked, it should be used to describe the objective finding of a decrease in the amount of saliva secreted as measured through a clinical assessment technique. Such a finding could also be called, salivary hypofunction [16]. During this clinical assessment there may also be a finding of a change in the physical composition of saliva such as its viscosity (provided mostly by mucins) – that can be evaluated by collecting samples on paper strips from different mucosal surfaces- or color (clear or cloudy) that may indicate infection or be a further indication of decreased volume [17–19].

The term “dry mouth” has also been used to describe the patient’s subjective sensation, which is correctly called “xerostomia.” Such a sensation may also be found even in patients with normal salivary gland function [20]. Studies have demonstrated that dry mouth is a very common symptom. Hopcraft and Tan indicate that there is a 20% prevalence of dry mouth complaints in the general population [15].

Typical saliva production has been measured at 0.5–1.5 l per day in the healthy adult [21]. Saliva is produced by three pairs of major salivary glands (parotid, submandibular and sublingual), which make a significant contribution to the overall amount of mixed saliva found in the mouth (90% by some estimates) with the remainder coming from the minor salivary glands located throughout the oral cavity on the mucosal surfaces. Saliva is produced by acinar cells of two types: serous and mucous cells with serous cells making up the majority of the parotid gland, mucous cells making up the sublingual gland and the submandibular gland containing a combination of mucous and acinar cells [22]. For the most part the minor salivary glands are mixed glands although there are a few that are strictly mucous (palatinal glands) and some that are serous (lingual von Ebner’s glands) [23,24].

The sympathetic and parasympathetic nervous systems are independently involved in the secretion of saliva with the fluid component including ions, responding to the parasympathetic system and a protein component responding to sympathetic stimuli [22,25]. Control of salivary secretion is complex with the sympathetic and parasympathetic systems regulating not only the secretory function but also the reabsorption process that goes on in the striated ducts of salivary glands [26,27]. In addition to conditioned reflexes (remember Pavlov’s dog studies), unconditioned reflexes can also stimulate salivary flow [28]. For example, mastication affects the salivary flow rate via periodontal mechanoreceptors and mechanical stimulation of the oral mucosa and tongue.

3. Salivary gland hypofunction in aging

3.1. Epidemiology

Epidemiologic studies have revealed increases in the prevalence and incidence of dry mouth with age [29,30]; however, in most studies aging per se is not indicated as the cause or a major risk factor for dry mouth. It has been hypothesized that this is due to the reserve functional capacity of the salivary glands usually compensating for the loss of acinar tissue that is associated with aging changes in the glands [29]. In contrast to this finding, a recent paper by Smith et al. examined a 1-min stimulated flow collection of whole saliva from three different age groups (n = 180 per group) and did find that with aging (≥70 years) there was a significantly decreased flow rate [31]. This paper is noteworthy in that the stringent exclusion criteria ensured that individuals with medical conditions and/or medications that could impact salivary flow were excluded from participating.

3.2. Effects of salivary hypofunction

Reduced salivary flow has many detrimental effects on oral health including increasing the risk of dental erosion, demineralization, dental caries, periodontitis, and intra-oral infections such as candidiasis [13,14,32]. Halitosis, burning mouth, oral soreness, difficulty in mastication, speech dys-function, dysgeusia (taste disturbance) and dysphagia (difficulty swallowing) have all been linked to this finding [33,34].

3.3. Causes of hypofunction

Salivary gland hypofunction (SGH) may result from many conditions directly or indirectly affecting the salivary glands [16,35,36]. Such hypo-function may signal the presence of serious underlying systemic diseases such as Sjogren’s syndrome [37] and by itself can have overwhelming effects on the oral health that may be observed in both the hard and soft tissues of the mouth [34]. The oral mucosa may become atrophic predisposing the individual to frequent ulcers and trauma and the teeth can become carious as a result of the shift in the acid/base balance or pH of the saliva, thereby diminishing its buffering capacity. Changes in the concentration of immune-proteins especially when they are related to radiation therapy can also be found [38,39].

3.4. Salivary hypofunction flow values

The cut-off salivary flow values in individual glands for a diagnosis of SGH are based on the following flow rates: unstimulated submandibular/sublingual (sm/sl) or parotid
saliva flow of <0.05 mL/min; stimulated sm/sl or parotid saliva flow <0.15 mL/min [40–42].

As has been previously mentioned, xerostomia is the subjective sensation of oral dryness. When it does correlate with clinical findings of salivary hypofunction, typically the salivary flow has decreased by more than 40–50% from its usual rate [41,43].

4. Risk factors for either salivary hypofunction or xerostomia

Female sex is another known risk factor for dry mouth. Epidemiologic studies have demonstrated that female patients have a higher prevalence of the perceived symptoms of a dry mouth sensation or xerostomia than males do at all ages [30]. Even though female patients are likely to take more medications than the male patients, the prevalence of xerostomia was still high in non-medicated females compared to their male counterparts [30,44]. However, in the study by Smith et al. healthy females did not differ significantly from healthy males in the same age group when stimulated salivary flow was measured objectively [31].

