Effects of Mouth-rinse with Sesame Oil On Chemotherapy-Induced Oral Mucositis In Patients with Hematologic Cancer

SunSook Moon

The Graduate School

Yonsei University

Department of Nursing

Effects of Mouth-rinse with Sesame Oil On Chemotherapy-Induced Oral Mucositis In Patients with Hematologic Cancer

A Dissertation

Submitted to the Department of Nursing

And the Graduate School of Yonsei University

In partial fulfillment of the

Requirements for the degree of

Doctor of Philosophy of Nursing

SunSook Moon

Jun 2006

This certifies that the doctoral dissertation of

SunSook Moon is approved

Thesis Chair: Won-Hee Lee, PhD, RN

Thesis Committee Member: Ji-Soo Yoo, PhD, RN

Thesis Committee Member: Soon-Bok Chang, PhD, RN

Thesis Committee Member: Duck Hee Kang, PhD, RN, AAN

Thesis Committee Member: ChaeWeon Chung, PhD, RN

The Graduate School
Yonsei University
June 2006

ACKNOWLEDGEMENTS

First of all, I would like to thank to God for all things that he works for the good in my lives.

I would like to express thanks to dissertation committee members who were as talented and generous with their time and energies.

I would like to express sincere gratitude to Dr. DuckHee Kang for her constructive advices and clear explanations in completion of the dissertation.

Also special thanks are given to my friend, Dr. KwangSook Kim whose enthusiasm for helping me get through the difficult times, and for all the emotional support and caring she provided.

I also wish to acknowledge the cooperation of patients and their families. Without their unwavering support and participation, this research would not have been possible.

I also wish to thank my parent and parent-in-law's enduring support which has been my greatest source of support.

Finally, I would like to take this opportunity to express my deepest appreciation to my wonderful husband DongUn Park, my beloved two daughters JiWon and SooHyun and unborn our family member HeeSoo for their sacrifices, love and support.

TABLE OF CONTENTS

TABLE

FIGURE

APPNDIX

Abstract

Oral mucositis is a significant health concern in patients with hematologic cancer who are undergoing chemotherapy. It causes pain, interferes with nutritional intake and communication, and decreases well-being of the patients. It can also serve as a source of serious infection. Current management of oral mucositis has not always been effective. The purpose of this study was to examine the effect of sesame oil on oral mucositis induced by chemotherapy in patients with hematologic cancer.

Using a nonequivalent control group and non-synchronized design, a clinical trial was conducted to compare the effect of sesame oil mouth-rinse with that of usual care. Patients diagnosed with hematologic cancer who had developed chemotherapy-induced oral mucositis were recruited and assigned into either the experimental (sesame-oil, n=9) or control (usual care, n=9) group. Participants in the experimental group received sesame oil gargle 5 times a day, whereas participants in the cont기 group received the usual care consisted of chlorhexidine gargles 5 times a day. Data collection was initiated at the onset of oral mucositis daily at 10 a.m. using the Oral Assessment Tool until the resolution of oral mucositis. The data were collected between March 2004 and August 2005 in G university hospital in Seoul.

The data were analyzed using SPSS/WIN 12.0. Baseline group differences in demographic and clinical data were analyzed using t-tests and chi-square tests. Group differences changes over time and the group by time interactions for oral mucositis score, duration of oral mucositis, and pain were analyzed using Repeated

measures ANOVA. Differences between the control and experimental group for oral mucositis scores, oral mucositis duration and pain scores according to daily time interval were analyzed using MANOVA. The results of the study are as follows:

1) For the 1st hypothesis, “the severity of oral mucositis in patients in the experimental group receiving sesame oil will be lower than those in the control group receiving usual care with chlorhexidine”, there was a significant difference in oral mucositis score between the two groups ($F = 6.55$, $p = 0.0184$), indicating that the experimental group had significantly lower severity of oral mucositis than the control group. Similarly, there were significant changes over time ($F = 8.19$, $p = 0.0001$) and the group by time interactions ($F = 4.22$, $p=0.0001$) indicating that the severity of oral mucositis decreased over time was also statistically different. Moreover, the oral mucositis according to daily time interval between the control and experimental group was significantly different from day 9. Therefore, the 1st hypothesis was supported.

2) For the 2nd hypothesis, “oral mucositis duration in participants in the experimental group receiving sesame oil will be shorter than those in the control group receiving usual care with chlorhexidine”, there was a significant group difference in the duration of oral mucositis ($F = 10.05$, $p = 0.008$) between the two groups. The mean duration of oral mucositis in experimental group treated with sesame oil was 10.67 (±3.46) days, compared with 19.11 (±7.20) days in the control group. The duration of healing ranged 6-18 days in the experimental group compared with 8-25 days in the control group. Therefore, the 2nd hypothesis was supported.

