



## Review Article

# Xerostomia: The Causes and Clinical Management Including Acupuncture and Herbal Medicine

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### Abstract

**Background:** Xerostomia is chronic sensation of a dry mouth and affects a large part of the population. Xerostomia often severely impairs quality of life with patients experiencing tooth caries, altered taste and smell, difficulty talking, problems with chewing, burning tongue, candida infection and so on. The pathology and course of xerostomia are not well described, many factors could cause xerostomia. It is usually the complex reasons for patients with xerostomia and identifying the causes will help guide clinical management. Several therapeutic strategies are available for

xerostomia. However, these treatments achieve limited effects and often induce adverse effects.

**Main Body of the Abstract:** This review focus on the causes and clinical management of xerostomia, including acupuncture and herbal medicine.

**Short Conclusion:** The complementary and alternative medicine such as acupuncture and herbal medicine could be helpful in patients suffering from xerostomia.

**Keywords:** Acupuncture; Causes; Clinical management; Herbal medicine; Xerostomia

## 1. Background

Xerostomia is the subjective feeling of dry mouth. This symptom is more common in ageing populations but is not caused by ageing. Saliva protects all the tissues of the oral cavity and is fundamental to our oral health and our wellbeing. Hyposalivation usually results in the feeling of xerostomia and other consequences including increased caries formation, gingivitis, dysarthria, dysgeusia, taste aberrations, poor denture retention, increased rate of candida infection and burning tongue [1-2]. All these distressing symptoms have a profound negative impact on patients' quality of life. The etiology of xerostomia is not well described, many factors could cause xerostomia as the secretion of saliva is regulated by the autonomic nervous system and is subject to reflex stimulation from physical and psychic causes. From the clinician's perspective, identifying the causes will help guide clinical management. This review focus on the causes and clinical management of xerostomia including complementary and alternative medicine such as acupuncture and herbal medicine.

## 2. Main Text

### 2.1. The Causes of Xerostomia

Many factors could cause xerostomia. It is usually the complex reasons for patients with xerostomia. It is important to identify the causes for guiding clinical management. Saliva is secreted by the major salivary glands including the parotid, submandibular or submaxillary, sublingual and minor salivary glands sited on the oral mucosa. Saliva is primarily made up of water (99%) and many electrolytes which include sodium, potassium, calcium, magnesium,

bicarbonate, and phosphate. The pH values of this biological fluid basically vary from 6 to 7 [3-4]. Therefore, individuals' saliva is affected by their systemic water and electrolyte balance and acid-base balance. An adult usually needs 6 to 8 glasses of fluid per day. If no enough fluids are drunk, the salivary glands will not produce enough saliva. The patients with fluid intake restriction for some medical reasons could cause xerostomia either. And any condition which creates a loss of body fluid—such as vomiting, diarrhea, sweating or hemorrhage—will cause xerostomia, as will the polyuria of diabetes [1]. The deficiency of body fluid leads to the hyposalivation and xerostomia, which generally is defined as deficiency of Qi, blood and body fluid in traditional Chinese medicine. While in the cases without deficiency of body fluid, the reduced rate of saliva secretion could cause xerostomia either, which generally is defined as disorders of distribution of Qi, blood and body fluid in traditional Chinese medicine. The secretion of saliva is regulated by the autonomic nervous system and is subject to reflex stimulation from physical and psychic causes. Both afferent and efferent stimuli modulate neural control of salivation. Apart from taste and mastication, which play a key role, the former also include smell, sight, and thought. Input to the solitary nucleus from afferent stimuli is integrated via the facial (VII) and glossopharyngeal (IX) nerves [5].