Common habits such as smoking, alcohol use (including its topical use such as in mouthwashes) and the drinking of caffeine containing beverages such as coffee and soft drinks can result in a clinical finding of oral dryness. In these instances dry mouth is reversible by avoiding or reducing the habit or consumption of the implicated products [25]. Other temporary causes of dry mouth include heavy snoring, mouth breathing, upper respiratory tract infections, dehydration and fear [45]. Salivary gland atrophy will result in decreased salivary flow and can occur when there are prolonged periods of autonomic denervation such as liquid diet feeding, thus reducing the salivary flow reflex; or salivary duct ligation, which may be done to decrease or eliminate drooling. However, with intact autonomic innervation, there is regenerative capacity in the glands and they regain normal function upon removal of the ligation or reintroduction of feeding by mouth [46].

Various conditions can lead to a major reduction in secretion of saliva (e.g. Sjogren’s and radiation therapy) but it is also a frequent occurrence as a side effect of multiple medications.

5. Diagnosing xerostomia and salivary gland hypofunction (SGH)

There are numerous questionnaires used to assess dry mouth symptoms, including various quality of life scales and some specific instruments such as the Xerostomia Questionnaire (XQ) [22] and the Xerostomia Inventory (XI) [47,48]. An extensive discussion of the different instruments (objective and subjective) to measure xerostomia is available in the article by Sasportas et al. [49].

5.1. Diagnosing xerostomia

The Xerostomia Inventory (XI), is reliable, reflects many manifestations of the xerostomic experience, has appropriate wording, is grounded in the experiences of xerostomic sufferers and is easy to administer. For example, it could be mailed to the patients for them to fill out and bring to their next appointment; it does not need the presence of the dentist or a trained staff member to collect the information. The XI consists of an 11-item summed rating scale with each response assigned a score between 1 and 5 and the combined total score calculated into a sum ranging from 11 to 55, that represents the severity of the underlying xerostomia. A score of 11 is characterized as very mild xerostomia and 55 represents severe xerostomia [50].

The XI has been validated to provide a both a discriminative measure of the severity of dry mouth symptoms as well as serve as a responsive measure to determine the success of interventions for dry mouth. A change in XI score of 6 or more points is likely to be clinically meaningful [20,50]. These are the 11 questions from the XI that individuals are asked to choose a response for, from neuer 1, hardly ever 2, occasionally 3, fairly often 4, very often 5.

1. My mouth feels dry
2. I have difficulty in eating dry foods
3. I get up at night to drink
4. My mouth feels dry when eating a meal
5. I sip liquids to aid in swallowing food
6. I suck sweets or cough lollies to relieve dry mouth
7. I have difficulties swallowing certain foods
8. The skin of my face feels dry
9. My eyes feels dry
10. My lips feel dry
11. The inside of my nose feels dry

5.2. Diagnosing salivary hypofunction

There are many ways to measure salivary flow from individual glands, combined oral surfaces (whole mouth measurement), during rest (drooling) or when stimulated (chewing a neutral substances or gustatory stimulants) [51]. Some of the methods are more relevant for research based collections [51,52] and others are more practical for the clinicians to perform in their practice. Navazesh et al. provides an extensive review on saliva collection methods [51–54].

Smith recommended a whole stimulated saliva collection consisting of having each subject chew on two pieces of gauze for 1 min, the weights of the gauzes having been measured before and after the exercise. This method is simple and inexpensive, and requires minimal equipment. It has been demonstrated to be a reliable method of assessment of the function of the salivary glands in patients with dry mouth [55]. Another method of interest is an adaptation of the Schirmer Test used to measure eye dryness [56]. Chen et al. recommended the Modified Schirmer Test (MST) to provide a quick screening for salivary gland hypofunction in any office setting; as it is performed in less than 5 min, is inexpensive, does not need sophisticated equipment and has acceptance from the patients [14].

6. Medications and their effects on saliva

By far, the most common cause of long standing dry mouth particularly in older adults is the use of xerogenic medications
Table 1 – Etiology or causes of salivary gland hypofunction and xerostomia [25,29,44,46,58,64,65].

