Review Article

Indian Journal of Dental Education
Volume 8 Number 3, July - September 2015
https://dx.doi.org/10.21088/ijde.0974.6099.8315.6

Xerostomia: An Updated Review

Pankaj Datta*, Sonia Sood Datta**

Abstract

Xerostomia can have a significant adverse effect upon oral health and quality of life. A variety of new therapies are continuously being developed and assessed, but in general the treatment of the underlying salivary gland disease remains difficult. It is important, however, that all patients with xerostomia are appropriately investigated to establish the underlying aetiology, and to receive professional oral health care.

Keywords: Xerostomia; Saliva; Dry Mouth; Salivary Gland Diseases; Xerostomia Management.

Introduction

Xerostomia refers to a subjective sensation of dry mouth [1]; it is frequently, but not always, associated with salivary gland hypo function or their symptoms may be secondary to qualitative and/or quantita-tive changes in the composition of saliva [2]. This term was derived from Greek word 'xeros' (dry) and 'stoma' (mouth).

Most individuals have short-term xerostomia due to emotional disorders, such as a panic attack caused by severe anxiety, stress or "flight or fight" which reduces saliva production in the mouth. In such condition patient complains of dryness of mouth but on sialometry there is no abnormality detected. Long-standing (chronic) xerostomia is a common complaint among the elderly and much more troublesome clinically [3]. According to a study approximately 20% of the population aged 65 and above experience this disorder [4]. A possible explanation is that older individuals take several xerogenic drugs for their chronic conditions and this may lead to an overall reduction of the unstimulated salivary flow rate [5]. The present article highlights problems associated with dry mouth and their management in order to improve the oral health and quality of life of the elderly.

Author's Affiliation: *Dean, Professor and Head, Dept of Prosthodontics, ** Assistant Professor, Dept of Public Health Dentistry, Inderprastha Dental College & Hospital, Sahibabad- Ghaziabad, India.

Reprints Requests: Pankaj Datta, C-86 AnandVihar, Delhi-110092, India.
E-mail: pankajdatta97@gmail.com

Clinical features

Chronic xerostomia gives rise to a variety of clinical symptoms and signs (Table 1) that can adversely affect quality of life. Combination of dryness and burning sensation of oral mucosa causes difficulty with speech (dysarthria) and swallowing (dysphagia) to the patient. Patient may have an increased need to sip or drink water when swallowing, difficulty with swallowing dry foods or an increasing aversion to dry foods [6].

The tongue may be erythematous pebbled, cobblestoned or fissured with atrophy of the filiform papillae. The oral mucosa may appear parched. Palpation of the oral mucosa may result in the finger's adhering to the mucosal surfaces instead of readily sliding over the tissues. Along with this the patient experiences reduced taste sensation, oral mucosal soreness, and halitosis [3,7]. Xerostomia can cause difficulties in denture wearing, as well as exacerbating chewing difficulties [8], thereby affects patient' nutrition as well as psychological health [9]. Patients with significantly decreased salivary output due to prolonged xerostomia have an increased risk of developing dental caries and oral fungal infections (e.g. candidiasis) [10,11]. Patients who develop Sjögren's syndrome secondary to a connective tissue disease also may complain of having dry eyes, and progressive parotid gland enlargement.

Table 1: Oral problems of xerostomia

Mucosal dryness
Liability to dental decay
Liability to gingival inflammation
Possible fungal infection
Loss of denture retention
Salivary gland infection
Oral manifestations of any associated disease

Aetiology

There are many causes of long-standing oral dryness as summarised in Table 2. The most frequent cause of hyposalivation is the use of certain medications (Table 3) followed by therapeutic radiation to head and neck, Sjögren's syndrome and systemic diseases (diabetes mellitus, HIV, emotional stress) [12,13]. Other factors include depression, anxiety and stress, or malnutrition [14].

