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Xerostomia – A Review

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Abstract: ***Xerostomia, or dry mouth, is a very common symptom amongst the terminally ill and can have profound negative effects on patients' quality of life. It predominantly affects the middle aged and elderly people. Patients with a persistently dry mouth may develop a burning or scalded sensation and have poor oral hygiene. They are prone to increased dental caries, periodontal disease, intolerance of dentures and oral infections, particularly candidiasis. The aim of this report is to review the causes, diagnosis and management of dry mouth patients and also to review the physiological and pathological changes in the salivary secretion in these patients.***

Keywords: Dry Mouth, Hyposalivation, Drugs Associated, and Palliative Treatment.

1. Introduction

Xerostomia refers to a subjective sensation of dry mouth; it is frequently, but not always, associated with salivary gland hypo function (1). It predominantly affects the middle aged and elderly people with an estimated prevalence of 21% and 27% in men and women respectively (2). Common causes of xerostomia include medications with antimuscarinic properties, radiotherapy for head and neck cancer, uncontrolled diabetes (3). The variety of local and systemic conditions, treatments and medications alter salivary secretion and composition. The degree of salivary glands dysfunction as well as the accompanying oral morbidity as a complication of dry mouth makes xerostomia therapy complex and often refractory.

2. Saliva And Hyposalivation:

Saliva is a complex fluid, mostly composed of water (99%) and in minor part of variety of non-organic and organic substances such as enzymes, hormones, antibodies, antimicrobial constituents and growth factors. Most of the constituents are produced within the glands; others are transported from the blood (4). Many of the compounds found in blood could be also detected in saliva, thus saliva is functionally equivalent to serum in reflecting the physiological state of the body, including emotional, hormonal, nutritional, and metabolic variations (5). Salivary gland hypo function or hypo salivation is the condition of having reduced saliva production due to various causes. It usually leads to the subjective complaint of oral dryness which is termed xerostomia. The term xerostomia comes from the Greek word xeros (dry) and stoma (mouth), which means dry mouth (6). Xerostomia is not a synonym for hyposalivation since it may also occur with the changes in the quality of saliva, while the amount of saliva stays unchanged (7). Therefore, a patient complaining of dry mouth cannot automatically be assumed to have salivary dysfunction, while oral dryness may have many causes (8).

3. Prevalence

Reports of the prevalence of xerostomia in general population are not conclusive and vary, ranging from 0.9% to 64.8%, mainly due to the small number of studies in population-based samples (9). It is estimated that about 30% of the population older than 65 suffer from xerostomia (10). Although previous opinion that salivary function declines with aging process, it is now accepted that salivary flow as well as salivary constituents are both age-stable in the absence of major medical problems and medications. Therefore, increasing age does not by itself cause hyposalivation (11).

4. Etiology

The dry mouth is common during periods of anxiety, mouth breathing and with advancing age. The causes of xerostomia are listed in Table1 (T-1).

a) Iatrogenic :
➢ Drugs
➢ Local radiation
➢ Chemotherapy
➢ Chronic graft-versus-host disease
b) Diseases of the salivary glands :
➢ Sjo¨gren's syndrome
➢ Sarcoidosis
➢ HIV disease
➢ Hepatitis C virus infection
➢ Primary biliary cirrhosis
➢ Cystic fibrosis
➢ Diabetes mellitus
c) Rare causes :
➢ Amyloidosis
➢ Hemochromatosis
➢ Wegener's disease
➢ Salivary gland agenesis (with or without ectodermal dysplasia)
➢ Triple A syndrome
d) Others

Table 1(T-1) :Common causes of Xerostomia (12)

Medications cause xerostomia by interfering with the transmission of signals at the parasympathetic neuro effector junctions, interfering with actions at the adrenergic neuro effector junctions, or causing the depression of the connections of the autonomic nervous system. Therapeutic doses of medications do not damage salivary gland anatomy and any damage is therefore reversible with discontinued use of xerogenic drugs (13). Drugs involved in causing xerostomia are included in the Table 2 (T-2).

a) Drugs which directly damage the salivary glands : ➢ Cytotoxic drugs **b) Drugs with anticholinergic activity** : ➢ Anticholinergic agents: Atropine and Hyoscine ➢ Anti-reflux agents: Omeprazole ➢ Psychoactive agents: Amitriptyline, Dothiepin ➢ Selective serotonin re-uptake inhibitors ➢ Fluoxetine ➢ Others: Phenothiazines, Benzodiazepines, ➢ Opioids, Antihistamines **c) Drugs acting on sympathetic system**: ➢ Drugs with sympathomimetic activity • Ephedrine ➢ Anti-hypertensive: • Alpha 1 antagonists: Terazosin, Prazosin • Alpha 2 agonists: Clonidine ➢ Beta blockers: Atenolol, Propranolol • Drugs which deplete fluid: Diuretics.
Table 2 (T-2): Drugs associated with dry mouth (5)