3) For the 3rd hypothesis, “The pain score for participants in the experimental group receiving sesame oil will be lowered than those in the control group receiving usual care with chlorhexidine”, there was a significant difference in pain score between the two groups ($F = 12.77$, $p = 0.018$), indicating that the experimental group had significantly lower pain score than the control group. Similarly, there were significant changes over time ($F = 9.12$, $p = 0.0001$) and the group by time interactions ($F = 2.19$, $p=0.0055$) indicating that the pain of oral mucositis decreased over time was also statistically different. The pain score according to daily time interval between the control and experimental group was significantly different from day 9. Therefore, the 3rd hypothesis was also supported.

In conclusion, the findings of the study demonstrate that mouth-rinse of sesame oil, containing abundant antioxidants, is more effective than the current usual care with chlorhexidine in reducing the severity, duration, and pain of chemotherapy-induced oral mucositis in patients with hematologic cancer.

I. INTRODUCTION

A. Significance of the Study

Despite the significant advances in health care, the incidence of cancer has been steadily increased, and the cause of cancer largely remains unclear. According to the American Cancer Society report (2005), more than 1.3 million people were diagnosed with various types of cancer in 2005, and cancer is the leading cause of mortality in Korea (NSO, 2005).

The typical modes of cancer treatment are surgery, radiation therapy and chemotherapy. Among these treatments, approximately 65% to 75% of all cancer patients receive chemotherapeutic agents at some time during the course of their cancer treatment (Rosenberg, 1990). The chemotherapeutic agents function at the cellular level, and they are the most effective when a high percentage of malignant cells are in active division. Unfortunately, these agents are not selective in their cytotoxicity on cells and affect all cells in active division, including the cells of bone marrow, hair and skin as well as epithelial cells of the gastrointestinal tract. Frequently the problems related to the destruction of these normal cells require more nursing care than the disease itself because of its life-threatening toxicity during the active treatment phase (Holmes, 1991).

The body of the literature in cancer treatment (Driezen, 1978; Baker, 1982) clearly documents the oral complications of chemotherapy. Wojtaszek (2000) states that oral mucositis occurs in approximately 40% of patients undergoing chemotherapy

and in more than 75% patients undergoing bone marrow transplantation. Because of the degree and duration of myelosuppression, the incidence of oral mucositis is estimated to be two to three times higher in patients with hematologic malignancies and patients undergoing bone marrow transplantation than in patients with solid tumors (McGuire et al., 1993; Woo et al., 1993).

Oral mucositis is an inflammation of the mucous membranes of the oral cavity. It typically begins in 5 to 10 days following the initiation of chemotherapy and lasts 7 to 14 days (Woo, 2003). The entire process of oral mucositis lasts 2 to 3 weeks in more than 90% of patients (Woo, 2003). During this period, an interruption in mucosal surface increases the risk of a secondary infection, which may progress into a life-threatening systemic infection and death, particularly in myelosuppressed patients (Driezen et al., 1974, 1977; McElroy, 1984; Wight et al., 1985; Bensadoun et al, 2001). In previous studies, infection was found to be associated with approximately 50% of deaths in general cancer patients (McElroy, 1984) and up to 70% of death in those with hematological and advanced metastatic disease (Klastersky et al., 1972; Inagki et al., 1974; Ambrus et al., 1975).

Discomfort and pain accompanying oral mucositis lead to impaired oral intake of fluids and calories necessary for treatment, resulting in anorexia, cachexia, dehydration and severe malnutrition (De Conno et al, 1989). Such conditions cause a delay or interruption of chemotherapy schedules or a dose reduction compromising the efficacy of cancer treatment and survival. Biron and his colleagues (2000) pointed

out that oral mucositis could be the most frequent dose-limiting factor in chemotherapy.

Oral mucositis almost always accompanies oral pain decreasing the individual's comfort, ability to eat and communicate, and general well-being. It significantly diminishes quality of life among cancer patients (NIH, 1989; Petersen, 1999; Epstein et al., 1999). The clinical significance of pain related to oral mucositis was highlighted in the National Institutes of Health (NIH)-sponsored consensus conference, "Oral Complication of Cancer Therapies: Diagnosis, Prevention, and Treatment" (NIH, 1989). Symptom management of illness and treatment is a priority area of research identified in the NIH National Institute of Nursing Research (NINR) strategic plan for the 21st century (NINR, 2006) in the United States. Accordingly, the prevention and treatment of oral mucositis and the management of mucositis-related pain are significant areas for nursing research. However, little is known about optimal care for patients with oral mucositis and the management of related pain (Fall-Dickson, 2000).

In addition to patient suffering, oral mucositis significantly increases health care costs. On one study it was found that patients with oral mucositis stayed in hospital 3 to 6 days longer and had an elevated temperature for 2 to 4 days longer than patients who did not have oral mucositis (Manzullo et al., 1998). Similarly, patients with oral mucositis required extra analgesics to relieve the oral pain. Thus, the significant economic burdens for more hospital days and extra uses of analgesics raised the concerns in the oncology community (Elting et al, 2002; Bensadoun et al,

1998; Magne et al, 2001; Marcy et al, 2000). Furthermore, analgesic use can be problematic in patients who may inadvertently traumatize the membrane of the oral cavity, which has been numbed with a topical anesthetic and/or aspirate their medications. Each event can further aggravate their clinical conditions of these patients.

