

difficulty participating in normal training and competition, 3.8% having reduced training volume, 5.8% having their performance affected, and 29.9% experiencing oral pain. The odds of having an oral impact on their sports performance was 41.0% in men compared to women. Thirty-one percent of athletes reported a non-zero score for the severity of the oral impact. With the possibility of a top severity score of 100, the highest score was a 94.

## EFFECTS OF ORAL HEALTH

When these data were evaluated for effect/no effect, various relationships were noted. Dental caries was associated with difficulty eating. Any PUFA lesion was associated with difficulty eating, participating in normal training or competition, experiencing oral pain, and “any sport performance impact.”

Oral health status and psychosocial impacts, including pain, were also associated. Relaxing and all sport performance impacts showed relationships. Among the self-reported oral health problems related to athlete-reported impacts on their well-being or sports performance were current pain or tooth problems, sensitivity to hot or cold, bleeding when cleansing teeth, and history of swelling or infection around the wisdom teeth.

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# XEROSTOMIA

## Update on dry mouth therapies



### BACKGROUND

Salivary dysfunction includes xerostomia and hyposalivation and is a common oral disorder. Causes include drugs, aging, radiotherapy, chemotherapy, and systemic diseases of various types. Among the drugs that induce hyposalivation and xerostomia are tricyclic antidepressants, antihypertensive agents, diuretics, and antispasmodic drugs. Salivary dysfunction causes a negative impact on the patient's quality of life and can predispose to the development of problems in the oral mucosa and teeth. These include the progression of dental caries, gingivitis, halitosis, mucositis, oropharyngeal candidiasis, poor denture fit, and bacterial sialadenitis. The primary therapeutic options to address salivary hypofunction were noted, with updates as to the current best options.

### METHODS

A review of the MEDLINE/PubMed database was done. Twenty-five clinical trials that investigated the effects of various salivary treatments were selected. The treatments for xerostomia were divided into those addressing symptomology, topical or systemic stimulants, regenerative treatments, and other approaches.

### RESULTS

#### Symptomatic Treatments

Among the modalities considered symptomatic treatments were salivary substitutes, which act directly on the surface of the mucosa, and the use of topical agents such as oral xanthan gum, mucin, linseed extract, and aloe vera, which are found in mouthwashes, sprays, or gels. The most common salivary substitutes

are animal mucin, carboxymethyl cellulose (CMC), hydroxypropyl methylcellulose (HPMC), hydroxyethylcellulose (HEC), and polyglycerylmethacrylate (PGM). Three studies addressed these types of treatments. The number of participants was low in all 3. No evidence supports the use of HEC, PGM, or xanthan gum to reduce the symptoms of xerostomia. Salivary substitutes overall tend to be easily removed from the mouth by swallowing, and their effects are short-lived. Some should not be used by dentate patients because of the risk of causing tooth enamel demineralization.

#### Salivary Stimulants

Citric acid and malic acid delivered in rinses, topical applications, and sprays were evaluated in 3 randomized controlled clinical trials (RCTs). Both agents were associated with improvements in xerostomia, but the numbers of participants was low and follow-up times were short. In addition, the use of acidic substances to stimulate salivary function has the adverse effect of increasing the risk of dental hypersensitivity, erosion, and dental caries.

Chewing gum containing xylitol is also used to stimulate salivary flow and provide temporary relief from xerostomia. However, the evidence does not indicate a positive effect of chewing gum on xerostomia or hyposalivation.

The mechanism of action for acupuncture with respect to xerostomia and hyposalivation is based on stimulating the autonomic nervous system through afferent neurons. Four RCTs provided

information regarding the effect of acupuncture on salivary dysfunction. These studies suggest that acupuncture may have efficacy in addressing xerostomia. One study of cancer patients who had undergone neck dissection noted significant reductions in pain, dysfunction, and xerostomia with acupuncture compared to usual care approaches. A study of acupuncture for the prevention of radiotherapy-induced xerostomia found that unstimulated and stimulated salivary flow was greater with acupuncture compared to the control group and xerostomia scores were significantly lower in patients who underwent acupuncture treatments.