Xerostomia is one of the most common complications during high-dose radiation therapy (RT) for head and neck cancer (HNC) and has a significant impact on quality of life, requiring careful planning of long-term dental and oral care (8). Radiotherapy (RT) of the head and neck region causes both acute and long-term complications on salivary gland tissue and function, as well as radiation-induced compositional salivary change (14). Acute effects of radiation on salivary function occur during the first week of RT and deterioration continues until flow rates are barely measurable at 6 to 8 weeks. Late complications are result of chronic injury on exposed tissue; mucosa, vasculature, salivary glands, connective tissue and bone. Qualitative changes in saliva include increased viscosity, increased organic component, altered pH, decreased transparency and yellow brown discoloration (15). The most radiosensitive salivary gland is parotid gland followed by submandibular, sublingual and minor salivary gland. A radiation dose as low as 20 Gy can cause permanent cessation of salivary flow if given as a single dose. At doses above 52 Gy, salivary dysfunction is severe (12). Radiation-induced xerostomia starts in the first week of RT during which salivary flow decrease for 50%-60% and after 7 weeks of RT diminishes to approximately 20% (16). Salivary function continues to decline for up to several months after RT (15). To spare salivary function and improve quality of life, salivary gland exposure to radiation can be minimized by utilizing intensity modulated radiation therapy and three dimensional treatment planning and dose delivery techniques. A reduction in radiation induce hypo salivation was noted with the use of the radio-protective agent amifostine which provides cyto-protection to salivary glands (4) (17).

Xerostomia is a well-known complication of chronic graft-versus host disease (cGVHD). The squamous epithelium of the oral mucosa and the epithelium of salivary glands are affected early in the course of cGVHD but the major salivary functional injury in cGVHD occurs later, with the target of destruction possibly being the muscarinic receptor, water transporter or calcium ions (18). Levels of diabetes associated xerostomia are reported in upwards of 40 to 80 percent of patients. Stimulated parotid flow rates are observed to be the lowest in patients with poorly controlled diabetes mellitus as compared to well controlled diabetes mellitus. Diabetic patients are also predisposed to develop oral candidiasis, median rhomboid glossitis, denture stomatitis and angular chelitis associated with denture use and poor glycemic control. It is believed that patient xerostomia is one possible cause for this predisposition (19). Sjögren's Syndrome (SS) is the most common autoimmune disease characterized by inflammation of the exocrine glands and may occur independently (as primary Sjögren's syndrome or Sicca syndrome limited to the eyes and mouth, SS-1) or in association with other autoimmune diseases such as rheumatoid arthritis, systemic sclerosis or systemic lupus erythematosus (secondary Sjögren's syndrome that affects connective tissue, SS-2) (20). In Sjögren's syndrome the progressive lymphocytic infiltration gradually destroys the secretory acini of the major and minor salivary glands which results in hyposalivation and finally in xerostomia. Another explanation for the loss of glandular function may be related to an inhibition of nerve stimuli of the glands (21). Chronic Sarcoidosis can give rise to xerostomia and salivary gland enlargement in up to 9% of affected patients, often occurring as part of Heerfordt's syndrome (22).

Salivary gland disease can arise in 4% to 8% of adults and children with HIV infection. The principal clinical features of salivary gland disease in HIV infection includes associated xerostomia and salivary gland enlargement, Kaposi's sarcoma causing salivary gland enlargement, non-Hodgkin's lymphoma and intra glandular lymphadenopathy; and acute supportive sialadenitis (23).

5. Risk Factors

Patients with the following disorders as listed in Table 3 (T-3) should be considered at risk for xerostomia.

a) Risk factors for Xerostomia: (5) ➢ AIDS ➢ Systemic Lupus Erythematosus ➢ Thyroid Dysfunction ➢ Parkinson's Disease ➢ Cerebral Palsy ➢ Depression ➢ Anxiety ➢ Post-Traumatic Stress Disorder ➢ Dehydration ➢ Eaten-Lambert Syndrome ➢ Trauma to Salivary Glands ➢ Anorexia and Bulimia
Table 3 (T-3)

6. Treatment

Treatment should include local and systemic stimulation of salivary glands, palliative treatment for symptomatic relief, as well as preventing and treating oral complications. (4) Decreased mastication exacerbates the condition due to the fact that periodontal mechanoreceptors and mechanical stimulation of the oral mucosa and tongue are required stimulate salivation. Consequently, patients should be referred for nutritional counselling to educate them to minimize any negative effects from reactionary diet alterations (24).