Four basic reasons are proposed to describe the etiology of xerostomia as the secretion of saliva is regulated by the autonomic nervous system and is subject to body fluid or electrolyte balance [1]:

- A. Factors affecting the salivary centre
- B. Factors affecting the autonomic inflow and outflow pathway
- C. Factors affecting salivary gland function
- D. Factors affecting body fluid or electrolyte balance

Many cases of xerostomia are related to psychological conditions like depression and anxiety [1]. And brain tumor, encephalitis, stroke, drugs could be the factors affecting the salivary center and autonomic pathway. There are various diseases where the salivary glands are directly affected by the disease process including Sjogren's syndrome, obstruction and infection of salivary gland, tumors of salivary gland, stroke, Alzheimer's diseases, irradiation, excision of salivary gland, drugs and so on [1]. And salivary glands are involved due to many systemic diseases with the resultant complication of xerostomia. Autoimmune diseases such as Sjogren's syndrome and Systemic lupus erythematosus, endocrine diseases such as diabetes and thyroid disease, end-stage renal disease and chronic graft-versus-host disease are frequently associated with salivary hypofunction [1,6]. From an etiological perspective, the most common cause of xerostomia is the use of medications with potential xerostomia effects, especially in elder people. There is a large number of drugs with the side effect of dry mouth, such as anticholinergic and antimuscarinic agents, antidepressants, anticholinergic agents, anxiolytic, sedative, antihypertensive drugs and so on may lead to xerostomia [7-8]. Sjogren's syndrome is a relatively common systemic autoimmune disease characterized by lymphocytic infiltration of the secretory glands. This process leads to sicca syndrome, which is the combination of dryness of the eyes (xerophthalmia), oral cavity (xerostomia), pharynx and/or larynx, which are the classical symptoms [9]. In other situations, dry mouth is mainly due to the radiation received by patients with head and neck cancer. Radiotherapy plays a pivotal role in the treatment of patients with head and neck cancer. Some head and neck cancer patients will receive radiotherapy. No technology can entirely protect normal tissues from irradiation and patients will always experience some degree of radiation-associated toxicity. The most

prevalent adverse effect of radiotherapy is the impaired functioning of the salivary glands and xerostomia [10]. Sometimes dry mouth could also be caused by opening the mouth for breathing due to rhinitis or snoring, especially during sleep.

## **2.2. Clinical Management of Xerostomia**

Commonly the xerostomia patients should be advised to avoid dry foods, spicy foods, alcoholic beverages, carbonated beverages, and tobacco. A high fluid intake should be encouraged unless it is medically contra-indicated. Maintenance of optimal air humidification in the home is helpful. And a visit to the dentist to make sure that all sharp cusps of teeth, irregular fillings and dentures are smoothed is advised [1]. If the cause is body fluid loss, then stopping the loss and increasing body fluid will eliminate the problem. If the cause is a medication, then the therapeutic strategy is to modify drug scheduling, adjust doses or terminate the drug causing the sensation of dryness or substitute it for another with less xerostomia effect [1,11]. In cases where salivary gland remains and there is some residual function of the parenchyma, it may be possible to use cholinergic to stimulate the salivary glands to produce more saliva [11-12]. Cholinergic drugs such as pilocarpine may be tried, unless medically contra-indicated. And pilocarpine should be withdrawn if there is no response. The patient also may get some relief by chewing a sugarless gum or use of malic acid [11-12]. There has been a lack of important developments in recent years in terms of drug treatment. Pilocarpine remains the only drug used in trials showing clear improvements in salivary flow and symptoms, but always where there is some residual function of the parenchyma [8,11-12]. The main problems related to pilocarpine treatment are the fact that the beneficial effect of the drug expires soon after termination of drug administration, and the adverse reactions due to

cholinergic stimulation such as sweating, nausea, fever or diarrhea [8,11-12]. When stimulated saliva secretion is much reduced or when stimulation of saliva secretion is impossible, palliative oral care can alleviate xerostomia. There are many distinct products included within this group such as commercial artificial salivas, toothpaste, mouthwash, moisturizing gel, chewing gum, and salivary flow stimulating tablets. These products are useful to alleviate the discomfort, but often help only for a short period of time [13-14]. Due to the limitations of the therapies described above, complementary and alternative medicine have become more popular among patients suffering from xerostomia.

