

Herbal Medicine Treatment for Xerostomia in Elderly Patients and Salivary Gland Regeneration Research

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ABSTRACT

Xerostomia often occurs in elderly patients due to Sjögren's syndrome, sialadenitis, IgG4-related disease, diabetes, dyslipidemia, and side-effects from certain medications. It is defined as a disturbance in saliva secretion, which can be triggered by radiation therapy and causes many oral and dental problems. Therefore, it is necessary to ameliorate oral symptoms and regenerate salivary glands in patients with these diseases. To relieve xerostomia and stomatitis, herbal medicines such as Japanese traditional medicine (Kampo) are often applied. Kampo therapy is effective for dry mouth symptoms. However, the salivary gland is complex and it is difficult to regenerate the salivary gland through clinical treatment. Byakkokaninjinto and Goreisan are often used as Kampo therapy for xerostomia through regulation of aquaporins. To investigate salivary gland regeneration after inflammation and atrophy, duct-ligation animal models were used in our previous studies. This model revealed that cytoskeletal changes and the distributions of small Rho GTPases, fibroblast growth factors, and β -catenin have important roles in cell proliferation and differentiation during submandibular gland regeneration.

Keywords: Xerostomia; Herbal medicine; Oral mucosa; Candidiasis; Potentially malignant disorders; Regeneration; Duct ligation model

INTRODUCTION

Xerostomia often occurs in elderly patients due to Sjögren's syndrome, sialadenitis, IgG4-related disease, diabetes, dyslipidemia, stress, and side-effects from certain medications. It is defined as a disturbance in saliva secretion, which can be triggered by radiation therapy and causes many oral and dental problems. Therefore, it is necessary to rescue oral symptoms and regenerate salivary glands in patients with these diseases. To relieve xerostomia and stomatitis, herbal medicines such as Japanese traditional medicines (Kampo) are often applied [1]. Kampo therapy is effective for dry mouth symptoms. However, the salivary gland is complex and it is difficult to regenerate the salivary gland through clinical treatment [2-4].

SALIVARY GLANDS IN HUMANS

Salivary glands are roughly divided into major and minor salivary glands. The major salivary glands include the parotid, submandibular, and sublingual glands, which occur as pairs (left and right) in the head and neck. Minor salivary glands are located

in the lip, cheek, tongue, oral floor, palatal, and molar gingival mucosae.

XEROSTOMIA LEADS TO CANDIDIASIS

Xerostomia occurs in 12%-28% of elderly individuals [5]. It leads to oral dysfunctions such as mastication disorder, dysphagia, taste disturbance, and burning sensations. Because of the reduction in saliva volume, the oral mucosa becomes more susceptible to infection [5]. Xerostomia can lead to the development of candidiasis in elderly individuals. Chronic candidiasis was classified as a potentially malignant disorder by the World Health Organization in 2017 [6]. Therefore, treatment for xerostomia is required to reduce the risk of oral cancer.

KAMPO TREATMENT FOR XEROSTOMIA

Herbal medicines, such as Kampo, are complex medicines derived from several kinds of natural resources and are useful for various diseases [1]. To our knowledge, Byakkokaninjinto (BKNT) and Goreisan (GRS) are the most popular forms of Kampo for

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patients with dry mouth. BKNT contains 5 constituent plant extracts: Anemarrhena rhizome, brown rice, ginseng, glycyrrhiza, and gypsum [1]. A previous report suggested that BKNT acted on aquaporins 2 and 3 in a mouse model of diabetes [7]. GRS has 5 natural components: Alisma rhizome, Astractylodes lancea rhizome, cinnamon bark, Polyporus sclerotium, and Poria sclerotium [1]. In an in vivo study of rat kidneys, it was suggested that GRS acted on aquaporins 1, 2, 3, and 4 [8].

IN VIVO STUDIES OF SALIVARY GLAND REGENERATION

To investigate salivary gland regeneration after inflammation and atrophy, duct-ligation animal models (DL models) were used in our previous studies [2-4,9]. In this model, ligation of the secretory duct eliminates most acinar cells and increases connective tissues, whereas release of ligation causes the appearance of transitional duct-like structures (DLSs) and proliferation of residual acinar cells. Additionally, DLSs are associated with the regeneration of acinar cells [2-4,9]. Temporospatial changes in the cytoskeleton maintains cell proliferation and differentiation during submandibular gland regeneration [2]. Additionally, small Rho GTPases and β -catenin have important roles in acinar cell regeneration [3], and saliva secretion is regulated by various factors, such as aquaporins [9]. DL models indicate that acinar cells regenerate through pathways other than the proliferation of residual acinar cells, suggesting that DLSs have progenitor cells that can differentiate into newly formed acinar cells [2-4,9]. However, the mechanisms by which progenitor cells proliferate and differentiate into acinar cells remain unclear. Therefore, we are currently investigating another experimental animal model [10]. We plan to carry out further research into salivary gland regeneration using this new method.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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