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Review Article

Xerostomia Diagnosis and Management

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Abstract

Xerostomia, or dry mouth, is a common complaint that may be caused by several conditions, which include side effects of a wide variety of drugs, such as antidepressants, therapeutic radiation to the head and neck, dehydration, diabetes, and diseases involving salivary glands, such as Sjogren's syndrome. The complaint of dry mouth may or may not be associated with decreased salivary gland function. Individuals with xerostomia complain of problems with eating, speaking, swallowing, and wearing dentures. Some people also complain of salivary gland enlargement or changes in taste. Lack of saliva may predispose one to oral infections, such as candidiasis, and increase the risk of dental caries. Management of the individual patient with xerostomia includes assessment of salivary gland function, replacement therapy, and prevention of caries and oral candidiasis. Early recognition and management of xerostomia may prevent devastating dental disease and help to improve the quality of life.

Keywords: Dry mouth, etiology, xerostomia

Introduction

Xerostomia, or dry mouth, is a fairly common finding and may be related to a variety of conditions including systemic disease, radiation therapy involving the salivary glands, and drug therapy. Individuals with a dry mouth may have complaints that are due to changes in quality as well as quantity of saliva and also may not be related to the degree of salivary dysfunction. Without the protective functions of saliva that include antimicrobial activity, control of the potential of hydrogen, and removal of food debris from the oral cavity, the risk of developing *Candida* infection and dental caries increases.[1,2] Diagnosis of xerostomia requires careful evaluation of signs and symptoms, with clinical extraoral and intraoral examinations, assessment of salivary gland function by measurement of resting and stimulated flow rates, and, in some cases, biopsy of minor salivary glands.

Diagnosis

Signs

Examination of the entire oral cavity is an important part of the assessment. In an individual with xerostomia, the mucosa may be dry and sticky, with the saliva appearing stringy or foamy. There may be little or no pooled saliva on the floor of the mouth, and it may be difficult to express saliva from the ducts of the major salivary glands. Dental caries may be found at the cervical margin (neck of the teeth), the incisal margins, or the tips of the teeth. These may be recurrent or primary caries and may occur at the margin of existing restorations. This type of caries may be rapid and is particularly devastating in those with severe, permanent xerostomia.

The oral mucosa may appear erythematous, with areas of the dorsal tongue sometimes becoming atrophic. The redness may represent erythematous candidiasis due to an overgrowth of *Candida albicans*. The erythematous patches commonly affect the hard or soft palate and dorsal surface of the tongue. Occasionally, pseudomembranous candidiasis occurs, which presents as removable white plaque that can be found on any mucosal surface. Angular cheilitis presents as cracking or fissuring at the commissures and can occur either alone or with intraoral candidiasis. Angular cheilitis is commonly associated with *C. albicans* but may be caused by *Staphylococcus aureus*. Individuals with oral candidiasis may complain of a burning sensation and changes in taste. Some individuals are susceptible to oral ulceration because

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of trauma to the dry mucosa. Patients with systemic disease, such as Sjogren's syndrome and human immunodeficiency virus (HIV) infection, may have enlarged parotid glands and even submandibular glands.

Symptoms

Individuals with xerostomia complain of problems with eating, speaking, swallowing, and wearing dentures. They may experience difficulty in eating dry foods, wearing dentures for a long period of time, or speaking without taking frequent sips of water. Interference with eating may occur because of changes in taste and difficulty eating spicy or acidic food.

Causes

Many conditions can cause a reduction in salivary flow. Some produce reversible or temporary dryness, whereas others result in changes that are essentially permanent. Complaints of dry mouth in a geriatric population are more likely to be related to medications than to changes in the salivary glands. Temporary conditions include the use of certain drugs, viral infections, dehydration, and psychogenic causes, such as fear. Many different types of drugs have been associated with dry mouth. These include drugs to prevent motion sickness, antihistamines, antidepressants, antipsychotics, antianxiety agents, antiparkinsonism drugs, antihypertensives, decongestants, diuretics, narcotics, and meperidine. Many of these drugs, including antihistamines, antidepressants, antipsychotics, antianxiety medications, and decongestants, cause dryness because of their anticholinergic action.