A. Local Stimulation

The combination of chewing and acidic taste, as provided by chewing gums or solid food or fruits can be very effective in stimulating salivary flow for patients who have remaining salivary function. The use of laser infrared light of 904nm (low level laser therapy, LLLT) on salivary glands in the treatment of xerostomia has proved to be not only stimulative but also regenerative in nature (25). Electrical stimulation has also been used as a therapy for salivary hypofunction but has been inadequately investigated clinically. A device that delivers a very low voltage electrical charge to the tongue and palate has been described although its effect was modest in patients with dry mouth (26).

B. Systemic Stimulation

Any agent that has the ability to influence salivary glands to increase production of saliva is termed a secretagogue. Among 24 examined agents only four sialagogues have been examined extensively in controlled clinical trials; these are bromhexine, anetholetrithione, pilocarpine hydrochloride (HCl), and cevimeline HCl, but with mixed results (8). Pilocarpine is a potent and naturally occurring nonspecific cholinergic agonist which stimulates muscarinic receptor leading to the secretion of water and electrolytes, if the patients has sufficient amount of functional salivary gland tissue. Initial dose of pilocarpine should be administered 30 minutes before meals, in 5 mg tablets 3 to 4 times a day, with the usual dose range being approximately 3 to 6 tablets a day, not to exceed two tablets per dose. New modes of delivery are also being researched including loading nanoparticles with pilocarpine (27).

Cevimeline is another parasympathomimetic agonist that has been recently approved for the treatment of oral dryness in patients with Sjögren's syndrome. Recommended dosage for Cevimeline is 30 mg, 3 times a day. It is capable of inducing salivation with minimal adverse cardiac and pulmonary effects. Animal studies have shown that Cevimeline has adverse effects on the fetus but its use during pregnancy is considered acceptable if the benefits are considered acceptable (4) (28).

Bethanecol found to increase the stimulated and unstimulated salivary flow rates of patients with xerostomia secondary to radiation, but objective changes in salivary flow rates did not always correlate with symptomatic improvement. It is given in a dose of 25 mg; 3 times daily orally (27).

C. Symptomatic treatment

Palliative treatment remains as only choice in cases when there is no functionally salivary tissue present as is in the disorders of irreversible damage of salivary secretory cells. A number of saliva substitutes have been developed for the palliative care of patients with salivary hypofunction, these agents, in liquid, spray, or gel form have moistening and lubricating properties, and their purpose is to provide prolonged wetness of the oral mucosa. Salivary substitute tend to be short acting, providing relief for a limited period of time. They are most effective when applied before sleeping or speaking. Patients affected with xerostomia should also increase their fluid intake due to the fact that most people do not drink enough water, contributing to the condition. The patients should be encouraged to place ice chips in their mouth and sip water throughout the day to provide moisture and possibly provide relief to dry mouth symptoms (4) (24). Acupuncture has been reported to increase parasympathetic activity, causing a release in neuropeptide, stimulating salivary flow and secretions. Three points are treated in each ear, and one in the radial aspect of each index finger. Preliminary data revealed that many patients achieve relief, even for symptoms refractory to pilocarpine therapy (29). Future treatment for some of the salivary gland disorders may require the use of gene therapy and tissue engineering, 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.

References

[1] Fox PC, Eversole R. Diseases of the salivary glands. Essentials of Oral Medicine. 2001:260–76.
[2] Nederfors T, Isaksson R, Morestad H et al. Prevalence of perceived symptoms of dry mouth in an adult Swedish population: relation to age, sex and pharmacotherapy. Community dental oral Epidemiol 1997; 25: 211-6.
[3] Moore PA, Guggenheimer J, Etzel KR et al. Type 1 diabetes mellitus, xerostomia and salivary flow rates. Oral surg Oral med Oral pathol Oral radiol Endod 2001; 92: 281-91.
[4] Guggenheimer J, Moore PA. Xerostomia: etiology, recognition and treatment. J Am Dent Assoc. 2003; 134(1):61-9.
[5] Lee YH, Wong DT. Saliva: an emerging biofluid for early detection of diseases. Am J Dent. 2009; 22(4):241-8.
[6] Thomson WM. Measuring change in dry-mouth symptoms over time using the Xerostomia Inventory. Gerodontology. 2007; 24(1):30-35.
[7] Ship JA, Fox PC, Baum BJ. How much saliva is enough? 'Normal' function defined. J Am Dent Assoc. 1991; 122(3):63-9.
[8] Grisius MM, Fox PC. Salivary gland diseases. In: Burket's Oral medicine. Diagnosis and treatment. Eds. Greenberg MS, Glick M., 10th edition, 2003.
[9] Orellana MF, Lagravère MO, Boychuk DG, Major PW, Flores-Mir C. Prevalence of xerostomia in population-based samples: a systematic review. J Public Health Dent. 2006;66(2):152-8
[10] Ship JA, Pillemer SR, Baum BJ. Xerostomia and the geriatric patient. J Am Geriatr Soc. 2002; 50(3):535-43.
[11] Ship JA, Nolan NE, Puckett SA. Longitudinal analysis of parotid and submandibular salivary flow rates in healthy, different-aged adults. J Gerontol A Biol Sci Med Sci. 1995;50(5):M285-9
[12] Porter S, Scully C, Hegarty A. An update of the etiology and management of xerostomia. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology & Endodontics. 2004; 97(1):28-46.