| General | • Old age  
|         | • Female sex  
|         | • Dehydration  
|         | • Disability (cognitive and physical)  
|         | • Institutionalization  
|         | • Habits (mouth breathing, smoking, alcohol and drug abuse)  
|         | • Compromised masticatory function  
| Iatrogenic | • Medications*  
|         | • Therapeutic irradiation*  
|         | • Chemotherapy/immunotherapy  
|         | • Chronic graft vs host disease  
|         | • Salivary duct ligation  
|         | • Liquid diet feeding  
| Diseases | Salivary gland diseases and disorders  
|         | • Agenesis of the salivary glands  
|         |   (with or without ectodermal dysplasia)  
|         | • Sialoadenitis  
|         | • Sialolithiasis  
|         | Chronic inflammatory autoimmune disease  
|         | • Sjogren’s syndrome  
|         | • Other rheumatologic diseases; Rheumatoid arthritis, SLE, scleroderma, mixed connective tissue disease, etc.  
|         | • Sarcoidosis  
|         | • Amyloidosis  
|         | • Crohn’s disease, ulcerative colitis  
|         | Endocrine diseases  
|         | • Diabetes mellitus  
|         | • Hyper- and hypothyroidism  
|         | • Cushing’s syndrome  
|         | • Addison’s disease  
| Neurologic diseases and disorders | Stroke  
|         | Parkinson’s disease  
|         | Bell’s palsy  
|         | Alzheimer’s disease  
| Psychogenic diseases and conditions | Stress  
|         | Anxiety and nervousness  
|         | Depression  
|         | Eating disorders (anorexia nervosa, bulimia)  
| Infections | HIV/AIDS  
|         | HCV  
|         | Tuberculosis  
|         | Human T lymphotropic virus (HTLV-1)  
| Others | Cystic fibrosis  
|         | Hypertension  
|         | Fibromyalgia  
|         | Chronic fatigue syndrome  
|         | Burning mouth syndrome  
|         | Primary biliary cirrhosis  
|         | Liver transplant candidates  
|         | Renal diseases and Renal dialysis  
|         | Anemia  
|         | Atrophic gastritis  

* Major causes of dry mouth.

commonly the inhibition is due to the impact of the drug on central and peripheral receptors resulting in anticholinergic activity against the M3 muscarinic receptors; the end result being reduced salivation [25,35,61].

A review of oral side effects of 131 of the most frequently prescribed drugs in the USA in 1992 showed dry mouth or xerostomia to be the most common oral side effect (80.5%) followed by alteration in taste (47.5%) and stomatitis (33.95%) [55]. In a study by Thomson et al., 42.3% of the medications taken by institutionalized older adults presented xerogenic effects [62].

Drugs most commonly implicated with subjective and objective dry mouth are the medications with anticholinergic actions, sympathomimetic actions, such as tricyclic antidepressants, antipsychotics, atropinic drugs to treat overactive bladder, decongestants, bronchodilators, anti-hypertensive drugs including beta-blockers and diuretics, anti-histamines, sedative hypnotics, opiates, and muscle relaxants [25,31,59,60,62]. Chemotherapeutic agents such as cytotoxic drugs and cytokines, retinoids, thyroid supplements, and anti-HIV medications are also known to cause dry mouth as the common adverse effect [55,60]. Selective drugs that may give rise to dry mouth are summarized in Table 2. A complete and searchable list of drugs associated with dry mouth with the frequency of dry mouth reported by patients taking these drugs, is provided on the following website: www.drymouth.info [59].

6.1. Medication effect on saliva in the older adult

The prevalence of dry mouth increases with increasing numbers of medications used for one or more conditions (polypharmacy) [25,29,30,44,62,63]. The prevalence of the perceived symptoms of dry mouth among subjects aged 20–80 years was 17% in patients taking no medication, 33.5% in patients taking 3 medications and 67% with the use of more than or equal to 7 medications [30,44]. In a study that focuses on only older adult patients (age > 65 years) with limited mobility, limited resources or complex health status, the prevalence jumps to 37% when taking 1 medication, 62% with 2 medications and reaches 78% when 3 medications were used [29]. Age and medication seemed to play a more central role when there was objective evidence of hypo-salivation while female gender and psychological factors were more related to the subjective sensation of oral dryness. Clearly the presence of medication is a more likely predictor of the risk of dry mouth than either age or gender [25]. When drug-associated symptoms of dry mouth occur, the timeline of the symptoms and the initiation of the medication are likely to be closely related [60].

7. Other conditions affecting salivary glands

7.1. Systemic diseases

Many systemic diseases are reported to cause or be associated with salivary gland hypofunction as mentioned in Table 1 [29,64]. Of these systemic diseases, Sjogren’s syndrome (SS) is the most common disease that causes both xerostomia and

[30]. There are now projected to be over a thousand medications associated with subjective and/or objective oral dryness either by interfering with the production of saliva or the pathways responsible for saliva secretions [31,57–60]. Most
salivary gland hypofunction with the incidence of xerostomia in the SS patient reaching nearly 100% [29,65]. SS is a chronic, autoimmune disease that is characterized by progressive injury to the exocrine glands, mainly the lacrimal glands and the salivary glands. Although the exact mechanism of SS is not known, it is associated with B lymphocyte hyper-reactivity, autoantibody production and T-cell lymphocytic infiltration to exocrine glands and other organs [65]. SS may present as a primary disease or a secondary disease that is associated with other autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus and systemic sclerosis [64,65]. All ages can be affected by SS but it generally becomes overt during the fourth and fifth decade of life [65] and elderly patients account for up to 20% of Sjögren’s cases [29]. As the HIV infected population ages, more salivary conditions are being noted as a result of the HIV virus or the anti-retrovirals used for its treatment. Mulligan et al. also found that women who are HIV positive presented salivary gland disease manifest by glandular enlargement, tenderness, and absence of saliva on palpation [66].