Table 2: Aetiology of xerostomia

Iatrogenic	Drugs Radiotherapy to head and neck Chemotherapy Chronic graft-versus-host disease
Diseases of the salivary glands	Sjo¨gren's syndrome Sarcoidosis HIV disease Hepatitis C. virus infection Primary biliary cirrhosis Cystic fibrosis Diabetes mellitus
Rare causes	Amyloidosis Hemochromatosis Wegener's disease Salivary gland agenesis (with or without ectodermal dysplasia) Triple A syndrome

Table 3: Drug-induced xerostomia

Drugs which directly damages salivary glands	Cytotoxic drugs
Drugs with anti cholinergic activity	Anticholinergic agents–Atropine, Atropinics and hyoscine
	Antireflux agents–Proton pump inhabitors
	Serotonin Reuptake Inhibitors
Central acting psychoactive agents	Antidepressants
	Phenothiazines
	Benzodiazepines
	Antihistamines
	Bupropin
Opioids	
Drugs acting on sympathetic systems	Drugs with sympathomimetic activity
	Anti hypertensive alpha 1 and alpha 2 antagonists and Beta blockers
Drugs that deplete fluids	Diurerics

Diagnosis

The diagnosis of xerostomia is very straightforward, and it involves the measurement of the quantity of both, resting and stimulated whole saliva [15]. The normal stimulated salivary flow rate averages 1.5–2.0 mL / min while the unstimulated salivary flow rate is approximately 0.3–0.4 mL / min [16]. A diagnosis of hyposalivation is made when the stimulated salivary flow rate is $\leq$ 0.5–0.7 mL / min and the unstimulated salivary flow rate is $\leq$ 0.1 mL / min [17].

Variety of other investigative methods are also used to evaluate the salivary gland secretion and to establish the precise cause of the xerostomia, some of these are summarized in Table 5.These methods includes self-reported questionnaires [18] (Table 4), visual analog scales (VAS), sialography, sialo-scintigraphy, sialo-ultrasonography, and biopsy [19]. Another way is by measuring volume of residual saliva on mucosal surfaces using filter paper and micromoisture meter and calculating thickness, and using mucosal wetness devices [20]. Patients who respond positive to these questions with salivary flow rate less than 0.1 mL / min are diagnosed as salivary hypofunction.

Table 4: The following questions should be asked to detect dry mouth.

• Does your mouth feel dry when eating a meal?
• Do you sip liquids to aid in swallowing dry foods?
• Do you have difficulties swallowing any foods?
• Does the amount of saliva in your mouth seem to be too little?
• Do you have a dry cough, hoarseness, nose bleeds or decreased sense of taste or smell?

Table 5: Investigation methods for xerostomia

Sialometry
Sialography
Ultrasound
Ultrasound-guided fine-needle or medium-needle biopsy
CT (+/- sialography)
MRI (+/- sialography)
Labial gland biopsy
Serology

Management and treatment of xerostomia

The general approach to treat patients with xerostomia is primarily; avoidance or drying agents (e.g. alcohol and tobacco), prescribing of salivary substitutes or salivary stimulants (sialogogues) and prevention of oral complications (Table 6).

Avoid oral dryness

Patients with dry mouth should increase intake of water and must be advised to sip water every 5-10 minutes to provide moisture in the mouth [21]. Water or non-alcoholic drinks with meals will also helps. Easy remedies are proper hydration; increase in humidity at night-time; avoidance of irritating dentifrices and crunchy / hard foods [22]. Lips can be protected by applying lip salve or petroleum jelly [18].

Intraoral topical agents

Intraoral topical agents are among the most common recommended treatments for the management of xerostomia. These include chewing gums, saliva stimulants, and substitutes.

Commercially available sugar-free chewing gums and candies can also be used to stimulate salivary flow [23]. In particular, chewing gums have been shown to increase saliva secretion and decrease oral mucosal friction [24]. Other efficacious remedies include mucoadhesive lipid-based bioerodible tablets [25] or mucin spray [25]. Other topical agents (toothpaste, mouth rinse, mouth spray, and gel) containing olive oil, betaine, and xylitol may be effective in improving xerostomia secondary to medication use [26].