Pilocarpine stimulates the secretion of exocrine glands and participates in the contraction of the smooth muscle, gastrointestinal tract, urinary tract, gallbladder, bile ducts, and bronchi. Its effectiveness for post-radiotherapy xerostomia has been attributed to stimulation of the minor salivary glands of the palate, which are resistant to radiation. The 5 RCTs evaluating pilocarpine indicated that it may be an alternative to decrease xerostomia and salivary hypofunction. The use of 5-mg pilocarpine tablets was well-tolerated by patients and improved xerostomia in patients who had radiotherapy and in those with Sjögren's syndrome. Because it is a cholinergic agent, patients can experience side effects such as nausea, lacrimation, sweating, frequent urination, rhinitis, low-intensity headache, and gastrointestinal upset.

Two RCTs in patients who were undergoing radiotherapy evaluated the use of bethanechol to reduce xerostomia. Because the results differed between the 2 studies, more RCTs are needed to investigate whether this drug may be beneficial to patients with salivary hypofunction.

Cevimeline increases salivary production, but the drug response mechanism remains to be elucidated. Four RCTs indicated that the use of 30 mg of cevimeline 3 times a day may be appropriate for the treatment of xerostomia in Sjögren's patients and those having radiation therapy.

### Regenerative Treatments

Stem cell therapy has been proposed as a regenerative therapy for the treatment of salivary dysfunction. One of the theories explaining a regenerative capacity in the glandular epithelium of the salivary glands relies on the ability of stem cells to differentiate into other types of cells. Extraction of mesenchymal stem cells from the parotid and submandibular glands has been done to take advantage of these cells' ability to differentiate both in acinar and ductal cells. Cells of mesenchymal origin can also be obtained from bone marrow, and multipotent cells can be obtained from adipose tissue. However, studies of stem cell regenerative therapy in salivary glands are currently scarce and limited to animal models. Many questions remain to be answered, but significant progress has been made in stem cell research. Cell-based therapies may restore function to radiation-damaged salivary glands in the future.

Gene therapy may also become a therapeutic option for radiation-induced salivary hypofunction. Salivary glands are readily accessed, they are well-encapsulated to limit vector spread, and clinical gene delivery to the major salivary glands does not require local anesthesia. Gene transfer can be accomplished using viral vectors. Studies of gene therapy for xerostomia and hyposalivation are few and limited to animal models. The treatment appears to be safe and may prove beneficial in the future. However, the translation of basic and preclinical research into clinical applications for gene delivery to salivary glands has not progressed very quickly.

### Other Approaches

Hyperbaric oxygen therapy increases the oxygen in the plasma as well as its distribution to tissues, which provides better tissue recovery and stimulation of physical functions. One RCT addressed the use of hyperbaric oxygen therapy to reduce the toxicity of radiotherapy to the head and neck region in cancer patients. Although a significant difference was found in the salivary consistency and degree of xerostomia between the treated and control groups, the current evidence is insufficient to recommend this treatment. It should also be noted that this treatment requires frequent sessions and specific equipment, making it a very expensive option.

## DISCUSSION

Most of the clinical trials addressing methods of treating xerostomia and hyposalivation have few participants and short follow-up times. The most promising treatments are pilocarpine and cevimeline. Citric and malic acids increase salivary flow but have the adverse effect of increasing the risk of erosion and dental caries. Clinical observations indicate promising effects for acupuncture, stem cell therapy, and gene therapy, but no controlled clinical trials support the efficacy of these approaches. No evidence supports the use of salivary substitutes, chewing gum, bethanechol, or hyperbaric oxygen to manage xerostomia or salivary hypofunction.

### Clinical Significance

Current evidence is limited regarding the use of any of the interventions outlined in this review. Patients may benefit from the use of pilocarpine and cevimeline as well as from citric and malic acids, although the latter should be used cautiously and with appropriate monitoring. Several therapies offer promise but are not yet at the stage where their use would be appropriate. Therapies such as stem cell therapy, gene therapy, and hyperbaric oxygen therapy also involve a significant cost component. Further research is needed.