Some drugs affect fluid and electrolyte balance. The antihypertensive medication methyldopa causes dryness because it is metabolized to methylnorepinephrine in the brain. This causes stimulation of alpha-2-adrenergic receptors in the brainstem. Dryness in the elderly appears to be related to medication use or systemic disease rather than to changes directly attributable to age.[2-5]

Chronic inflammatory diseases, such as Sjogren's syndrome, sarcoidosis, and amyloidosis, cause xerostomia because of changes in the salivary glands. Sjogren's syndrome is an autoimmune disease in which marked infiltration of exocrine glands, notably, the lacrimal and salivary glands, occurs. The lacrimal gland infiltrate causes dry eyes (keratoconjunctivitis sicca). The infiltrate, consisting predominantly of a cluster of differentiation 4 (CD4) lymphocytes, as well as a small number of plasma cells and macrophages, replaces the gland acinar or secretory cells.

The disease occurs in two forms. Primary Sjogren's syndrome is mostly confined to the salivary and lacrimal glands. Secondary Sjogren's syndrome is associated with rheumatoid arthritis and other autoimmune diseases, including systemic lupus erythematosus. Autoantibodies may be found that react against anaphylaxis, SS-A (Ro), and SS-B (La). The etiology of Sjogren's syndrome is unclear but probably includes viral, genetic, and immunological factors. Diagnosis of Sjogren's syndrome is made from clinical and laboratory assessments, including histopathology of labial salivary gland biopsy.

Sarcoidosis is another chronic inflammatory disease that causes xerostomia because of changes in salivary glands that include granulomatous inflammation with Langhans' type giant cells and epithelioid macrophages, forming noncaseating granulomas. In amyloidosis, deposits of amyloid occur in the salivary glands with the consequent development of xerostomia.

Some individuals infected with HIV experience salivary gland enlargement and xerostomia. HIV-associated salivary gland disease is similar, in some ways, to Sjogren's syndrome, with xerostomia and enlargement of the parotid glands and, occasionally, the submandibular glands. However, dry eyes are not a common complaint. In HIV-associated salivary gland disease, the T-lymphocytic infiltrate is composed predominantly of CD8+ cells, whereas CD4+ cells predominate in Sjogren's syndrome. HIV-associated salivary gland disease is more common in children but is occasionally seen also in adults. Other systemic diseases that can cause xerostomia includes diabetes, if uncontrolled, and cystic fibrosis.

Almost all patients who undergo radiation therapy to the head and neck develop xerostomia. Radiation causes changes to the secretory cells, particularly the serous cells, resulting in a reduction in salivary output and a change in the viscosity of the saliva. Thick or sticky saliva is a common early complaint. The degree of permanent xerostomia depends upon the volume of salivary glands included in the fields of radiation and the total radiation dose. Even low doses of radiation can cause changes in the quantity and quality of saliva. When the total radiation dose exceeds 5,200 cGy, salivary flow diminishes, the mouth feels extremely dry, and little or no saliva is expressible from the salivary ducts. These changes are essentially permanent, with little or no recovery of salivary gland function.[6,7]

Some patients undergoing chemotherapy have reported dryness during therapy, but these changes are usually temporary.[8] Xerostomia may also be a feature of graft-versus-host disease. Changes occur when donor lymphocytes proliferate and infiltrate the recipient tissues, including salivary glands, in a pattern with clinical results resembling those seen in Sjogren's syndrome.

Methods of Assessment

Xerostomia may be evident from the examination of the oral mucosa. Complaints of dryness should be further evaluated by careful questioning. Problems with eating and swallowing have been shown to have a close association with xerostomia.[9]

Salivary flow measurement (sialometry) is an important part of the evaluation of dry mouth. It can be used to investigate and establish the diagnosis of xerostomia. The efficacy of interventive regimens, such as discontinuing medications or the use of sialagogues, can be evaluated by repeated salivary

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flow measurements. Standardized techniques must be used. These have the advantage of being relatively easy to perform, are reproducible, and give a quantitative assessment of salivary production.

Measurement of resting or unstimulated whole saliva is an easy way to evaluate complaints of dryness. Resting flow may be reduced in association with fear or anxiety, depression, and diabetes,[3] and with the use of certain drugs. Reduced flow usually correlates with complaints of dryness. Normal resting flow during the day is about 0.3 mL/min.[10]

Salivary flow rates from the parotid gland or the submandibular/sublingual glands can be assessed by the use of collection devices placed over the duct orifices. Saliva is stimulated with citric acid. The normal flow rate from the parotid gland is usually within the range of 0.4–1.5 mL/min/gland.[2,10] Reduced parotid flow is seen in diseases such as Sjogren's syndrome, following radiation therapy, and with some medications. Reduced flow may not always be associated with complaints of dryness.