Saliva substitutes aim to increase viscosity and mimic natural saliva without altering the salivary flow [27]. Artificial saliva substitutes have been shown to give relief by rehydrating the oral mucosa and help to clean teeth from bacteria and debris [28]. Artificial saliva (Table 7) contains minerals (eg, fluoride, calcium, and phosphate ions), carboxymethy lcellulose or hydroxyethylcellulose, flavoring agents, and preservatives (eg, propyl or methyl paraben) [29. Saliva substitutes are available as lozenges, rinses, sprays, swab sticks and as reservoirs in dentures [30].

Table 6: Management of oral mucosal dryness

Avoid drying agents	Tobacco, Alcohol
Salivary substitutes	Saliva Orthana, Glandosane, Luborant, Oral Balance BioXtra, Salinum
Salivary stimulants	Pilocarpine (Salagen), Cevimeline, Others
Other methods	Acupuncture, Neurophysiological stimulation

Table 7: Composition of artificial saliva

Components	Quantity
Water	500ml
Xylitol	20gm
Potassium chloride	1.2gm
Sodium chloride	0.843gm
Magnesium chloride	0.051gm
Tricalcium phosphate	20ml
Peppermint food flavour	5ml
Carboxymethylcellulose	10gm
Sodium hydroxide	20ml

Salivary Secretion Stimulants - Cholinergic Agonists

For patients with remaining viable salivary gland tissue, stimulation techniques are helpful. Pilocarpine and cevimeline are two systemic sialogogues for treatment of dry mouth. These drugs provide a similar benefit in patients with dry mouth [31]. Oral pilocarpine and cevimeline are parasympathomimetic medications with muscarinic action [32].

Pilocarpine is a non-selective muscarinic agonist, whereas cevimeline reportedly has a higher affinity for M1 and M3 muscarinic receptos [33,34]. Pilocarpine is typically administered at a dose of 5 mg three times a day for at least 3 months and cevimeline is prescribed at a dose of 30 mg three times a day for at least 3 months [35].

Side effects include: excessive sweating, cutaneous vasodilatation, emesis, nausea, diarrhea, persistent

hiccup, bronchoconstriction, hypotension, bradycardia, increased urinary frequency, and vision problems. Both pilocarpine and cevimeline are relatively contraindicated in patients with uncontrolled asthma or chronic pulmonary disease and in â-adrenergic blocker users, and should be used with caution in patients with active gastric ulcers or uncontrolled hypertension [36].

Dental Caries Prevention

With reduction in saliva, the patients are more prone to cervical and root caries and therefore diligent oral hygiene and regular dental care is essential. It primarily consists of rigorous attention to personal oral hygiene (keeping mouth very clean by brushing twice daily and flossing), frequent dental and oral evaluations, strict adherence to a non-cariogenic diet (reducing sugar intake, avoiding sticky foods), placement of sealants, the application of topical fluorides and antimicrobial mouth rinses. Such preventive measures are critical to help prevent dental caries [37], periodontal diseases, mucosal infections and other oral complications. Supplements that contain sodium fluoride, acidulated phosphate fluoride or sodium monofluorophosphate are available for professional application as well as for home use [38].

Oral candidal infection

Oral candidiasis is commonly seen in patients with xerostomia. These patients should be prescribed topical antifungal agents. Topical application of miconazole gel (e.g. placed on the fitting surface of a denture is helpful along with systemic antifungal medications. Oral lubricants like vitamin E or oral balance also helpful in case of dry mucosa and cracked lips [39].

Radiotherapy-associated xerostomia

A variety of methods have been recently proposed to lessen the severity of the likelihood of radiotherapy- induced xerostomia, these include confocal radiotherapy, which allows precise radiation targeting without causing significant salivary gland destruction, and the implementation radioprotectants such as amifostine. Future radioprotectants may include Tempol [40,41].