## Diagnosing oral hypofunction



### BACKGROUND

Older adults gradually become dependent and just as gradually change in oral health status. Declines in oral function accompany the declines in systemic function. To prevent oral function from becoming oral dysfunction, a means to diagnose the patient's condition is essential. The study group of the National Center for Geriatrics and Gerontology in Japan has developed a concept regarding the progressive process of general functional decline related to decreased oral function. Oral frailty was defined as frailty that manifests only in the oral cavity. Its signs and symptoms have been specified as decreased articulation, slight choking or spillage while eating, and an increase in the number of unchewable foods. To recover from oral frailty requires not only maintenance of oral hygiene to prevent oral disease but also restoration of function by providing any needed prostheses to counter the effects of tooth loss. Oral hypofunction was proposed as a term referring to the stage at which recovery can be expected and occurs before oral dysfunction develops. The concepts related to oral hypofunctional state were defined, along with signs and symptoms of the condition, and a method was developed to establish diagnostic criteria for oral hypofunction.

### CONCEPTUAL DEFINITIONS

A conceptual diagram was created to guide diagnosis from the healthy state through oral frailty, oral hypofunction, and oral dysfunction (Figure 1). Both oral frailty and oral hypofunction can be restored to a previous stage by specific remedies.

Seven conditions were selected as part of the diagnostic process used to identify oral hypofunction. These included poor oral hygiene, oral dryness, reduced occlusal force, decreased tongue-lip motor function, decreased tongue pressure, decreased masticatory function, and the deterioration of swallowing function. In addition, the initial thresholds for entering these conditions were defined. Oral hypofunction was defined as the state when 3 or more of these diagnostic criteria are present.

### SIGNS AND SYMPTOMS

Poor oral hygiene was defined as an increased number of microorganisms in the mouths of older adults. Various methods are available to measure the number of microorganisms present. The diagnostic criterion is based on the total number of microorganisms expressed as colony-forming units per milliliter and was

determined to be  $10^{6.5}$  CFU/mL or more. If the Tongue Coating Index (TCI) is measured, the criterion is 50% or higher.

Oral dryness, which is an abnormally dry state in the oral cavity or a subjective perception of intraoral dryness, contributes to loss of homeostasis of the oral structures. An oral moisture checker measures mucosal wetness, but the Saxon test can also be used. The diagnosis of oral dryness is made if the oral moisture checker obtains a value less than 27.0 or the Saxon test results are 2 g/2 min or lower.

Reduced occlusal force is strongly correlated with masticatory ability, influenced by the number of natural teeth present and the occlusal support. Muscular weakness can also contribute. If the occlusal force is less than 200 N or the number of natural teeth, excluding roots and highly mobile teeth, is less than 20, reduced occlusal force is diagnosed.

Both speed and dexterity are reduced in decreased tongue-lip motor function, which results from a decline in brain function and perioral muscle function, often caused by systemic disease and changes related to aging. Oral diadochokinesis is used to measure motor speed and dexterity of the tongue and lips. Decreased function is diagnosed when the number of any of the /pa/ta/or/ka/ produced per second is less than 6.

Patients with decreased tongue pressure suffer chronic functional decline in the muscles that move the tongue. With progression, normal mastication, bolus formation, and swallowing become impaired, which can lead to insufficient food intake to meet nutritional requirements. Maximum tongue pressure is measured by having the patient compress a balloon attached to a tongue pressure probe onto the anterior palate for a few seconds using the tongue's maximum voluntary force. The diagnosis of impairment is made when the pressure is less than 30 kPa.

Decreased masticatory function results in frequent spillage while eating and choking when swallowing, as well as having more foods considered unchewable. These events lead to a loss of appetite and reduced numbers and types of foods that are consumed. The state can progress to malnutrition and decreased metabolic rate. Glucose concentration obtained from chewed gummy jelly is used to evaluate a patient's masticatory function. The degree of eluted glucose is measured using a masticatory ability testing