Chemotherapy generally takes 3 days during each cycle and patients are discharged from hospital after chemotherapy. Because the symptoms of oral mucositis do not begin until 5 to 10 days after chemotherapy (Harris & Knobf, 2004), the management of severe pain and oral mucositis are frequently left to the patients and family at home without adequate preparations. Borbasi and colleagues (2002) stated that patients believed that health care professionals did not fully understand the problems which they faced.

There are more than 50 published studies focusing on the palliation, prevention and/or reduction of the severity of oral mucositis. The range of medications tested for the management of oral mucositis includes chlorhexidine, sucralfate, topical antimicrobials, marrow-stimulating cytokines, vitamins, inflammatory modifiers, palliative rinses, amino acid supplements, cryotherapy, laser treatment and antioxidants. Chlorhexidine has been the most frequently used gargling agent for oral mucositis. Its effectiveness, however, has been inconsistent partly because of the irritation to the sense of smell and increased pain due to the interrupted oral surface in these fragile patients with cancer (Foote et al., 1994). Researchers reported that cell protective agents such as granulocyte colony stimulating factors (G-

CSFs) and granulocyte-macrophage colony stimulating factors (GM-CSFs) are economically burdensome for patients with cancer (Bianco et al., 1991; Macieiewski et al., 1991, Loprinz et al., 1990; Pfeiffer et al., 1990; Epstein et al, 1989). Although various agents have been studied as prophylactic or therapeutic agents for improving oral mucositis, none has been fully effective (Valcarcel et al., 2002). There is no unified recommendation for a gargling agent in the management of oral mucositis. The existing agents do not meet the standards of a gargling agent, such as the effectiveness of sterilization, economical feasibility, and convenience for the use and patient satisfaction (Chung, 1998).

In Oriental Medicine, sesame oil has been used effectively for burns and other problem of the skin and mucous membrane including toothaches, gum disease and oral mucositis. Sesame oil is known to contain a large amount of antioxidant. Despite its potential for efficacy in the management of oral mucositis, there has been no research investigating its efficacy or the biological mechanisms underlying its effect on oral mucositis. Only one anecdotal report (Rosenfeld, 1996) suggests the effectiveness of sesame oil for oral mucositis management in patients with chemotherapy.

Therefore, the purpose of this study was to examine the effects of sesame oil mouth-rinse, compared with that of chlorhexidine mouthwashes, on the severity and duration of oral mucositis and the degree of pain in hematologic cancer patients undergoing chemotherapy,

The results of the study potentially offer not only an important role of

sesame oil in relieving and treating oral mucositis but also in minimizing individual economic burden resulting from oral mucositis and thereby, improving the well-being and quality of life of these patients. Furthermore, sesame oil can be used as a new nursing intervention in clinical practice.

B. Purpose of the study

The purpose of the study was to test the effectiveness of mouth-rinse with sesame oil, compared with that of chlorhexidine mouth-rinses on oral mucositis in hematologic cancer patients undergoing chemotherapy. The specific aims of the study were as follows:

1) To examine the effect of mouth-rinse with sesame oil on the severity of oral mucositis induced by chemotherapy compared with chlorhexidine mouth-rinse.
2) To examine the effect of mouth-rinse with sesame oil on duration of oral mucositis induced by chemotherapy compared with chlorhexidine mouth-rinse.
3) To examine the effect of mouth-rinse with sesame oil on degree of pain related to oral mucositis induced by chemotherapy compared with chlorhexidine mouth-rinse.

.

C. Definitions

1. Oral mucositis

Oral mucositis is an inflammation of the mucous membranes of the oral cavity and oropharynx, which may range from redness to ulceration, secondary to intensive chemotherapy and is not associated with trauma (Hyland, 1997). In this study, the severity of oral mucositis was measured using the oral mucositis assessment tool (OAT) developed by the London Standing Conference work group.

2. Duration of oral mucositis

Duration is “the length of time that something lasts or continues” (retrieved from http://kr.dic.yahoo.com). In this study, the duration of oral mucositis refers to the number of days the study participants experienced the symptoms of oral mucositis from the onset to the complete disappearance of the symptoms. Therefore, the duration of oral mucositis was number of days as measured by the research assistant in the study.

3. Oral pain

Pain is “unpleasant sensory and emotional experience associated with actual

or potential tissue damage, or described in terms of such damage" (International Association for the Study of Pain, 1986, p. S217). In this study, oral pain was the subjective feeling experienced by the study participants with oral mucositis and was measured by a numerical rating of pain by the participants on a visual analogue pain scale.