### 2.3. Acupuncture and Herbal Medicine

Acupuncture, herbal medicine or the combination of both are the most popular alternative treatment for xerostomia in China. The treatment principle is according to the theories of Chinese traditional medicine. The basic theories of Chinese traditional medicine include the theory of Yin Yang and five elements theory, viscera theory and meridian theory. These theories constitute a complete diagnosis and treatment system of Chinese medicine. There are mutual promotion and restraint between Yin and Yang. Among the five elements, there is a network of mutual promotion and restraint in constant motion and change. The Yin Yang and five elements theory, viscera theory and the meridian collateral theory are concerned with the physiological functions and the pathological changes of the viscera organs system and meridian system, and the relationships with each other. The overall concept, Yin and Yang, five elements, viscera organs, meridians network coincide to maintain and adjusting the internal balance for individuals. It is considered that the pathogenesis of dry mouth is mainly caused by disorder of distribution of body fluid or body fluid deficiency including insufficient generation or excessive loss of body

fluid. The disorder of distribution of body fluid is mainly related to lung, spleen, kidney, Sanjiao, Shaoyang and liver, while the body fluid deficiency is mainly caused by deficiency of Yin, deficiency of Qi and Blood, or by dry heat damaging body fluid.

### 2.4. Acupuncture

The principle of acupuncture treatment should be clearing away heat and toxic material, promoting blood circulation to remove meridian obstruction, supplementing Qi, nourishing Yin and promoting the production of body fluid. The method of acupoints selection for the treatment of xerostomia is mainly local acupoints selection combined with acupoints selection along meridians.

The earliest medical classic in China, Huangdi Neijing (Huangdi's internallassic), came out more than 2,000 years ago. It mentioned that the meridians related to the mouth, tongue, lip, and pharynx include "Large Intestine Meridian of Hand-Yangming", "Spleen Meridian of Foot-Taiyin", "Stomach Meridian of Foot-Yangming", "Heart Meridian of Hand-Shaoyin", and "Kidney Meridian of Foot-Shaoyin". Especially, dry mouth is most frequently associated with the pathological changes of "Large Intestine Meridian", "Heart Meridian" and "Kidney Meridian".

Based on ancient documents, Chen [15] and colleagues researched the acupoints selection to treat thirst symptom in traditional Chinese medicine. By querying articles related to thirst from ancient documents, they noted down the related meridians and the acupoints. They sequenced the results and figured out the rules of applying these meridians and acupoints. They found the first 10 acupoints that were most frequently used for thirst or dry month symptom based on ancient documents were as follows: Qu Ze (PC3), Tai Chong

(LR3), Shao Ze (SI1), Chi Ze (LU5), Tai Yuan (LU9), Shang Yang (LI1), Guan Chong (TE1), Zhao Hai (KI6), Da Zhong (KI4) and Fu Liu (KI7). They found the ideas to treat thirst symptom were to decrease the overheat in lung and large intestine meridians and the blocked heat in liver and gallbladder meridians with nourishing Yin in kidney meridian, in addition to local acupoint selection of Dui Duan (GV27). Chen [15] also researched the acupoints selection to treat for “Xiao Ke” symptom which is mostly like dry mouth associated with diabetes in traditional Chinese medicine. By querying articles related to “Xiao Ke” from ancient documents, they found the most frequently 6 acupoints for “Xiao Ke” were Cheng Jiang (RN24), Yi She (BL49), Ran Gu (KI2), Shui Gou (GV26), Xing Jian (LR2) and Yin Bai (SP1). The treatment ideas for “Xiao Ke” were to decrease heat in spleen meridian, to balance the Yin and Yang in kidney meridian and local acupoint selection of Cheng Jiang (RN24). Liu [16] and colleagues studied the therapeutic effect of acupuncture in 60 cases of Sjogren Syndrome and found it was effective and safe. The treatment group were treated with acupuncture of collaterals at Qu Ze (PC3), Tai Chong (LR3), Xue Hai (SP10), San Yin Jiao (SP6), Tai Xi (KI3), Lian Quan (RN23), Jin Jin and Yu Ye (EX-HN12). Qing Ming (BL1) and Si Bai (ST2) were added for patients with xerophthalmia.