Imaging techniques may provide additional important information in some cases, although they may not be useful in assessing salivary gland function. Sialography involves the injection of a radiopaque material into the salivary glands. It may be useful in identifying salivary gland stones and salivary gland masses. Sometimes, the contrast medium can cause damage and can be retained in people with xerostomia because the material is not cleared from the gland.

Scintigraphy of the major glands using sodium pertechnetate can be helpful in assessing salivary gland function. Biopsy of minor labial salivary glands is used in the diagnosis of Sjogren's syndrome, HIV-associated salivary gland disease, sarcoidosis, amyloidosis, and graft-versus-host disease. Biopsy of major glands should be reserved for investigation of salivary gland enlargement when malignancy is suspected.

Management

Therapy for radiation-induced xerostomia includes the use of salivary substitutes or salivary stimulants. Water, glycerin preparations, and artificial saliva are often used as substitutes for saliva. Some patients experience temporary relief of symptoms with artificial substances, such as carboxymethyl cellulose and hydroxyethyl cellulose solutions, such as Salivart, VA OraLube, or Xero-Lube, mucopolysaccharide solutions, such as MouthKote, or the glycerate polymer Oral Balance. Several studies have shown that artificial salivas are more effective than agents containing water or glycerin. Saliva stimulants or sialagogues, such as sugarless candies and chewing gum, or certain pharmacologic agents may be used to stimulate saliva. These agents are effective when functional salivary glands remain. After radiation therapy, although a significant proportion of the salivary glands may have been included in the radiation fields, it is rare that all the minor and major glands will be totally compromised by the radiation therapy. In systemic diseases, such as Sjogren's syndrome, the salivary gland involvement may be more widespread, leaving less functional glands available for stimulation.

Several drugs, including bromhexine, anethole trithione (Sialor, Sulfarlem), pilocarpine hydrochloride, anecdotally, and bethanechol hydrochloride, have been evaluated for their effectiveness as sialagogues.[11-16] Anethole trithione has been used in the treatment of chronic xerostomia, but reports differ as to its efficacy. Some studies found improvements in salivary flow in drug-induced xerostomia, while trials in people with Sjogren's syndrome showed conflicting results.

Pilocarpine has been effective in clinical trials in individuals with Sjogren's syndrome and those who developed xerostomia following radiation therapy.[12,13] Among 31 patients with xerostomia secondary to radiation therapy or Sjogren's syndrome, pilocarpine relieved complaints of oral dryness in nearly 90% who completed the 6-month study.[12] Although side effects, such as sweating, flushing, or polyuria, were common, they were generally tolerable. In a double-blind crossover study in 12 patients with postradiation xerostomia, nine experienced significant improvement in salivary flow with pilocarpine, whereas only two showed any improvement with placebo.[13] Valdez *et al*.[16] in a 3-month trial of pilocarpine treatment of patients undergoing radiation, demonstrated a lower incidence of oral symptoms during drug treatment compared with placebo treatment.

The safety and efficacy of oral pilocarpine hydrochloride were more thoroughly evaluated in two large, multicenter, placebo-controlled clinical trials.[17,18] Pilocarpine was shown to improve the ability to speak, the comfort of mouth and tongue, and to reduce the need for oral comfort agents.

Saliva production in pilocarpine-treated patients was significantly increased over that found in placebo-treated patients when measured postdose each time. Adverse effects associated with pilocarpine were mild in both studies, appeared to be dose related, and were generally consistent with the known pharmacologic effects of a cholinergic agonist. Sweating, transient in nature, was the most common side effect and usually occurred 20–60 min after taking the drug.

Anethole trithione and pilocarpine were reported to be useful in the treatment of radiation xerostomia in patients who have not responded to other treatments.[19] Electrical stimulation used intraorally has also been tried, with limited effectiveness.[20,21]

The oral cavity has a unique environment as it has a continuous interaction among its components– tooth surfaces, saliva, mucous membranes, and microflora. Saliva is an important component as it maintains the oral tissues in a physiologic state. Hence, correct diagnosis and management of xerostomia are paramount.[22]

Conclusion

A standardized definition and protocol to diagnose xerostomia need to be developed to facilitate comparison between studies

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and communication between researchers. Studies evaluating younger age groups should be conducted to understand the impact throughout the lifespan. Most of the current literature focuses on the prevalence of xerostomia in the Scandinavian population. More population-based studies in other regions are needed.

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Conflicts of interest

There are no conflicts of interest.

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