Ⅱ. LITERATURE REVIEW

A. Chemotherapy & Oral Mucositis

1. Direct / Indirect Stomatotoxicity

The primary mode of action of the chemotherapeutic agents involves interfering with the supply and utilization of building blocks of nucleic acids, such as enzymes for purines and pyrimidines, as well as interfering with the intact molecules of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), which are needed for replication and growth of cells (See-Lasley, 1982). The characteristic capability of cancer cell is of having a high rate of cellular replication and proliferation which cannot be controlled. Chemotherapeutic agents are particularly toxic to these highly proliferative cells. The body contains three regions in where cell divisions are as active as in malignant cells. These regions are the bone marrow, the hair follicles, and the gastrointestinal tract. Because of their active cell division, these regions are most vulnerable to the toxicity of anticancer drugs. Particularly, oral mucosa is in the process of constant epithelial renewal and thus is highly vulnerable to the direct cytotoxic effects of antineoplastic agents (Dreizen, 1990). This is called direct stomatotoxicity. Antineoplastic agents, such as 5-flourouracil (5-FU), methotrexate, bleomycin, doxorubicin, cyclophosphamide, isophamide, cisplatin, VP-16, and high doses of cytarabine, rinblastine, mitoxantrone and the taxanes, are well known to induce oral mucositis (Awidi et al, 2001; Epstein et al, 2002). Direct stomatoxic

effects of these agents lead to reduced production, decreased differentiation, and accelerated detachment of epithelial cells resulting in a denuding of the mucosa (Squier, 1990). Once the continuity of the epithelial lining is disrupted, a painful and debilitating mucositis results from the sequence of tissue destruction, inflammation, and infection (Sonis & Clark, 1991).

Chemotherapy is also believed to have an indirect stomatotoxic effect via suppressed bone marrow function during the nadir of treatment. The nadir is the time at which the platelet and granulocyte counts are lowest due to the cytotoxic effect of the chemotherapeutic drugs on the precursor cells of the bone marrow. The individual is immunosuppressed and extremely susceptible to infection during this time. Research (Bensadoun et al, 2001) indicates that increased stomatotoxicity is associated with a decrease in granulocyte counts that occurs during the nadir. Oral infections, which may be due to bacteria, viruses (mainly herpes simplex), or fungal organisms (*Candida albicans*), can further exacerbate the mucositis and may lead to systemic infections. Gonzalez-Barca and colleagues (1996) pointed out that an upward trend in gram-positive bacteremia was significantly related to an increase in oral mucositis. Peterson and Schubert (1977) stated that up to 54% of neutropenic individuals develop septicemia related to oral infections. Furthermore, infection is responsible, solely or in part, for approximately 50% of deaths in the general cancer patient population (McElroy, 1984), and in those with hematological and advanced metastatic disease, accounts for 70% (Klastersky et al., 1792; Inagki et al., 1974; Ambrus et al., 1975). Woo (2003) reports that mortality rates from oral mucositis

range from 6% to 30%. In immunosuppressed cancer patients, ulceration, severe inflammation, infection, and bleeding develop due to loss of mucosal integrity, cellular destruction, neutropenia, and thrombocytopenia (Beck, 1999).

Chemotherapy causes a systemic immunosuppression with severe depression of the bone marrow (Jensen et al, 2003). It also impairs the local humoral defense mechanism in the oral cavity. The salivary immunoglobulins (Igs) play an important part in protecting the oral cavity from diseases (Jensen et al., 2003). IgA in the saliva originates both from plasma cells in the bone marrow and the salivary glands (Jensen et al., 2003). A secretory component produced in the acinus and ductal cells of the salivary glands is coupled to the IgA, after which the complex is secreted into the oral cavity as secretory IgA (Jensen et al., 2003), called s-IgA. Secretory-IgA is the predominant immunoglobulin in the saliva, and the concentration in saliva is normally ten-fold the saliva concentrations of IgG and IgM. Chemotherapeutic agents have been reported to decrease saliva production and alter the composition of saliva (Epstein, 2002). Studies have shown that when bone marrow is severely depressed during treatment with a variety of chemotherapeutic agents, the concentrations of s-IgA, IgG and IgM in stimulated whole saliva are significantly decreased and those of s-IgA are markedly decreased (Epstein, 2002). The results suggest qualitative and quantitative changes in saliva can have deleterious consequences for oral mucosal health, especially in the presence of oral mucositis. Furthermore, it has been reported that mucosal damage is caused by the direct contact of chemotherapeutic agents on the oral epithelium through salivary secretion (Ishii et al., 1989). Several studies (Ishii

et al., 1989; Oliff et al, 1989; Slavik, 1993; Svojanovsky et al., 1999) have demonstrated a correlation between the severity of oral mucositis and the amount of stomatotoxic agents secreted in the saliva.