Several studies have explored the effect of acupuncture on radiation-induced xerostomia among patients with head and neck cancer. It is reported that acupuncture was found to be effective also in pilocarpine-resistant patients and as a preventive treatment of xerostomia following radiotherapy for head and neck malignancies [17-18]. Zhao [19] and colleagues studied the effect of acupuncture on radiation-induced xerostomia among patients with head and neck cancer. They found that the position of Xia Guan (ST07), Da

Ying (ST05) and Lian Quan (RN23) is close to the position of parotid gland, submandibular gland and sublingual gland respectively. By the acupuncture of these three acupoints with other acupoints including Tian Rong (SI17), Zhao Hai (KI6), Ye Men (SJ02), Tai Xi (KI03) to replenish Qi, nourish Yin, promoting blood circulation to remove meridian obstruction, and clear away heat, the dry mouth of patients after radiotherapy could be alleviated. If the sublingual vein of the patient is obviously varicose, combined with prick bloodletting in Jin Jin and Yu Ye (EX-HN12) to activate blood circulation and resolve stasis. Jia [20] and colleagues found that Zu San Li (ST36) and He Gu (L14) acupoints had obvious effects in regulating neuroendocrine immunity and could be used as the acupoints in the prevention and treatment of precancerous lesions of oral mucosa. Acupuncture treatment indicated a promising therapeutic option for the treatment of xerostomia.

### 2.5. Herbal medicine

According to Traditional Chinese Medicine, four Qi (cold, hot, warm and cool), five flavors (acid, bitter, sweet, pungent and salty), meridian tropism and efficacy of different herbs could play a fundamental role in adjusting the imbalance of human life state to rebalance. Chinese herbal compound doesn't mean adding single herb simply. Based on Chinese herbal compatibility theory, Chinese herbal compound is a combination of several herbs and deployment of the four Qi, five flavors, meridian tropism of herbs to achieve the overall synergy and to maximize efficacy, and to reduce the toxicity and bias of single herb. The prescription rules in the treatment of xerostomia include: nourishing Yin and promoting the production of body fluid, supplementing Qi, Blood and promoting the production of body fluid, promoting blood circulation and removing stasis, clearing away heat. And clearing heat and toxic material, anti-

radiation injury, promoting the recovery of radiation-induced immune function injury should be considered for radiation-induced xerostomia patients with head and neck cancer as well. Chen [21] and colleagues analyzed the prescription rules of xerostomia in the Traditional Chinese Medicine Prescription Dictionary by data mining. They analyzed the frequency, four Qi (the four natures), five flavors and meridian tropism of drugs and get the link relationship between drugs through the network diagram. They found that there were 46 prescriptions and 98 kinds of drugs for xerostomia in the dictionary, among which the most frequent drug was Zhi-Gan-Cao (Roasted licorice), followed by Wu-Mei (Fructus Mume), Mai-Dong (Ophiopogon Japonicus) and Fu-Ling (Poria Cocos). Among the four Qi, cold drugs are the most frequently used; Among the five flavors sweet drugs are the most frequently used; Lung meridian appears the most frequently, followed by spleen meridian and stomach meridian. Three main drug combinations were obtained from modular analysis of complex network diagram:

1. Mai-Dong (Ophiopogon Japonicus), Tian-Hua-Fen (Trichosanthin), Huang-Lian (Coptis Chinensis) and Di-Gu-Pi (Cortex Lycii Radicis);
2. Wu-Mei (Fructus Mume) and Ge-Gen (Pueraria Lobata);
3. Zhi-Gan-Cao (Roasted licorice) and Ren-Shen (Ginseng).

