Xerostomia: Diagnosis and Management

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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 Sjögren'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. [ONCOLOGY 10(Suppl):7-11, 1996]

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 pH, and removal of food debris from the oral cavity, the risk for developing Candida infection and dental caries increases [1]. Diagnosis of xerostomia requires careful evaluation of signs and symptoms, with clinical extra-oral and intra-oral 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 in 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 intra-oral 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 of trauma to the dry mucosa. Patients with systemic disease, such as Sjögren'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, while 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 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, anti-psychotics, antianxiety agents, antiparkinsonism drugs, antihypertensives, decongestants, diuretics and the narcotic, meperidine. Many of these drugs, including the 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 methyl-norepinephrine 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 disease, such as Sjgren's syndrome, sarcoidosis, and amyloidosis, cause xerostomia because of changes in the salivary glands. Sjgren's syndrome is an autoimmune disease in which marked infiltration of exocrine glands, notably, the lachrymal and salivary glands, occurs. The lachrymal gland infiltrate causes dry eyes (keratoconjunctivitis sicca). The infiltrate, consisting predominantly of 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 Sjgren's syndrome is mostly confined to the salivary and lachrymal glands. Secondary Sjgren's syndrome is associated with rheumatoid arthritis and other autoimmune diseases, including systemic lupus erythematosus. Autoantibodies may be found that react against ANA, SS-A(Ro), and SS-B(La). The etiology of Sjgren's syndrome is unclear but probably includes viral, genetic and immunological factors. Diagnosis of Sjgren'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-salivary gland disease is similar, in some ways, to Sjgren'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-salivary gland disease the T-lymphocytic infiltrate is comprised predominantly of CD8+ cells, whereas CD4+ cells predominate in Sjgren's syndrome. HIV-salivary gland disease is more common in children but is occasionally seen also in adults. Other systemic diseases that can cause xerostomia include 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 gland 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 [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-vs-host disease. Changes occur
when donor lymphocytes proliferate and infiltrate the recipient tissues, including salivary glands, in a pattern and with clinical results resembling those seen in Sjögren's syndrome.

Methods of Assessment

Xerostomia may be evident from 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 interventional regimens, such as discontinuing medications or the use of sialagogues, can be evaluated by repeated salivary 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 [10], 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 [11].

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 to 1.5 mL/min/gland [11,12]. Reduced parotid flow is seen in diseases such as Sjögren'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 radio-opaque 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 Sjögren's syndrome, HIV-salivary gland disease, sarcoidosis, amyloidosis, and graft-vs-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 carboxymethylcellulose and hydroxyethylcellulose 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 Sjögren's syndrome, the salivary gland involvement may be more widespread, leaving less functional gland available for stimulation.

Several drugs, including bromhexine, anethole-trithione (Sialor, Sulfarlem), pilocarpine hydrochloride, and anecdotally, bethanecol hydrochloride, have been evaluated for their effectiveness as sialagogues [13-18]. 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 Sjögren's syndrome showed conflicting results. Pilocarpine has been effective in clinical trials in individuals with Sjögren's syndrome and those who developed xerostomia following radiation therapy [14,15]. Among 31 patients with xerostomia secondary to radiation therapy or Sjögren's syndrome, pilocarpine relieved complaints of oral dryness in nearly 90% who completed the 6-month study [14]. 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 post-radiation xerostomia, 9 experienced significant improvement in salivary flow with pilocarpine, while only 2 showed any improvement with placebo [15]. Valdez et al [18], 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 was more thoroughly evaluated in two large, multicenter, placebo-controlled clinical trials [19,20]. 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 post-dose 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 to 60 minutes 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 treatment [21]. Electrical stimulation used intra-orally has also been tried, with limited effectiveness [22,23].

**Caries**

Caries is a common occurrence in association with permanent reduction in salivary flow. The cervical and incisal areas of the teeth are frequently affected and recurrent caries may be found at the margins of existing restorations. The risk of developing caries can be minimized by following a careful regimen of diet control, dental prophylaxis, and the use of topical fluorides. Frequent visits to the dentist and the use of fluoride toothpaste, as well as home-applied topical fluoride, will help reduce the risk of caries.