The model for direct-indirect stomatotoxicity is supported for several reasons. The first reason is that most high dose cancer therapies affect rapidly replicating cells, thus, oral mucosal epithelium with approximately a 1-2week mucosal turnover rate is typically damaged (Squier, 1990) and is even more severe in pediatric patients (Peterson & Sonis, 1983; Sonis, 1998; Sonis et al, 1978) who typically have a higher proliferating fraction of basal cells. They are three times more likely to develop mucositis than are elderly adults in whom the basal cell proliferative rate has slowed down (Sonis & Sonis, 1979). Secondly, oral mucositis closely parallels timing of impairment and subsequent recovery of marrow function. For example, mucositis severity increases as the number of white blood cells decreases. Conversely, resolution of oral mucositis coincides with recovery of the white cell count, specifically when the absolute neutrophil count becomes greater than 500 cells/mL (Woo, 2003).

Although the direct/indirect mechanism of oral mucositis is supported for the above mentioned reasons, it still does not explain why similar patients receiving comparable chemotherapy regimens develop different degrees of oral mucositis. Therefore, Sonis (2004c) proposed a new model hypothesizing the mechanisms of the development and healing of oral mucositis induced by chemotherapy.

2. The Five Phases of Oral Mucositis

Although speculative, Sonis (2004c) proposes the five phases in oral mucositis based on animal and clinical data. Oral mucositis is hypothesized to be a complex biologic process consisted of five phases: initiation, primary damage response, signal amplification, ulceration, and healing.

The initiation phase is associated with tissue injury that occurs following the administration of radiation or chemotherapy (Sonis, 2004c). During the initiation phase, radiation and chemotherapy cause both DNA and non-DNA damage, resulting in direct cellular injury that disrupts normal cellular function in the cells of the mucosal epithelium and underlying mucosa (Sonis, 2004c). At the same time, the primary damage response of oral mucositis begins through generation of reactive oxygen species (ROS) or free radicals. ROS play an important role in subsequent biological events and may directly damage cells, tissues, and blood vessels (Sonis, 2004c). The activation of ROS and the subsequent stimulation of transcription factors determine the extent of the acute oral tissue response (Spielberger, 2005). Although the mucosa appears to be normal at this stage, a cascade of events has begun in the submucosa, which ultimately leads to epithelial destruction.

During the phases of the primary damage response and the signal amplification, there is a complex series of events leading to the activation of transcription factors. In particular, nuclear factor-kappa B (NF-kB) is activated in

response to radiation or chemotherapy or indirectly by ROS in epithelial, endothelial cells and macrophages (Kostler et al, 2001; Sonis, 2004b; Sonis, 2002). NF-kB controls almost 200 genes associated with oral mucositis (Sonis, 2004a). The activation of NF-kB leads to the up-regulation of these genes and ultimately the production of pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-6, which can damage connective tissues and endothelium result in cell death. Furthermore, TNF-α has been found to be an important regulator of early endothelial changes associated with mucosal injury and is an efficient activator of NF-kB (Sonis, 2004c). Proinflammatory cytokines amplify the primary signal and activate NF-kB in other cells, which results in transcription of gene encoding mitogen-activated protein-kinas (MAPK), cyclooxegenase2 (COX2) and tyrosine-kinase signaling molecules. These transcription factors induce activation of matrix metalloproteinases (MMPs) 1 and 3 in cells of the epithelium and lamina propria (Bamba et al, 2003; Sesaki et al, 2000) leading to apoptosis in the submucosa and basal epithelial cells of the mucosa (Sonis, 2003c). In addition, MMP1 causes destruction of the collagenous subepithelial matrix, and MMP3 breaks down the epithelial basement membrane and potentially promotes the dissemination of other destructive signals, thus, ultimately resulting in tissue injury (Sonis, 2004c; Spielberger, 2005).

Both TNF-α, and IL-6 induce matrix metalloproteinases (MMPs) 1 and 3 activation (Bamba et al, 2003; Sesaki et al, 2000) leading to apoptosis in the submucosa and basal epithelial cells of the mucosa and destruction of the subepithelial matrix and basement membrane (Sonis, 2004c). These processes provide

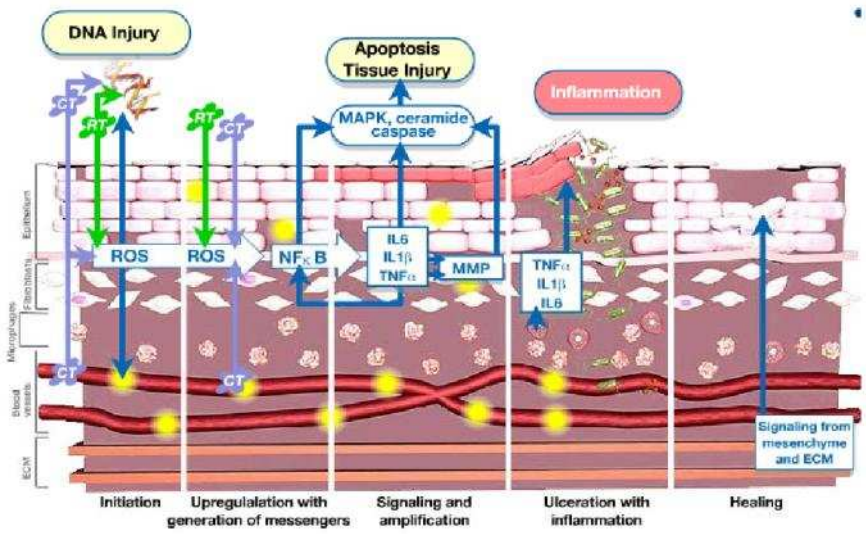
a positive-feedback loop by further activating NF-kB, thus amplifying the primary damage response (Sonis, 2004c). During the signal amplification, there may be some mucosal erythema, but tissue integrity remains intact with few symptoms.