Based on the Traditional Chinese Medicine Prescription Dictionary, herbs of replenishing Qi, nourishing Yin and clearing away heat are commonly used in the treatment of xerostomia [21].

Sun and Wang [22] studied the medication regularity of compound herbal formulae in treating patients with Sjogren's disease published on journals from China National Knowledge Infrastructure (CNKI) for database establishment. There were 126 compound herbal formulae (involving 234 Chinese medicinal herbs and 1080 frequency) for Sjogren's disease. Among the four Qi, cold drugs showed the highest frequency. Among the five flavors, sweet was the highest. Among the meridians, lung meridian had the highest frequency.

The top 5 herbs were Gan-Cao (licorice), Mai-Dong (Ophiopogon japonicus), Bai-Shao (Radix Paeoniae Alba), Sheng-Di-Huang (raw Rehmannia glutinosa Libosch) and Dang-Gui (Angelica sinensis). The most commonly used herbal combinations are "Bai-Shao (Radix Paeoniae Alba) and Gan-Cao (licorice)", "Sheng-Di-Huang (raw Rehmannia glutinosa Libosch) and Mai-Dong (Ophiopogon japonicus)", "Gan-Cao (licorice) and Mai-Dong (Ophiopogon japonicus)", "Shan-Zhu-Yu (Cornus officinalis), Ze-Xie (rhizoma alismatis) and Fu-Ling (Poria Cocos)". Chang [23] et al evaluated frequencies and patterns of Chinese herbal medicine used for Sjogren's syndrome in Taiwan by analyzing the National Health Insurance Research Database for cases in which Chinese herbal medicine was used as an alternative therapy to Western medicine for improving patients' discomforts. They found that "Qi-Ju-Di-Huang-Wan" and "Xuan-Shen" (Scrophularia ningpoensis Hemsl.) was the most commonly used formula and single herb, respectively. "Qi-Ju-Di-Huang-Wan", "Gan-Lu-Yin", "Xuan-Shen", "Mai-Dong (Ophiopogon japonicus), and "Sheng-Di-Huang" (raw Rehmannia glutinosa Libosch)" were the core pattern prescriptions in treating Sjogren's syndrome. Many herbs and herbal formula with effects of anti-radiation injury and promoting the recovery of



radiation-induced immune function injury were reported. Among these, the most popular herbs and herbal formula include Ren-Shen (Ginseng), Huang-Qi (Astragali Radix), Dang-Gui (Angelica Sinensis), Hong-Jing-Tian (Rhodiola Crenulatae Radix), Gou-Qi-Zi (The fruit of Chinese wolfberry), Sha-Shen (Adenophora Stricta) and classical Chinese herbal compound for nourishing Qi and Blood such as “Si-Wu-Tang”, “Si-Jun-Zi-Tang” and “Bu-Zhong-Yi-Qi-Wan” [24]. Herbal medicines had potential benefits for improving salivary function and reducing the severity of dry mouth patients. However, methodological limitations and a relatively small sample size reduced the strength of the evidence [25].

### 3. Conclusions

Many factors could cause xerostomia. Sometimes, it is the complex reasons for patients with xerostomia. Identification of the main reason of xerostomia helps attain timely diagnosis and more appropriate treatment plan. If the cause is a medication, then the therapeutic strategy is to modify drug scheduling. Despite the different etiological origins of dry mouth, pilocarpine is the most used parasympathomimetic drug for xerostomia. Acupuncture and herbal medicine had potential benefits for improving salivary function and reducing the severity of dry mouth patients, and anti-radiation injury, promoting the recovery of radiation-induced immune function injury, so could be a promising therapeutic option for the treatment of xerostomia but need further research to strengthen the evidence.

### Declarations

#### Ethical Approval and Consent to Participate

Not applicable.

### Consent for Publication

Not applicable.

### Availability of Supporting Data

Not applicable.

### Competing Interests

The author has declared that no competing interest exists.

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### Author contribution

Zhao Min was the contributor in writing the manuscript.

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