7.2 Radiation therapy effects

Another major cause of dry mouth is head and neck radiation with or without chemotherapy for cancer treatment at or near salivary glands. Radiotherapy in the head and/or neck region can cause temporary or permanent damage to the salivary glands [25,29,58,65,67]. Salivary flow rates were the most severely reduced in patients with a history of radiation therapy when compared with patients with SS patients or patients on xerogenic medications [68]. Once head and neck radiation therapy is begun, salivary gland flow decreases as does oral health related quality of life; these reductions often continue on a chronic basis and may result in a lifelong condition [68,69]. The prevalence and the severity of xerostomia and salivary gland hypofunction in head and neck cancer patients depends on the tumor site, stage, type of radiation therapy, the cumulative dose of irradiation, and the volume of salivary gland tissue included in the treatment portals [69].

The highest prevalence and severity of salivary gland hypofunction and xerostomia has been reported in nasopharyngeal [29,69] and oropharyngeal carcinoma where all salivary glands bilaterally are included in the radiation treatment. In contrast, the least prevalence of these conditions are when the cancer is located in the laryngeal/epilaryngeal area, which is more remote from the salivary glands [69]. Conventional radiotherapy doses of ~60 Gy to the glandular tissue results in high rates of tissue destruction and the described sequelae [69]. The treatment of head and neck cancer with radiation usually is extended over 5–7 weeks and

| **Table 2** - Partial list of medications that have the potential to cause dry mouth [44,45,58,59,64,65]. |
|---|---|---|
| **Action by which the drug causes dry mouth** | **Pharmacologic group** | **Partial list of drugs** |
| Anticholinergic action | Tricyclic antidepressants | Amitriptyline, Nortriptyline, Clomipramine, Imipramine |
| | Antipsychotics | Phenothiazine, Clozapine, Olanzapine, Quetiapine, |
| | Muscarinic receptor antagonist | Prochlorperazine, Respiridone, Lithium |
| | Alpha-receptor antagonists | Oxybutynin |
| | Diuretics | Tamsulosin, Terazosin |
| | Antihistamine | Furosemide, Bumetanide, Torsemide |
| | Antiinetics/drugs for vertigo | Loratidine, Promethazine, Chlorpheniramine, Hydroxyzine, |
| | Anti-Parkinson’s drugs | Diphenhydramine, Cetirizine |
| | Bronchodilator | Scopolamine |
| | Atropine and analogs | Biperiden, Amantadine, Levodopa Carbipoda |
| | | Propanolol bromide |
| | Sympathomimetic | Ipratropium bromide, Tiotropium bromide |
| | Antidepressants: SSRI, SNRI | Atropine, Benzoprine |
| | Antihypertensive | Venlafaxine, Duloxetine, Mirtazapine, Bupropion |
| | Appetite suppressants and | Metoprolol, Timolol, Clonidine, Prazosin, Terazosin |
| | CNS stimulants | Phentermine, Amphetamine/Dextroamphetamine |
| | Decongestants and cold cures | Pseudoephedrine |
| | Bronchodilators | Albuterol, Formoterol, |
| | Skeletal muscle relaxants | Cyclobenzaprine, Tizanidine, |
| | Antimigraine agents | Zolmitriptan, Rizatryptan |
| Synergistic action (Anticholinergic + Sympathomimetic) | Opioids | Fentanyl, Tramadol, Oxycodone |
| | Nonbenzodiazepine hypnotics | Zolpidem, Eszopiclone, Zopiclone |
| | Benzodiazepine | Alprazolam, Lorazepam, Diazepam, Triazolam, |
| | Drug of abuse | Temazepam Methamphetamine |
| Others | H2 antagonists, proton pump inhibitors | Omeprazole |
| | Antibiotics | Amoxicillin, Tetracycline, Metronidazole |
| | Antineoplastic/cytotoxic drugs | Interferon Alpha, Fluorouracil, IL2 |
| | Anti-HIV drugs | Didanosine, Protease inhibitors such as indinavir |
| | Supplements | Retinoids |
includes a total dose of 50–70 Gy delivered in daily allotments of 1.8–2.0 Gy [70]. Salivary flow begins to be impacted fairly quickly after initiation of therapy, falling to 50–70% of baseline once 10–16 Gy is delivered. Flow becomes nearly undetectable after the cumulative doses of 40–42 Gy [68,70].