Regenerative Medicine and Tissue Engineering

Muscarinic agonist medications have very limited effect on the recovery of damaged tissue. Recently, the occurrence of proliferative, multipotent salivary gland stem / progenitor cells has been reported in neonatal mice. A similar cell type was also reported in adult mice, although their pluripotency was limited [42,43]. More recently, the potential of mesenchymal stem cells to regenerate salivary glands was reported using a radiation-damage mode [43,44].

Gene therapy

If immunologically-mediated therapy is proven to be effective for the treatment of Sjogren's syndrome, it is likely to require administration over many months, if not years, and has the potential to give rise to adverse side effects. Thus it has been suggested that gene therapy may be a more effective means of managing disorders such as Sjogren's syndrome. These methods, which are still in the early stages of development, entail the placement of a low pathogenic virus equipped with a gene coding for an important protein of salivary gland function into the salivary tissue (via the duct of a major gland). The most promising data has come from studies on animals with radiotherapy- induced xerostomia. Adenovirus transfected with the human acquaporin-1 gene has been found to enhance salivary gland function, and not give rise to any significant host immune response. Interestingly, this intra-salivary gene transfer method has also been found to be a means of transferring non-salivary genes such as those for human growth hormone and insulin such that increased levels of the hormones appear in systemic circulation [45].

Alternate modalities of treatment

Other modalities such as intraoral electro – stimulation [46] and Acupuncture [47] have been helpful to increase salivary flow. Advice the patient to avoid taking medications before bedtime because salivary flow rate is low during sleep [48].

Conclusion

Xerostomia is a subjective perception of oral dryness. There may be various degree of salivary hypofunction depending upon the causes. Early diagnosis and treatment can slow progression of dry mouth and improve the quality of life of the patient. Current xerostomia-based treatments include replacement therapies, stimulants and systemic agents such as pilocarpine or cevimeline. Future treatment for some of the salivary gland disorders may require the use of gene therapy and tissue

engineering for atrophic salivary gland, but at present there is a need to have a greater understanding of the causes and pathogenesis of salivary gland disease before specific therapies can be developed. Oral healthcare professionals can play a vital role in identifying patients at risk for developing salivary dysfunction, and should provide appropriate preventative and therapeutic techniques that will help to preserve a person's health, function, and quality of life.