The ulcerative phase of mucositis is the most symptomatic phase (Sonis, 2004b; Sonis et al, 2004). As shown in Figure 1, degradation of the mucosa causes extremely painful lesions that are prone to superficial bacterial colonization. These ulcerations often require secondary supportive care and increase the risk of other complications. In immunosuppressed patients, breaks in the mucosal barrier serve as portals of entry for the numerous microorganisms that reside in the mouth. Opportunistic bacteria or other infective agents may attack and increase the risks of sepsis and bacteremia that may become life-threatening. Inflammatory cells then migrate by chemotaxis to the base of the lesion, where they produce damaging enzymes (Sonis, 2004c). Severe ulcerations may force the clinician to reduce the dose of the chemotherapeutic agents and delay the treatment of the primary malignancy (Peterman et al 2001).

In the final phase, signals from the extracellular matrix initiate the healing and renewal process of epithelial proliferation and differentiation (Sonis, 2004b; Sonis et al, 2004c). The mucosa returns to a normal appearance, but the patient continues to be at increased risk for future episodes of mucositis with subsequent cancer therapy (Sonis et al 2004; Denham & Hauer-Jensen, 2002). This process summarizes the current understanding of cytokine activity and integrates the direct-indirect effects of local immunity and microflora (Barasch & Peterson, 2003). Based

on the biological complexity of oral mucositis, therapeutic interventions targeting specific biologic responses have been suggested.

Figure 1. Five pathological phases of chemotherapy induced oral mucositis.



(from Sonis, 2004, p26)

3. Other Risk factors related to Oral Mucositis induced by Chemotherapy

Both direct and indirect factors appear to contribute to oral mucositis (Bensadoun et al, 1999; Kaanders et al, 1992; Macmilla et al, 1991). Direct factors include the chemotherapeutic agent, dosage, and cycles (Adelstein et al, 1993; Taylor et al, 1994; Vokes et al, 2000), the total dose and days of radiotherapy (Bourhis et al, 1995; Fu et al, 2000; Horiot et al, 1992; Kaanders et al, 1997), pre-existing mucosal damage from ill-fitting dental prostheses, periodontal disease, salivary gland dysfunction, and patient susceptibility (Borowski et al, 1994). Indirect factors include myelosuppression, immunosuppression, reduced secretory IgA, and bacterial, viral, or fungal infections (Borowski et al, 1994; Raber Durlacher et al, 1989). It has been suggested that the repair of ill-fitting prostheses, extraction of offending teeth, elimination of periodontal disease, and effective oral hygiene reduce the incidence and severity of mucositis (Raber Durlacher et al, 1989). A patient might develop more severe mucositis if his or her nutrition is poor, and poor nutrition may impair mucosal regeneration. The importance of good nutrition (through a feeding tube or percutaneous gastrostomy) is emphasized before, during and after specific cancer treatments (Sprinzl et al, 2001; Dazzi et al, 2003). Xerostomia that develops as a result of irradiation or drug use contributes significantly to the development of oral mucositis (Fu et al, 1995; Wagner et al, 1998). Drugs resulting in xerostomia include antidepressants, opiates, antihypertensives, antihistamines, diuretics and sedatives. Finally, both alcohol and tobacco can impair salivary function. It has been known that

the use of tobacco during radiation significantly increases the intensity of radiation-induced mucositis (Trotti, 2000).

B. Studies Related to Interventions on Oral Mucositis

A variety of agents have been used to prevent or treat oral mucositis, but there is no consensus as to the most effective management of oral mucositis (Biron et al., 2000). The agents used for oral mucositis are classified into four broad categories;

1) antimicrobials/anti-inflammatory; chlorhexidine, Povidone-iodine
2) physical barriers; sucralfate
3) mucosal proliferation modifiers; colony stimulating factors (CSFs)
4) biological approaches; Amifostine, antioxidants (vitamin E)

