CHAPTER I

INTRODUCTION

Rationale and Background

Radiotherapy is an important modality as primary and adjuvant treatment for primary head and neck malignancies. An annual incidence of head and neck cancers is 12.7 per 100,000 in general population, and they are ones of the leading cancers in Thailand [1]. Radiation portals always include a large part of the parotid, submandibular gland and/or minor salivary gland volume.This is often complicated by xerostomia which creating many problems with swallowing, speaking, mucosal burning pain, dental, periodontal disease and lower quality of life.

This insufficient salivary flow can result from the inflammatory and degenerative effects of ionizing radiation on salivary gland parenchyma, especially serous acinar cells [2, 3]. The salivary flow measurably decreases within 1 week after starting the radiation treatment and progressively diminishes with further continued treatment [3]. Parotid gland may be more susceptible to its radiation effect than submandibular, sublingual or other minor salivary glandular tissues. At dose above 50 Gy, salivary dysfunction is severed [4, 5] and permanently damaged but some of the minor salivary gland function still exist.

The diagnosis of xerotomia is based on subjective impressions by patients and clinicians. However, many researchers have tried to quantify the xerostomia state by an objective measurement of the salivary flow rate, but the standard methods have not been established. The salivary flow rate quantification was composed of resting saliva measurement and stimulated saliva measurement. The resting saliva measurement is done by letting the patients drool over a plastic container or tube glass for 3-5 minutes, and the saliva will be weighed. Additionally, stimulated saliva is collected by letting the patient chew on paraffin or tasteless parafilm for 3-5 minutes, so the saliva can be weighed.

Management of xerostomic includes 3 modalities: oral hygiene care, topical therapies and systemic therapies. In cases of post-irradiation xerostomia, the salivary

function is severely affected; as a result, only hygiene oral cares are not proved effective. The topical and systemic therapies are beneficial in this situation. Topical therapy agents may be in forms of sugar-free gum, candies, liquid [6, 7], mouthwashes, [8] salivary stimulant pastilles [9, 10], humidifiers [11] and saliva substitutes.

Saliva substitutes, in general, comprise 4 base compounds [12]: oil, mucin [13], lubricating gels [14, 15] and carboxymethylcellulose. Oil has the worst taste. Mucin is better for normal oral floras because it has antimicrobial properties, but it is expensive and difficult to be manufactured. Gel has high viscosity and enduring effect, but it has problems with the application and handling, so it is preferred to be used at night. [12]

The last one, carboxymethlycellulose, which is the polymer-base, is inexpensive, good taste and is the most conventional daily used regimen including at our institute. It is easy to be handled and delivered to the mouth during the daytime. However, the drawback is that it is easily removed from the mouth and has short duration effects.

Roles of saliva substitutes in xerostomia patients are to lubricate, hydrate the oral mucosa and/ or mineralized the teeth. Their roles are able to reduce xerortomia symptoms, but the results are not obvious and depended on the compounds used. [12, 16]

Systemic therapy has focused on pilocarpine which was approved by the U.S. Food and Drug Administration [17] to increase saliva secretion in the head and neck radiation and Sjogren syndrome.

Pilocarpine is a parasympathetic agonist of acetylcholine muscarinic M3 receptors. Thus, it stimulates secretion of exocrine glands such as the salivary, sweat, lacrimal, and respiratory mucous glands [18]. Also, it stimulates contraction of the smooth muscles, the motility of the gastrointestinal and urinary tracts, gall bladder, biliary ducts, and bronchi. [19] These latter effects have dissuaded some clinicians to use pilocarpine. Weaver [20] found pilocarpine absorption in dog to be 72.9±38.5μg/kg per hour at a pH of 7.6. The time to appearance in the blood stream was 0.31±0.32 hours. A threshold dose of 32.9± 7.5 μg/kg was required to induce secretion.