Review

Xerostomia: An Overview

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Abstract: (1) Background: Xerostomia is a subjective symptom of dry mouth resulting from various causes, including side effects of medication, systemic disorders, radiation, and Sjögren's syndrome. Recently, the number of patients afflicted with xerostomia has increased due to an increase in the elderly population and patients on medication.; (2) Methods: A systematic approach is required to determine the etiology and management of xerostomia. This review summarizes recent literatures on the diagnosis and management of xerostomia.; (3) Results: A patient with xerostomia experiences difficulty in chewing, swallowing, speaking, tasting, and maintaining oral hygiene. Xerostomia and hyposalivation are uncomfortable side-effects in many patients. Assessing the function of the salivary gland is essential for selecting an appropriate treatment, improving symptoms, and preventing oral complications. Also, a more systematic approach is required to differentiate the subjective symptoms of the patient from the objective hyposalivation.; and (4) Conclusions: Although there is no standardized treatment for xerostomia, doctors need to endeavor and adapt the various treatments of xerostomia, to unearth the optimal treatment required for the patient.

Keywords: Xerostomia; Dry mouth; Salivary hypofunction; Saliva

1. Introduction

Xerostomia generally refers to subjective symptoms of dry mouth. [1] Even with no reduction in salivary secretion, xerostomia occurs if the composition of saliva changes. [2] Generally, adults excrete 1 to 1.5 liters of saliva per day. Normally, saliva is secreted at 0.3 to 0.4 ml per minute without stimulus, and 1.5 to 2.0 ml per minute with stimulus.[3] Symptoms of dry mouth are usually seen in patients whose saliva secretion is reduced by more than 50%, and patients with xerostomia with decreased salivary secretion are usually diagnosed when saliva secretion is less than the sum of saliva absorbed from oral mucosa and saliva evaporated from the oral cavity.[4] However, hyposalivation is defined as saliva secretion less than 0.1 ml per minute without stimulus, or less than 0.5 to 0.7 ml per minute with stimulus.[3]

Patients with xerostomia may have difficulty in speaking and eating foods, and patients with reduced saliva may also suffer from symptoms such as dental cavities, bacterial infections, taste alterations, bad breath, or burning of the mouth. [5]

The elderly is further at an increased risk of systemic diseases such as aspiration pneumonia, due to oral hygiene deterioration and dysphagia. [6] The prevalence of xerostomia is 0.9-64.8%, [7] and approximately 30% of people over 65 years have xerostomia. [8] The prevalence of xerostomia is

nearly 100% in patients who have received radiation therapy for head and neck tumors, and those who suffer from Sjögren's syndrome. [9, 10]

Many factors, including physiological dehydration, neurological or cognitive dysfunction, nutritional disorders, and emotional changes such as depression, anxiety and stress, could result in xerostomia. One of the most common causes of xerostomia is medication. Anticoagulants, antidepressants, antihypertensive agents, antiviral agents, and diabetic agents are common drugs causing xerostomia. Sjögren's syndrome, radiation therapy in the head and neck region, systemic disease or salivary trauma and tumors, are other causative factors. [11]

In this paper, we present a systematic approach to diagnose the increasing incidence of xerostomia, and further introduce several known treatments.

2. Materials and Methods

Reviewing the article was conducted using a PubMed search from Jan 2015 to 31 Jul 2020. Search terminologies were utilized as below: ("xerostomia" OR "Dry Mouth" OR "Mouth Dryness" OR "Hyposalivation"). A total of 1775 articles were identified. Materials not written in English and for which full text was not obtained were excluded. After reading the titles and abstracts, articles that were not directly related to xerostomia were excluded, and 42 papers were finally selected and reviewed with priority on the materials of meta-analysis and well-organized clinical trial researches.

3. Diagnosis of xerostomia

A systematic approach is important for the diagnosis of xerostomia or hyposalivation. First, it is necessary to pay attention to the subjective symptoms of the patient and confirm them medically. The specific symptom/s of the patient may be important clues to predict xerostomia and hyposalivation. Dryness of mouth when eating, the requirement of water when eating dry foods, and discomfort during swallowing, are likely to be accompanied by an actual decrease of salivation. However, even if there is no reduction of objective salivary secretion, xerostomia discomfort is known to occur in patients. [12] Other symptoms such as uncomfortable speech, change in taste, burning sensation in the mouth, and bad breath may also occur. Ascertaining the patient's detailed history and medication record is, therefore, a necessary procedure.