References

1. Hopcraft MS, Tan C. Xerostomia: an update for clinicians. Aust Dent J. 2010; 55(3):238–44; quiz 353.
2. Van der Putten GJ, Brand HS, Schols JM, de Baat C. The diagnostic suitability of a xerostomia questionnaire and the association between xerostomia, hyposalivation and medication use in a group of nursing home residents. Clin Oral Investig. 2011; 15(2):185–92.
3. Porter SR, Scully C, Hegarty AM. An update of the etiology and management of xerostomia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004; 97(1):28-46.
4. Turner M, Jahangiri L, Ship JA. Hyposalivation, xerostomia and the complete denture: A systematic review. The Journal of the American Dental Association. 2008; 139(2):146-50.
5. Liu B, Dion MR, Jurasic MM, Gibson G, Jones JA. Xerostomia and salivary hypofunction in vulnerable elders: prevalence and etiol-ogy. Oral Surg Oral Med Oral Pathol Oral Radiol. 2012; 114(1): 52–60.
6. Loesche W J, Bromberg J, Terpenning M S, et al. Xerostomia, xerogenic medications and food avoidances in selected geriatric groups. J Am Geriatr Soc 1995; 43: 401-07.
7. Ritter AV. Xerostomia (dry mouth). J Esthet Restor Dent. 2006; 18(5): 306.
8. Cassolato SF, Turnbull RS. Xerostomia: clinical aspects and treatment. Gerodontology. 2003; 20(2): 64–77.
9. Helen L Craddock. An aid to the management of xerostomia in the partially dentate patient. Dent Update 2004; 31: 302-04.
10. Villa A, Polimeni A, Strohmenger L, Cicciù D, Gherlone E, Abati S. Dental patients' self-reports of xerostomia and associated risk factors. J Am Dent Assoc. 2011; 142(7): 811–16.
11. Ekström J, Khosravani N, Castagnola M, Messana I. Saliva and the control of its secretion. In: Ekberg O, editor. Dysphagia: Diagnosis and Treatment. Berlin: Springer-Verlag; 2012: 19–47.
12. Michael D Turner, Jonathan A Ship. Dry mouth and its Effects on the oral health of elderly people. JADA 2007; 138: 15-20.
13. Thomson WM. Issues in the epidemiological investigation of dry mouth. Gerodontology. 2005; 22(2):65–76.
14. Bergdahl M, Bergdahl J. Low unstimulated salivary flow and subjec-tive oral dryness: association with medication, anxiety, depression, and stress. J Dent Res. 2000; 79(9): 1652–58.
15. Wiener RC, Wu B, Crout R, Wiener M, Plassman B, Kao E, et al. Hyposalivation and xerostomia in dentate older adults.J Am Dent Assoc 2010;141:279-84.
16. Humphrey SP, Williamson RT. A review of saliva: normal composition, flow, and function. J Prosthet Dent. 2001; 85(2): 162–69.
17. Sreebny LM, Vissink A, editors. Dry Mouth: the malevolent symptom. A clinical guide. Ames: Wiley-Blackwell; 2010.
18. Singh T. Xerostomia: Etiology, diagnosis and management. Dent today. 2012; 31: 82-83.
19. Grisius MM, Fox PC. Salivary gland diseases. In: Greenberg MS,Glick M, editors. Burket's Oral medicine. Diagnosis and treatment.10th ed Hamilton, Ontario: BC Decker; 2003.
20. Takahashi F, Koji T, Morita O. Oral dryness examinations: Use of an oral moisture checking device and a modified cotton method. Prosthodont Res Pract 2005; 5: 26-30.
21. Visvanathan V, Nix P. Managing the patient presenting with xerostomia: a review. Int J Clin Pract. 2010; 64(3): 404–07.
22. Scully C, Felix DH. Oral medicine — Update for the dental practitioner: Dry mouth and disorders of salivation. Br Dent J 2005; 199: 423-7.
23. Furness S, Worthington HV, Bryan G, Birchenough S, McMillan R. Interventions for the management of dry mouth: topical therapies. Cochrane Database Syst Rev. 2011(12):CD008934.
24. Olsson H, Spak CJ, Axéll T. The effect of a chewing gum on salivary secretion, oral mucosal friction, and the feeling of dry mouth in xeros-tomic patients. Acta Odontol Scand. 1991; 49(5): 273–79.
25. Aframian DJ, Mizrahi B, Granot I, Domb AJ. Evaluation of a mucoadhesive lipid-based

bioerodable tablet compared with Biotène mouthwash for dry mouth relief – a pilot study. Quintessence Int. 2010; 41(3): e36–e42.