Chlorhexidine gluconate has been widely studied over the past 30 years as to its prophylactic and therapeutic efficacy in oral mucositis (Wojtaszek, 2000) because of its broad-spectrum antimicrobial effect that is capable of sustained binding to oral surfaces (Rutkauskas & Davis, 1993). Some researchers have found chlorhexidine to be effective in preventing and treating chemotherapy- and radiotherapy-induced oral mucositis (Ferreti et al, 1990; Ferreti et al, 1988; MaGaw & Belch, 1985; Rutkauskas & Davis, 1993). However, others have failed to identify clinical benefits for chlorhexidine in the prevention and treatment of oral mucositis (Epstein et al., 1992; Ferretti et al., 1990; Weisdorf et al, 1989; Wahlin, 1989; Spijkervet et al, 1989; Foote et al, 1994; Ferretti, 1990; Epatein et al, 1992). Moreover, other researchers have indicated the emergence of gram-negative bacilli infections despite the chlorhexidine mouthwashes, and oral discomfort and interference with the

nystatin treatment (Weisdorf et al, 1989; Wahlin, 1989; Foote et al, 1994; Raybould et al, 1994; Barkvoll & Attramadal, 1989). Other researchers (Parulekar et al, 1998; Rosenberg, 1990) have indicated that commercial mouthwashes containing alcohol such as chlorhexidine are particularly hazardous because of they tend to dry oral tissues and alter oral flora (Parulekar et al, 1998; Rosenberg, 1990). Hydrogen peroxide and povidone-iodine also are antimicrobial agents. Hydrogen peroxide, however, is known to delay antifibroblast healing and possibly promote carcinogenic activity (Carl & Emrich, 1991). In addition, some researchers found that frequent mechanical cleansing of the mouth with saline was more beneficial than using hydrogen peroxide (Tombe & Gallucci, 1993). Another disinfection agent, povidone-iodine solution also reduced the incidence, severity, and duration of oral mucositis in 40 patients with head and neck cancer in a prospective randomized trial (Rahn et al, 1997). Others (Tombe & Gallucci, 1993; Rosenberg, 1990) have demonstrated that topical antimicrobial agents H_2O_2 and Povidone alter oral flora and inhibit mucosal tissue granulation in persons with oral lesions (Daeffler, 1981). Moreover, Tombe and Gallucci, (1993) reported that patients were irritated by the unpleasant taste of the mouthwashes in their research. Based on finings of randomized clinical trials, researchers were unable to make recommendation for chlorhexidine, hydrogen peroxide or povidone-iodine as a standard preventive or therapeutic regimen, although these agents are commonly used for prevention and treatment of oral mucositis.

In the next category, physical barriers, sucralfate has been used to treat gastric ulcer disease and is known to act by forming a physical barrier coating over

the damaged surface of the mucosa protecting it from acid, bile salt and pepsin. Sucralfate also has the biological effect of inducing prostaglandin production and the binding of growth factors to tissue (Castagna et al., 2001), a process which is known to play a part in the healing of ulceration (Biron et al, 2000). Sucralfate has been used in patients with oral mucositis for the same pharmacologic action. Out of three randomized trials evaluating the efficacy of sucralfate in prevention of chemotherapy-induced oral mucositis, the findings were mixed: In one study, sucralfate was found to be moderately effective; in another, the mucositis-associated oral discomfort was reduced; and in the third study, there were no differences between the sucralfate and placebo groups (Shenep et al, 1989; Chiara et al, 2000; Pfeiffer et al, 1990; Loprinzi et al, 1997). In addition, others reported that sucralfate failed to alleviate symptoms in patients experiencing 5-FU induced oral mucositis despite oral cryoprophylaxis (Loprinzi et al., 1997)

Granulocyte-colony-stimulating factor or granulocyte-macrophage colony-stimulating-factor (CSFs) are growth factors that promote proliferation and differentiation of neutrophil and monocyte/macrophage lineages (Biron et al, 2000). These factors also have a direct stimulating effect on the growth or regeneration of the cells of the oral mucosa (Hallahan et al, 1996). The proposed mechanism of systemic use of CSFs could derive from a primary direct effect on epithelial cells and secondary to enhancement of immune system recovery (Barasch & Peterson, 2003; Chi et al, 1995; Gabrilove et al, 1998; Gordon et al, 1994). Several researchers propose that the effects of CSFs on mucosal repair is mediated by the shortened

duration of neutropenia (Nemunaitis et al, 1995; Symonds, 1998; Katano et al, 1995; Kannan et al, 1997; Klawford, 1991) or by the migration and proliferation of non-hematological cells such as keratinocytes (Karthaus et al, 1999). However, others have urged caution in the systemic use of CSFs (Wardley et al, 2000; Legros et al, 1997), which increase the incidence of oral mucositis. Growth factors have also been used topically for prevention or treatment of oral mucositis. Recently in four randomized trials using CSFs topical administration, the researchers concluded that CSFs did not improve oral mucositis (Valcarcel et al, 2002; Karthaus et al 1998; Sprinzl et al, 2001; Dazzi et al, 2003). Furthermore, cell protective agents such as CSFs can significantly increase the economic burden for cancer patients (Bianco et al., 1991; Macieiewski et al., 1991, Loprinz et al., 1990; Pfeiffer et al., 1990; Epstein et al, 1989). Taken together, the effectiveness of CSFs on oral mucositis has been inconsistent.