A questionnaire related to dry mouth was developed by various institutions to confirm xerostomia. Sreebny et al. reported that the comment "mouth always feels dry" is predictive of a decrease in saliva secretion, having a sensitivity of 93% and a specificity of 68%. [13] A very important factor that induces xerostomia and hyposalivation is medication (Table 1). The dosage of the drug is proportional to the extent of xerostomia and hyposalivation. [14] Psychiatric drugs, diabetic drugs, respiratory drugs, and antihypertensive drugs need to be assessed. [15] In addition, Sjögren's syndrome, radiation therapy, hypertension, asthma, diabetes, hematologic disease, thyroid disease, rheumatic disease, and psychiatric history should also be confirmed.

Oral abnormalities are also known to bring about hyposalivation or xerostomia. Physical examination, other than the oral cavity, is another necessary procedure. Osailan et al. reported that the sticky mucous membrane of the mouth, bubbly saliva, invisible saliva reservoir on the oral cavity, loss of the taste bud of the tongue, depressed gums, smooth mucosa of the palate, fissured tongue, and dirty secretion of saliva are helpful in diagnosing hyposalivation. However, no correlation has been reported between these findings and the patient symptoms. [16]

Measurement of saliva secretion is an indispensable test to determine whether the cause of dry mouth lies within the salivary glands or is due to other reasons. Measurement of saliva flow should be easy and short; it is usually measured for at least 5 minutes, and measurements are taken after

fasting of at least 2 hours to rule out other confounding variables. Generally, the saliva flow is measured in a sitting position. The saliva is collected by a commercially available apparatus or by cotton swab placed in the oral cavity. The cotton should be located on the floor of the mouth or opening of the salivary duct. The salivary flow test is measured by assessing the unstimulated and stimulated salivary flow rates (stimulation of saliva secretion is achieved through chewing, or citric acid and vitamin C). The amount of saliva secreted indicates the total weight of the saliva released during a specific time in hours. Since the specific gravity of saliva is 1, the weight can be directly converted into the volume, thereby enabling measurement of the amount of saliva secreted. The saliva flow rate is measured using a specially designed instrument, a pipette, and a paper patch. [17]

Salivary gland function is measured via salivary scintigraphy. After administration of ^{99m}Technetium pertechnetate, the amount absorbed into the salivary glands and the residual amount in the salivary gland after secretion of saliva are measured to know the uptake rate and secretion rate, respectively. The function of the salivary gland can be confirmed by imaging studies such as magnetic resonance imaging or computer tomography. These methods are useful for observing salivary glandular abnormalities. Ultrasonography is also useful for non-invasive observation of the parenchyma of the salivary gland. Sialography, a useful method for monitoring the anatomy of salivary gland ducts and the appearance of tumors and stone, utilizes the injection of a radiopaque contrast into the opening of salivary gland ducts. Recent studies have employed MR Sialography, which has the advantage of confirming the pathologic status of salivary gland using saliva as the contrast agent. [18, 19] For diagnosis of the salivary gland in Sjögren's syndrome, a biopsy of the minor salivary gland in the lips and a fine needle aspiration is performed.

Type of medicine	Drugs
Anticholinergic drug	Tricyclic antidepressants, Antipsychotics,
	Anticonvulsants, Drugs for Parkinson's disease,
	Antihistamines, Anti-reflux agent, Antiemetics,
	Agents for urinary incontinence
Sympathetic stimulating drug	Antidepressant, Appetite suppressants,
	Decongestants, Bronchodilators, Skeletal
	muscle relaxants, Amphetamines
Antihypertensive agent	Angiotensin-converting enzyme inhibitors,
	Angiotensin II receptor antagonists, Calcium
	channel blockers, Alpha Adrenergic blockers,
	Beta-Adrenergic blockers, Alpha2 agonists,
	Diuretics
Anticancer drug	
Antiviral agent	

Table 1. Various drugs causing xerostomia.

Narcotic analgesics, Opiates, Sedative

4. Treatment of xerostomia

Since there is no single therapeutic policy to relieve the symptoms of dry mouth, a step by step treatment with various methods is employed, to optimize selection of the most effective method (Table 2). The primary goal of various therapeutic strategies for treating xerostomia being studied is to reduce the symptoms and increase salivation for the patient. Some of the easiest methods are to use appropriate amounts of water, avoid toothpaste or food intake that worsen xerostomia, and use of chewing gum that induces saliva secretion. [20] Lubricants, saliva substitutes, and sialogogues are also helpful in alleviating symptoms.