Topical fluoride rinses or gels should be used once or twice a day. Sodium fluoride mouth rinse should be held in the mouth for at least one minute before expectorating. A 0.05% sodium fluoride rinse used twice daily was shown to be effective in preventing demineralization of enamel in individuals with xerostomia following radiation therapy [24]. Fluoride gels can be applied with a toothbrush and left in place for 2 to 3 minutes before expectorating. The gel can also be applied in a close-fitting custom-made plastic tray that is placed over the teeth and left in place for several minutes before removal. The choice of topical fluoride preparation should depend on patient preference and ability to comply. Chlorhexidine rinses, by reducing lactobacillus count, may also be useful in preventing caries [25].

**Oral Candidiasis**

Oral candidiasis is one of the most common oral infections seen in association with xerostomia. Pseudomembranous candidiasis may appear as removable white plaques that can appear on any mucosal surface. Erythematous candidiasis appears as red patches, most commonly seen affecting the palate and dorsal surface of the tongue. Fissuring of the dorsal surface of the tongue may be seen in association with erythematous candidiasis. Symptoms include change in taste and complaints of a burning sensation in the mouth and difficulty eating spicy foods. These complaints in people with dry mouth are suggestive of oral candidiasis.

Diagnosis can be made by microscopic examination of smears taken from the suspected lesion and examined with a potassium hydroxide preparation. The presence of hyphae and blastospores confirm a clinical diagnosis of candidiasis. In erythematous candidiasis, these hyphae may be sparse and the diagnosis is often made on response to therapy. Cultures can be useful for species determination, although C albicans is most commonly found. Angular cheilitis appears as cracking at the commissures and may occur alone or in combination with intraoral lesions. Angular cheilitis may also be a mixed bacterial and fungal infection.

Treatment of oral candidiasis involves the use of topical or systemic antifungal drugs. Care must be taken in the choice of antifungal medication, as many contain a cariogenic sweetening agent. The ideal topical antifungal medication allows a long contact time. Oral rinses, such as oral nystatin suspension, are usually not effective because of the presence of sucrose as a sweetener and short contact time in the oral cavity. Oral topical medications include clotrimazole (Mycelex-oral troche), 10-mg tablets, 1 tablet dissolved slowly in the mouth five times a day; nystatin (Mycostatin-oral pastille), 200,000 units, 1 or 2 tablets dissolved slowly in the mouth five times a day; or nystatin vaginal tablets, 100,000 units, 1 tablet dissolved slowly in the mouth three times a day. Both clotrimazole oral troche and nystatin oral pastille contain sweetening agents that are cariogenic, and
therefore, should be used with care in people with xerostomia. All three topical agents need sufficient moisture in the mouth in order to dissolve, and instructions should be given to those with a dry mouth to sip water while using the medication. People who wear dentures should be instructed to remove them before using topical antifungal agents. Nystatin and triamcinolone acetonide cream, clotrimazole cream, or ketoconazole cream (Nizoral) are useful adjuncts in the treatment of angular cheilitis. Dentures should also be treated, as Candida can be harbored in the denture material. Patients should be advised to leave their dentures out at night and soak them in 1% sodium hypochlorite solution. The dentures should be rinsed well before use.

If the denture has metal parts, other agents such as benzalkonium solution should be used. The choice of topical medication may also depend on patient preference as effective therapy depends on good patient compliance. Systemic medications include fluconazole (Diflucan), 100-mg tablet taken daily, and ketoconazole, one or two 200-mg tablets taken daily with food. Candidiasis is a recurrent problem in those with dry mouth. The choice of an effective prophylactic agent depends on patient preference and the presence of systemic disease.

Conclusions

Xerostomia is a common problem and if not recognized can lead to significant morbidity. Daily activities of living for patients with xerostomia can become overwhelming. They frequently have problems with such basic needs as speaking, eating, and sleeping. As a result, patients may become depressed or emotionally distressed due to their diminished functional capacity and overall quality of life.

Xerostomia may have devastating consequences for the oral cavity. Individuals can suffer from rampant dental caries, requiring extraction of all the teeth. Dry mouth can lead to lack of efficacy of certain medications, such as sublingual nitroglycerin. Opportunistic candidiasis causes soreness but is treatable. However, the loss of taste and difficulty in speaking and swallowing attendant on severe xerostomia can be very difficult to manage, as well as to endure.

Strategies for replacement of saliva and stimulation of natural salivary flow are important components of the management of xerostomia caused by medications, diseases such as Sjögren's syndrome, or radiation therapy for head and neck cancer. In particular, drugs such as oral pilocarpine hydrochloride tablets show much promise and can be an important therapeutic option in managing xerostomia.

References:

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