Radiation induced salivary hypofunction is accompanied by changes in the composition of saliva, including the lowering of salivary pH and therefore buffering capacity, and decreases in amylase activity, while at the same time it demonstrates increasing osmolality and viscosity, and higher concentrations of lactoferrin, protein, sodium, chloride, alterations in mucin and calcium concentration [29,70]. Using 3D conformal radiation therapy can reduce the radiation dosage to the contralateral parotid gland and Intensity-Modulated Radiation Therapy (IMRT) allows more accurate delivery of specific radiation dosage and distribution to the tumor mass, while sparing the salivary glands. By doing so, both 3D conformal radiation therapy and IMRT can decrease the prevalence and severity of radiation induced salivary hypofunction [69]. In addition to salivary hypofunction, there are other head and neck radiation induced outcomes that can occur including taste loss, mucositis, radiation caries and susceptibility to osteonecrosis of the jaw bone, all of which can negatively impact oral health related quality of life (Fig. 1) [64,69,71].

Other treatments for cancer such as radioactive iodine therapy, total body irradiation/chemotherapy and hematopoietic stem cell transplantation, chemotherapy, and immunotherapy have also been reported to have the potential of causing dry mouth but there is not sufficient data to report on the severity and grading of the resulting dry mouth outcomes [69].

8. Management of dry mouth

The management of dry mouth includes two aspects: attempts to affect a change in the causative factors of the condition; and, the prevention of any potential or worsening of existing consequences of dry mouth on oral health.

8.1. Diagnosis directed management

In order to determine where intervention may benefit, an accurate diagnosis of the cause and severity of dry mouth is the most important prerequisite for its treatment. The diagnostic process should include a thorough history of the symptoms, the patient’s medication and medical history, a complete clinical examination with salivary flow rate measurements (both stimulated and unstimulated flow rates if possible), as well as imaging examinations, salivary gland biopsies and laboratory analysis when needed (Fig. 2) [63]. Subsequently treatment can be directed at providing salivary substitutes and/or oral mucosal lubricants for palliation of the symptoms and/or to stimulation of the salivary secretion from remaining glandular tissue. The sequencing of this process, as described by Närhi et al. can be found outlined in Fig. 2 [63].

8.2. Modifiable behaviors

An extensive list of the results of various investigations, including laboratory studies, imaging, biopsy and other measurement results for patients with prolonged dry mouth is reported elsewhere [58]. Temporary causes of dry mouth can be improved by avoiding or reducing intake of substances such as caffeine, alcohol or hot and spicy foods eaten. Other actions include the avoidance of mouth breathing and dehydration. Patients with long standing habits of smoking and alcohol usage may require the help of behavioral psychologists to wean them from the offending substance that is a causative or contributory factor to their dry mouth condition.

8.3. Medication substitution or dosing changes

Medication induced salivary gland hypofunction is often a reversible condition and ceasing the drug therapy, reducing the number or dosage of medications or substituting the medication for a less xerogenic alternative may bring the salivary flow back to normal [25,59,63]. However, it is important to note that only a few studies compare the relative xerogenic potential of one drug to another and the knowledge on the relative effects of drugs to induce dry mouth is limited. So, such a substitution process has to be done by trial and error and the result may vary for each patient [59]. If the value of medical treatment outweighs any substitution or dosage adjustments, symptomatic treatments for dry mouth are indicated [25,63]. In some cases, it may be possible to manage the dry mouth symptoms through optimal management of the underlying diseases such as better management of diabetes, Sjogren’s syndrome, sarcoidosis, or HIV.

8.4. Chronic conditions

Management strategies for long-standing symptoms in patients with histories of head and neck radiation or systemic diseases with prolonged salivary gland hypofunction include a variety of topical and systemic management options [58]. Almost all cases of dry mouth will benefit from symptomatic
therapy irrespective of etiology [63]. The goal is to moisten the oral mucosa. Non-specific palliative management of dry mouth includes sipping water and sucking on ice chips frequently throughout the day to provide moisture [44,58,63]. For elderly patients, the use of water or ice chips should not be dependent on thirst sensations since satiety and thirst reflexes are obtunded in older age groups [72]. Water and glycerin in small spray bottles can also be useful for some patients for periodic relief of dry mouth during the day; and adding moisture to the environment at night with a room humidifier may give some relief during sleep.

8.5. Various treatment modalities

Several mouth moisteners in the form of salivary substitutes or artificial saliva are available as rinses, aerosols, toothpastes, mouthwashes, lozenges or chewing gums in the U.S. and worldwide, Table 3 [58,59,73,74]. The principal idea of these salivary substitutes is to provide a long lasting coating of the oral soft tissues. But sprays, liquids or gels may need to be applied frequently throughout the day (at least 3–4 times a day) depending on their adherence and/or lasting abilities. Lozenges or pastilles may provide a more discrete and socially acceptable means of adding moisture to the mouth, since their usage may be better hidden, however one needs to be aware of hidden sugars in some of these products [73,74].