Pilocarpine® and cevimeline® are FDA approved salivation stimulants. Pilocarpine® stimulates the parasympathetic nerves of muscarine, while cevimeline® promotes salivary stimulation due to its strong affinity for M3 muscarinic receptors. Pilocarpine® has been approved for the treatment of dry mouth with Sjögren's syndrome and radiation therapy, and cevimeline® has approval for the treatment of Sjögren's syndrome. The indicated dosage for pilocarpine® is 5 mg and cevimeline® is 30 mg, three times a day for at least three months. [21-23] Pilocarpine® may cause side effects such as increased sweating, enlargement of skin vessels, nausea and vomiting, diarrhea, hiccups, bronchial constriction, hypotension, tachycardia, increased urinary frequency, and visual field abnormalities. Pilocarpine® and cevimeline® are relatively contraindicated in patients with uncontrolled asthma, chronic lung disease, and beta-blockers, and should be used with caution in patients with acute gastric ulcers or uncontrolled hypertension. Pilocarpine® can also be contraindicated in patients with glaucoma or iritis. Anethole trithione is a bile release promoter known to relieve the symptoms of oral dryness and promote salivation; however, more research is required for its extensive use. [24]

Drugs that are locally sprayed in the mouth are most commonly used for xerostomia patients. Many medications contain malic acid in topical spraying agents, which are effective in relieving the symptoms of dry mouth in patients using antidepressants or antihypertensive agents. [25, 26] Sugar-free gum not only increases the saliva secretion, but also plays an additional role in reducing the friction of the oral mucosa. Salivary stimulants and substitutes (as a gel, toothpaste, mouth rinse, and spray) are also commonly used drugs. Saliva substitutes mimic the saliva component without increasing the viscosity and altering the saliva secretion. These drugs include minerals such as fluoride, calcium and phosphorus, and carboxymethylcellulose, hydroxyethylcellulose, flavoring agents, and preservatives. [20] Oral sprays containing glycerol triester are also effective as salivary gland replacement agents, as are saliva substitutes including olive oil, betaine, and xylitol. [27] Fatty mucosal preservatives, natural mucins, and mucopolysaccharide-containing sprays are also used. Most of these saliva substitutes do not increase the secretion of saliva. [28]

Drugs that cause dry mouth can be reduced or replaced with other drugs. [29] However, such an alteration in therapy needs to be decided after consultation with the physician in charge of treating the disease. Another study indicates increasing the salivation through electrical stimulation of the oral cavity. [30] To stimulate saliva secretion, Saliwell Crown and the electrostimulating device GenNarino, as well as acupuncture were investigated. [31, 32]

Patients receiving radiation therapy in the head and neck area can consume drugs such as amifostine, a salivary cytoprotective agent, prior to irradiation. Recently, many efforts have been made to treat xerostomia with stem cells, growth factors, and natural antioxidant factors. [33-35]

During the treatment of xerostomia, it is important to change the lifestyle of the patient. Using humidifiers in the room, and avoiding dry foods, acid foods, caffeinated foods and alcoholic beverages that cause dehydration, are highly recommended. Regular dental or oral examinations every six months are helpful in preventing complications. Consuming less sugar and regular use of fluoride aids in preventing tooth decay and maintaining a good oral hygiene. Fungal infections in

the mouth are a common complication for xerostomia patients. A variety of antifungal agents made from rinses, ointments, candies, tablets, and mouthwashes can be used as a treatment. It is also important to treat the underlying diseases of patients, such as diabetes, renal failure, and autoimmune diseases. These remedies alleviate the symptoms, prevent deterioration, improve oral conditions, improve salivary functions, and maintain a systemic disease.

Category	Treatment	Effect
Lifestyle modification	Supply of water, Restrictions of dry, hard and acid food, Restrictions of caffeine and alcohol-containing beverages	
Systemic disease	Management of multidisciplinary underlying diseases, Control of drug dosage, Substitution of drug	
Saliva stimulating agent	Pilocarpine®, Cevimeline® Anethole trithione, Yohimbine, Anticholinesterase physostigmine	Increased salivation
Salivating agents and lubricants	Artificial saliva, Rinse agent, Gel, spray, Toothpaste	Increase of saliva viscosity
Masticatory movement	Sugar-free gum and candy	Increased salivation and reduction of mucosal friction
Salivary stimulation	Electrical stimulation, Acupuncture	Alleviation of symptoms and increased salivation
Tooth decay prevention / prosthetic care	Use of fluorine, Disinfection of prostheses, Regular screening and management	
Intraoral device	Night guard	Increased salivation and prevention of saliva evaporation
Prevention of bacterial and fungal infections	Use of antibiotics and antifungal agents	
Regenerative medicine	Stem Cells, Growth factors, Antioxidants	

Table 2. Managements of xerostomia

5. Conclusions

Xerostomia and hyposalivation are uncomfortable side-effects in many patients. This article summarizes the diagnosis and treatment of xerostomia and hyposalivation. Assessing the function of the salivary gland is essential for selecting an appropriate treatment, improving symptoms, and preventing oral complications. Also, a more systematic approach is required to differentiate the subjective symptoms of the patient from the objective hyposalivation. Although there is no standardized treatment for xerostomia, doctors need to endeavor and adapt the various treatments of xerostomia, to unearth the optimal treatment required for the patient.

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