26. Ship JA, McCutcheon JA, Spivakovsky S, Kerr AR. Safety and effec-tiveness of topical dry mouth products containing olive oil, betaine, and xylitol in reducing xerostomia for polypharmacy-induced dry mouth. J Oral Rehabil. 2007; 34(10):724–32.
27. van der Reijden WA, Vissink A, Veerman EC, Amerongen AV. Treat-ment of oral dryness related complaints (xerostomia) in Sjögren's syndrome. Ann Rheum Dis. 1999; 58(8): 465–74.
28. Smith G, Smith A J, Shaw L, et al. Artificial saliva substitutes and mineral dissolution. J Oral Rehabil 2001; 28: 728-31.
29. Visvanathan V, Nix P. Managing the patient presenting with xerostomia: a review. Int J Clin Pract. 2010; 64(3): 404–407.
28. Sinclair C F, Frost P M, Walter J D. New design for an artificial saliva reservoir for the mandibular complete denture. J Pros Dent 1996; 75: 276-80.
32. Takakura AC, Moreira TS, Laitano SC, De Luca Júnior LA, Renzi A, Menani JV. Central muscarinic receptors signal pilocarpine-induced salivation. J Dent Res. 2003; 82(12): 993–997.
31. Braga MA, Tarzia O, Bergamaschi CC, Santos FA, Andrade ED, Groppo FC. Comparison of the effects of pilocarpine and cevimeline on salivary flow. Int J Dent Hyg. 2009; 7(2): 126–30.
33. Iwabuchi Y, Masuhara T. Sialogogic activities of SNI-2011 compared with those of pilocarpine and McN-A-343 in rat salivary glands: iden-tification of a potential therapeutic agent for treatment of Sjorgen's syndrome. Gen Pharmacol. 1994; 25(1): 123–29.
34. Weber J, Keating GM. Cevimeline. Drugs. 2008; 68(12): 1691–98.
35. Aframian DJ, Helcer M, Livni D, Robinson SD, Markitziu A, Nadler C. Pilocarpine treatment in a mixed cohort of xerostomic patients. Oral Dis. 2007; 13(1): 88–92.
36. Wiseman LR, Faulds D. Oral pilocarpine: a review of its pharmacologi-cal properties and clinical potential in xerostomia. Drugs. 1995; 49(1): 143–55.
37. Joel JN, Michael TB, Philip CF. Diagnosis and treatment of xerostomia (dry mouth). Odontology 2009; 9:76-83.
38. Fox P C. Management of dry mouth. Dent Clin North Am 1997; 41: 863-75.
39. Brennan MT, Fox PC. Xerostomia: Diagnosis, management and sjogren's syndrome. In: Brennan MT, Fox PC, editors.Clinicians Guide to Salivary Gland and Chemosensory Disorders. Edmonds: American Academy of Oral Medicine; 1st ed 2009. p. 5-25.
40. Brizel DM, Wasserman TH, Henke M et al. Phase III randomized trial of amifostine as a radioprotector in head and neck cancer. J Clin Oncol. 2000; 18(19): 3339-45.
41. Epstein JB, Burchell JL, Emerton S et al. A clinical trial of bethanechol in patients with xerostomia after radiation therapy. A pilot study. Oral Surg Oral Med Oral Pathol. 1994; 77(6): 610-4.
42. Kishi T, Takao T, Fujita K. Clonal proliferation of multipotent stem / progenitor cells in the neonatal and adult salivary gland. Biochem Biophys Res Commun 2006; 340: 544-52.
43. H Kagami1, Wang S, Hai B. Restoring the function of salivary glands. Oral Diseases 2008; 14:15–24.
44. Lombaert IM, Wierenga PK, Kok T et al. Mobilization of bone marrow stem cells by granulocyte colony-stimulating factor ameliorates radiation-induced damage to salivary gland. Clin Cancer Res 2006; 12: 1804–12.
45. Lodde BM, Baum BJ, Tak PP, Illei G. Experience with experimental biological treatment and local gene therapy in Sjogren's syndrome: implications for exocrine pathogenesis and treatment. Ann Rheum Dis. 2006; 65(11): 1406-13.
46. Strietzel FP, Lafaurie GI, Mendoza GR, et al. Efficacy and safety of an intraoral electrostimulation device for xerostomia relief: a multicenter, randomized trial. Arthritis Rheum. 2011; 63(1):180–90.
47. O'Sullivan EM, Higginson IJ. Clinical effectiveness and safety of acupuncture in the treatment of irradiation-induced xerostomia in patients with head and neck cancer: a systematic review. Acupunct Med. 2010; 28(4):191–99.
48. Diaz-Arnold AM, Marek CA. The impact of saliva on patient care: A literature review. J Prosthet Dent 2002; 88:337-43.