[13] Pajukoski H, Meurman JH, Odont D, Halonen P, Sulkava R. Prevalence of subjective dry mouth and burning mouth in hospitalized elderly patients and outpatients in relation to saliva, medication, and systemic diseases. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology & Endodontics. 2001; 92(6):641-9.
[14] Sciubba JJ, Goldenberg D. Oral complications of radiotherapy. Lancet Oncol. 2006; 7(2):175-83.
[15] Valdez IH, Atkinson JC, Ship JA, Fox PC. Major salivary gland function in patients with radiation-induced xerostomia: flow rates and sialochemistry. Int J Radiat Oncol Biol Phys. 1993; 25(1):41-7.
[16] Franzen L, Funegard U, Ericson T, Henriksson R. Parotid gland function during and following radiotherapy of malignanciewsin the head and neck: a consecutive study of salivary flow and patient's discomfort. Eur J Cancer. 1992; 28:457-462.
[17] Antonadou D, Pepelassi M, Synodinou M, Puglisi M, Throuvalas N. Prophylactic use of amifostine to prevent radiochemotherapy-induced mucositis and xerostomia in head-and-neck cancer. International Journal of Radiation Oncology Biology Physics. 2002; 52(3):739-47.
[18] Nicolatou Galitis O, Kitra V, Vliet Constantinidou C, Peristeri J, Goussetis E, Petropoulos D, et al. The oral manifestations of chronic graft versus host disease (cGVHD) in paediatric allogenic bone marrow transplant recipients. Journal of Oral Pathology & Medicine. 2001; 30(3):148-53.
[19] Chavez EM, Taylor GW, Borrell LN, Ship JA. Salivary function and glycemic control in older persons with diabetes. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2000; 89(3):305-11.
[20] Fox PC, Bowman SJ, Segal B, Vivino FB, Murukutla N, Choueiri K, et al. Oral involvement in primary Sjogren syndrome. J Am Dent Assoc. 2008;139(12):1592-601
[21] Humphreys-Beher MG, Brayer J, Yamachika S, Peck AB, Jonsson R. An alternative perspective to the immune response in autoimmune exocrinopathy: induction of functional quiescence rather than destructive autoaggression. Scand J Immunol. 1999; 49:7-10.
[22] Drosos A, Voulgari P, Psychos D, Tsifetaki N, Bai M. Sicca syndrome in patients with sarcoidosis. Rheumatology International. 1999; 18(5):177-80.
[23] Schiødt M. HIV-associated salivary gland disease: A review. Oral Surgery, Oral Medicine, Oral Pathology. 1992; 73(2):164-7.
[24] Diaz-Arnold IS, Marek CA. The impact of saliva on patient care: A literature review. The Journal of Prosthetic Dentistry. 2002; 88(3):337-43.
[25] Lončar M, Mravak-Stipetić M, Risović D. The effect of low level lasertherapy on salivary glands in patients with xerostomia. Photomed Laser Surg. 2011; 29(3):171-5.
[26] Sreebny LM, Vissink A, editors. Dry mouth, the malevolent symptom: a clinical guide. Singapore: Wiley-Blackwell. 2010; 268 pp.
[27] Gorsky M, Epstein J, Parry J, Epstein M. ND Le en S. Silverman. The efficacy of pilocarpine and bethanechol upon saliva production in cancer patients with hyposalivation following radiation therapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004; 97:190-5.
[28] Suzuki K, Matsumoto M, Nakashima M, Takada K, Nakanishi T, Okada M, et al. Effect of cevimeline on salivary components in patients with Sjögren syndrome. Pharmacology. 2005; 74(2):100-5.
[29] Blom M, Dawidson I, Angmar-Månsson B. The effect of acupuncture on salivary flow rates in patients with xerostomia. Oral Surgery, Oral Medicine, Oral Pathology. 1992; 73(3):293-8.