

CHAPTER II

LITERATURE REVIEW

The search strategy used to locate the literature in this study was performed through MEDLINE database and additionally through the reference lists of the articles and institutional databases. The medical subject heading terms used for search strategy were (Pilocarpine OR artificial saliva OR saliva substitute OR *cellulose) AND (Irradiation OR radiation OR radiotherapy) AND (xerostomia OR hyposalivation), "LENT SOMA" AND xerostomia, "LENT SOMA" AND validity. 86 studies were found and 4 were randomized-controlled trials in topical pilocarpine.

Pilocarpine has been studied in many literatures in reducing xerostomia symptoms. Results of oral pilocarpine in some studies suggested that it might lessen the severity of radiation-associated xerostomia symptoms, [19, 21-27] but some study have contradicted these effects.[28, 29] Some articles reported high drop out rates (>20%) from side effects [27, 30]

In post radiotherapy, pilocarpine can stimulate residual major and minor salivary gland functions. It cannot increase the function of glands that are completely damaged. [17, 31] Moreover, the stimulation effects of salivary flow for post irradiation xerostomia are controversial problems. Some articles indicated improvement of subjective xerostomia symptoms [19, 21-26] (they did not study on objective salivary flow). Some studies reported both subjective and objective salivary flows. [27, 32] Some articles could not demonstrate any improvement of xerostomia subjectively and objectively [28, 29]. However, many literatures revealed the improvement of subjective xerostomia but not objective salivary flow. These studies have demonstrated that symptomatic improvement is not always correlated with the objective salivary flow. [10, 29, 33-36]

About the topical pilocarpines, they can directly stimulate the minor salivary gland function which has more tolerance to the damaging effects of the radiation compared with the major salivary glands. However, the topical pilocarpines have fewer side effects than the systemic route. The rationale of dispensing the drug is to avoid the "first pass" hepatic loss and obtain local response while avoiding systemic side effects. There were

reports of topical pilocarpine in subjective improvements of xerostomia symptoms. There was one trial using pilocarpine suspended in a candy like pastille compared with the placebo. [10] In this study, the sample size was limited and the statistic analysis was unclear because the placebo data was not be reported. Another study using pilocarpine eye drop added in artificial saliva also had limited sample sizes and used low concentration of pilocarpine (0.07 mg/ml), so the results did not reveal any significant effects. [34] The other article was studied the effects of mouthwash pilocarpine, but they were conducted with healthy volunteers who had normal salivary gland function and were not representatives of xerostomia state. [37] Provided an existing of residual functioning salivary tissue, pilocarpine administered in the form of an oral spray may be effective in relieving symptoms of dry mouth. But further investigation is warranted.

There were some studies on the effect of carboxymethylcellulose compounds in xerostomia patients. One cross –over single- blind study suggested that use of linseed oil and carboxymethylcellulose preparation does not influence oral flora, periodontis or oral mucous membrane infections.[38] One study found no effect of carboxmethylcellulose on gustatory function but these "simple lubricant" may had some positive effects on the symptoms of xerostomia. [39] Another controlled study of Biotene gel and carboxmethylcellulose gel found that microbial floras were more controlled, salivary flow was more improved and comfort was greater in biotene group in the first four weeks. [40]

The aim of this study is to investigate the efficacy of a combination of topical pilocarpine and carboxymethylcellulose saliva substitutes (providing both saliva stimulant and saliva lubricating effects) in postirradiation xerostomia patients compared with carboxymethylcellulose solution alone