Most of the currently available preparations to moisten the mouth contain either carboxymethylcellulose or mucins although preparations based on hydroxyethylcellulose, polyglycerylmethacrylate, hydroxypropylmethylcellulose, glycerol, canola oil, olive oil, and linseed extract are also reported to be useful [73]. Sugar free chewing gums of various types, sweetened with sugar substitutes, xylitol or sorbitol, can be used by patients during waking hours. These chewing gums stimulate salivary production by topical gustatory or masticatory action [25,73]. There is no evidence that gum is better or worse than saliva substitutes probably because gums are effective only if there is remaining salivary functional tissue [73,74]. However, chewing gums can be problematic for older adults especially those who wear removable appliances [45] or have arthritis effecting the temporo-mandibular joint (TMJ). Lozenges or pastilles containing Xylitol that dissolve on the tongue or are adherent to the buccal surface of the tooth and are not to be chewed, may give better patient comfort for these cases, with less likelihood of adhering to the denture component or aggravating TM joints.
Table 3 – Selective topical salivary stimulators, oral moisturizers and salivary substitutes for Dry Mouth signs and symptoms.a

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Products</th>
<th>Active ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugarless chewing gums</td>
<td>Biotene dry mouth gum (GlaxoSmithKline)</td>
<td>Sorbitol, xylitol, maltitol</td>
</tr>
<tr>
<td>Orbit (Wm. Wrigley Jr. Company)</td>
<td>Sorbitol, mannitol, xylitol</td>
<td></td>
</tr>
<tr>
<td>Eclipse (Wm. Wrigley Jr. Company)</td>
<td>Maltitol, sorbitol, mannitol</td>
<td></td>
</tr>
<tr>
<td>Extra (Wm. Wrigley Jr. Company)</td>
<td>Sorbitol, mannitol, maltitol</td>
<td></td>
</tr>
<tr>
<td>Trident/Stimoral (Mondelez International)</td>
<td>Xylitol, sorbitol, mannitol</td>
<td></td>
</tr>
<tr>
<td>Ice Breakers (The Hershey Company)</td>
<td>Xylitol</td>
<td></td>
</tr>
<tr>
<td>Xylifresh (Leaf International)</td>
<td>Xylitol</td>
<td></td>
</tr>
<tr>
<td>Spry Xylitol Gum (Spry Dental Defense System)</td>
<td>Xylitol, sorbitol</td>
<td></td>
</tr>
<tr>
<td>Smint (Perfetti Van Melle)</td>
<td>Xylitol</td>
<td></td>
</tr>
<tr>
<td>Sugarless tablets/discs/patches</td>
<td>Salix SST (Scandinavian Natural Health &amp; Beauty Products, Inc)</td>
<td>Sorbitol, fruit acid</td>
</tr>
<tr>
<td>Xylimefts (Orahealth Corporation)</td>
<td>Xylitol</td>
<td></td>
</tr>
<tr>
<td>Sugarless solution/spray</td>
<td>Mouth-Kote (Parnell Pharmaceuticals, Inc.)</td>
<td>Yerba santa, xylitol, lemon oil</td>
</tr>
<tr>
<td>Sugarless hard candy, mints, lozenges or lemon drops</td>
<td>Many preparations available</td>
<td>Sugar substitutes, citric acid, etc.</td>
</tr>
<tr>
<td>Mouth rinses/washes</td>
<td>Biotene Dry Mouth Oral Rinse (GlaxoSmithKline)</td>
<td>Glycerin, xylitol, sorbitol, propylene glycol, hydroxyethyl cellulose</td>
</tr>
<tr>
<td>Colgate® Dry Mouth Relief Fluoride Mouthwash (Colgate)</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>Spray Oral Rinse (Spry Dental Defense System)*</td>
<td>Xylitol, glycerin</td>
<td></td>
</tr>
<tr>
<td>Oasis Moisturizing Mouth Wash (Oasis Consumer Healthcare)</td>
<td>Glycerin, water, sorbitol</td>
<td></td>
</tr>
<tr>
<td>Act Total Care Dry Mouth Soothing Mouthwash (Chattem, Inc.)</td>
<td>Glycerin, sorbitol, xylitol, propylene glycol</td>
<td></td>
</tr>
<tr>
<td>Patches</td>
<td>Oramoist dry mouth Patches (Quantum)</td>
<td>Xylitol, polyvinylpyrrolidone, carborner homopolymer, hydroxypropyl cellulose, lysosome, lactoferrin</td>
</tr>
<tr>
<td>Spray</td>
<td>Water/Glycerine Spray</td>
<td>Glycerin</td>
</tr>
<tr>
<td>MOI-STIR (Pendopharm, Pharmascience Inc.)</td>
<td>Carboxymethylcellulose sodium, glycerin</td>
<td></td>
</tr>
<tr>
<td>Biotene Moisturizing Mouth Spray (GlaxoSmithKline)</td>
<td>Glycerin, xylitol, hydrogenated castor oil</td>
<td></td>
</tr>
<tr>
<td>Oralube (Perrigo Australia)</td>
<td>Methyl hydroxybenzoate, sorbitol</td>
<td></td>
</tr>
<tr>
<td>Spry Oral Mist (Spry Dental Defense System)</td>
<td>Glycerin, Xylitol, Sorbitol</td>
<td></td>
</tr>
<tr>
<td>Oasis Moisturizing Mouth Spray (Oasis Consumer Healthcare)</td>
<td>Glycerin, sorbitol, poloxamer 338, PEG 60, hydrogenated castor oil</td>
<td></td>
</tr>
<tr>
<td>CVS Dry Mouth Spray (CVS Pharmacy)/Rite Aid Dry Mouth Spray (Rite Aid Pharmacy)</td>
<td>Xylitol, aloe vera, lactoferrin, lysozyme, glucosidase, amylose, amylogucosidase, peptizyme</td>
<td></td>
</tr>
<tr>
<td>Gel</td>
<td>GC Dry Mouth Gel (GC America Inc.) Dentist dispensed</td>
<td>Not available</td>
</tr>
<tr>
<td>Biotene Oral Balance Moisturizing Gel (GlaxoSmithKline)</td>
<td>Glycerin, sorbitol, xylitol, carberner, hydroxyethyl cellulose</td>
<td></td>
</tr>
<tr>
<td>Orajel Dry Mouth Gel (Church &amp; Dwight, Inc.)</td>
<td>Glycerin</td>
<td></td>
</tr>
<tr>
<td>Toothpaste</td>
<td>Biotene Dry Mouth Fluoride Toothpaste (GlaxoSmithKline)</td>
<td>Glycerin, sorbitol</td>
</tr>
<tr>
<td>Spry toothpaste (Spry Dental Defense System)</td>
<td>Glycerin, xylitol, sorbitol</td>
<td></td>
</tr>
<tr>
<td>Saliva Substitute (Roxane laboratories)</td>
<td>Purified water, sorbitol, sodium carboxymethylcellulose, etc.</td>
<td></td>
</tr>
</tbody>
</table>

This table is based on the information acquired from http://www.drymouth.info/practitioner/treatment.asp and web searches.

a Some products contain citric acid and alcohol, which can irritate the mucosa of patients with dry mouth. Many dry mouth products contain fluoride.

8.6. Toothpastes, fluoride as treatment

Toothpastes designed for the treatment of dry mouth may subjectively improve symptoms but do not improve salivary gland function [73]. Many people with dry mouth prefer non-foaming gel type toothpastes that are less irritating than foaming toothpastes, which have surfactants in them that can prove to be problematic [25]. Since reduced salivary flow can have detrimental effects on the dentition, aggressive caries prevention and management play vital roles in maintaining the dentition for patients with dry mouth [32]. Regular dental visits and a meticulous oral hygiene regimen should be encouraged [32]. Both professionally applied varnish (2.26% fluoride or 5% Sodium fluoride varnish) and prescription-strength, home-use topical fluorides (0.5% fluoride or 1.1% neutral sodium fluoride gel/paste, 0.09% fluoride mouth rinse)
have been recommended as effective and beneficial measures for caries prevention in older adults [32,75].

8.7. Effectiveness of topicals

Although some topical agents, by patient report, do seem to cause a lessening of dry mouth symptoms, thus improving the quality of life for some, there is no strong scientific evidence that any topical treatment is effective for relieving the sensation of dry mouth [74] and recent literature indicates that no one topical agent is better than another [73]. Patient preference appears to play a significant role in the acceptance and attribution of efficacy [32,74]. The make-up of most lubricants and salivary substitutes do not duplicate the compounds found in saliva and therefore lack its protective effects although some of them contain fluoride and electrolytes to prevent demineralization [32,59]. Any preparation containing substances problematic for causing caries or tissue discomfort such as sugar, acid and/or alcohol should be avoided in patients with dry mouth [32].

8.8. Prescription medications to relieve symptoms

In cases when topical therapy cannot provide adequate relief of dry mouth symptoms or cannot control the complications of dry mouth, prescription strength systemic medication in the form of sialagogues such as pilocarpine and cevimeline, orally administered parasympathetic agonists of the acetylcholine muscarinic M3 receptors, may be considered. US Food and Administration approved these parasympathetic agonists to increase salivary secretion in patients with Sjögren’s syndrome (pilocarpine and cevimeline) and head and neck cancer patient with radiation induced salivary gland hypofunction (pilocarpine only) [25,32,58,63,65,70,73]. These sialagogues cannot increase the function of salivary glands that are completely destroyed but they can enhance the function when there is residual glandular tissue.

The optimal dosage of pilocarpine 5–7.5 mg three to four times daily or 10 mg 3 times daily is generally well tolerated [32,69,70]. Pilocarpine (SALAGEN; MGI Pharma, Bloomington, USA) should be prescribed for at least 8–12 weeks to see if there is a positive response and if long-term use would be planned due to the presence of residual salivary gland tissue that has become functional as a result of the medication [49,70]. Cevimeline (EVOXAC; Daichi-Sanky, Tokyo, Japan) 30 mg taken 3–4 times daily, increased salivary flow and improved subjective and objective symptoms of patients with dry mouth and is also well tolerated by patients [32,69,70]. Sialagogues need to be administered long term, basically life-long, since the observed clinical improvements in salivary gland hypo-function diminish after cessation of sialagogues. The side effects of these medications include but are not limited to sweating, increased urgency or frequency of urination, lacrimal and nasal secretion, and joint pain. Both medications, but this is true more so for pilocarpine, are contraindicated in patients with narrow angle glaucoma, acute iritis, uncontrolled asthma, chronic obstructive pulmonary disease (COPD), kidney stones, gall stones, and heart or liver disease. Both medications can cause dehydration as well. Hence, sialogogues must be given with a high rate of caution in our older adult population.

Another systemic sialogogue of interest is Bethanechol HCL with promising results in patients with radiation therapy induced hyposalivation. However, further studies are needed to determine the dose, frequency of use, long-term efficacy and safety for the use of Bethanechol [69,70,73].

8.9. Non-pharmacologic interventions

Non-pharmacologic interventions for dry mouth include electrostimulation of the salivary glands with hand-held battery operated devices or removable intraoral devices [49,69,70,73,76]; manual and electro acupuncture [49,69,70,73,77]; hyperbaric oxygen therapy [72,78] and application of low level laser therapy [79]. There is however little or insufficient evidence in the literature in definitive support of these interventions in the management of dry mouth [20,72,73].

Immunologically active agents such as interferon alpha, corticosteroids, hydroxychloroquine and other immuno-suppressants such as cyclophosphamide and thalidomide have been studied for the management of dry mouth by suppressing the glandular damage from immunologically mediated diseases such as Sjögren’s syndrome and others such as sarcoidosis, HCV and HIV infection related salivary gland diseases [58].

8.10. Cost effectiveness of treatment

Given the myriad of choices for the treatment of dry mouth, it is easy for a practitioner to be unsure as to what to recommend to a patient who has clinical signs with or without symptoms. A cost-effective study examining the various treatments that are currently available or in development for this condition when it occurs as an outcome of head and neck cancer therapy, was mounted by Saportas et al. Her group indicated that the most effective and attractive way to address dry mouth in these patients is by protecting the salivary glands from radiation damage in the first place [49]. To do so, changes to the conventional therapy techniques previously used must be employed. Several solutions that meet this objective are available and have demonstrated moderate effectiveness. For example, newer radiation techniques including not only Intensity-modulated RT (IMRT), but also Intensity modulated Proton Radiation Therapy (IMPRT), which uses protons instead of X-rays. When IMPRT is employed, reduced findings of hyposalivation function from 80% down to 25–40% have been reported [80,81].

Another protective action would be to institute the use of radioprotective drugs such as Amifostine, which has been approved for treatment of salivary hypofunction. However, this drug does have significant negative effects such as nausea and vomiting, and its use during IMRT has been indicated as possibly unnecessary since the major salivary glands are being spared in this type of therapy, unlike in conventional radiation therapy [82]. Surgical procedures, including salivary gland transfer to an area outside of the radiation field (e.g. transfer of the submandibular gland to the submental space) have been shown to spare the gland and its function [83].
Hydration devices [84] are also available as one of the current palliative treatments for radiation induced xerostomia in addition to the administration of sialagogues, acupuncture, saliva substitutes, and electrical stimulation of salivary secretion. Emerging preventive treatment solutions include systemic administration of growth factors such as insulin growth factor 1 (IGF-1) or keratinocyte growth factor (KGF) [85,86] administration of botulinum toxin (BoNT) [87], another radioprotective drug called tempol [88] and the regeneration of the salivary gland tissue by gene therapy or by transplantation to the salivary gland of bioengineered salivary gland germ cells [89]. Even with all of these existing and emerging therapies for radiation induced salivary hypofunction there is a large treatment gap, and the most efficacious treatment with the most cost-effective ratio is still not available (Fig. 3) [49]. Solving this treatment gap will not only serve the needs of the patients with radiation induced salivary gland hypofunction but also will help the majority of patients who are more likely to have dry mouth from more frequently seen conditions such as medication-usage.

9. Conclusions

When it comes to treatment of dry mouth conditions, either objective or subjective, there are no easy answers as to the best course of action for a specific individual. As previously noted, there are many conditions that can cause dry mouth. While most of the cited studies have examined the most difficult cases of dry mouth, that is, those that are a result of treatment for head and neck cancer, there are many individuals who demonstrate dry mouth from far less grievous circumstances. Taking a thorough history in an attempt to discover the contributor to and/or cause of the signs and/or symptoms and based on those findings, attempting to select the most appropriate intervention is the critical role of the practitioner. Additional factors such as patient comfort, motivation, access to the various treatments, and cost will also play a role in the selection of a successful therapy. It is important to recall that water is an essential component for life [90]. Begin by educating the patient about possible causes of dry mouth.
An analysis of fluid intake (e.g. a daily fluid diary) may be a good place to start and may also be the most practical, cost effective and efficient treatment with the best risk-benefit ratio.

**Conflict of interest**

Authors have neither affiliation nor financial conflict of interest with any organization or company producing the oral care products discussed and mentioned in this article.

**REFERENCES**