Researchers have also used antioxidants as biological approaches for prevention or treatment of oral mucositis. As described previously, the ubiquity of ROS as early drivers of mucosal injury has prompted the idea for targeting this agent (Sonis, 2004c). Antioxidants detoxify ROS and scavenge free radicals (Byrnes, 2005; Coklin, 2000). Amifostine is an antioxidant cytoprotective agent, and was originally developed by the United States army to protect troops who were exposed to radiation (Sonis, 2004c). Most studies using amifostine focus on its prophylactic efficacy for radiation-induced oral mucositis. The findings of the studies consistently indicated a reduction in the incidence and severity of oral mucositis. However, this treatment induces side effects, mostly nausea and hypotension (Foote, 2001), which seemed to

be more pronounced with high doses of the agent and upon intravenous administration (Kouokourakis et al, 2000; Bourhis et al, 2000). Data on the effects of amifostine in the prevention of chemotherapy-induced oral mucositis are very scant (Kostler et al, 2001). Another antioxidant used for chemotherapy-induced oral mucositis is topical Vitamin E. Its antioxidant and membrane stability potency is thought to interfere with the inflammatory damage caused by ROS and free radicals produced by chemotherapy or radiotherapy (Kostler et al, 2001). In a randomized clinical trial with patients who had oral mucositis induced by chemotherapy, the topical application of vitamin E was shown to be significantly more effective than the placebo (Wadleigh et al, 1990). Although the antioxidant effect of vitamin E was relatively weak, the duration of chemotherapy-induced oral mucositis was significantly shorter in patients treated with topical vitamin E than the placebo group in two small studies.

In summary, the review of the current practices clearly indicates that none of the gargling agents has consistently demonstrated the effectiveness in managing oral mucositis, nor have they met basic standards of gargling agents, such as effectiveness of sterilization, low expense, improved physical comfort, and convenience of purchase (Jung, 1998). These findings clearly suggest a need for further investigation as to the use of non-pharmacological interventions in the care of patients suffering from oral mucositis. The gargling agent should minimize physical discomfort and should be readily attainable in the home setting without a physician's prescription (Kostler et al., 2001).

C. Oral Mucositis, Antioxidants and Sesame oil

As reviewed above, chemotherapy or radiation induces excessive production of ROS or free radicals leading to the activation of transcription factors, such as NF-kB. Activated NF-kB, in turn, leads to the up-regulation of genes affecting mucosal toxicity and production of pro-inflammatory cytokines such as TNF-α, IL-1β as well as MAPK, COX2, and MMP1 and 3, all of which result in oral mucositis. Free radicals or ROS are a chemical species that possess an unpaired electron in the outer shell of the cell or molecule, so they are very unstable. To survive, they attack healthy cell to replace missing electrons. When the "attacked" molecule loses its electron, it becomes a free radical itself, beginning chain reaction. Once the process is started, it can cascade, finally resulting in the disruption of healthy cells. The only way to stop a radical reaction is to lose electrons without forming a chain reaction. Antioxidants are known to quench and detoxify ROS or free radicals as they catch free radicals and stabilize the cell membrane thus preventing damage to cellular macromolecules and organelles and promoting healthy cells. Coklin (2000) reports that antioxidants have the potential to enhance the anticancer effects of chemotherapy. Vitamin E, as an antioxidant, was examined for its efficacy in treating oral mucositis. Waddleigh and his colleagues (1992) investigated the therapeutic effects of topical vitamin E in oral mucositis. Eighteen patients with oral mucositis were randomized into either the experimental or the control group. Patients in the experimental group received the application of vitamin E oil (400IU/ml) on oral

lesions twice a day, whereas the control group received placebo oil (coconut or soybean oil) to oral lesions. Six of nine patients in the experimental group had complete resolution of their lesions within four days of initiation of therapy, whereas eight of nine patients in the control group receiving the placebo did not have complete resolution of their lesions during the study period of five days. Although the sample size was too small to make generalization of the findings, these findings suggest that topical treatment with an antioxidant may facilitate the healing of chemotherapy-induced oral mucositis.

Sesame is one of the oldest oilseeds known to man (Morris, 2002), and sesame oil is a commonly used seasoning oil in Korean household. Sesame oil is known not only for its nutritional value but also for medicinal properties. According to Oriental Medicine (Hur, 1999), sesame oil was used to treat dermatologic problems such as burns, scabies and oral mucositis as well as a remedy for toothaches and gum disease during the 4^{th} century in China (Morris, 2002). Furthermore, sesame oil is known to be an important ingredient in Ayurvedic remedy in India. Indians have used sesame oil as an antibacterial mouthwash for toothaches and gum disease (Morris, 2002) and to relieve anxiety and insomnia (Annussek, 2001). Other uses of sesame oil also include the treatment of blurred vision, dizziness, and headaches (Morris, 2002).

Sesame oil contains several antioxidants, which contribute to the stability of sesame oil (Fukuda, 1990). The antioxidants in sesame oil are formed and amplified during the roasting of seeds (Morris, 2002). The types of antioxidants contained in sesame oil include sesamin (Chavali, 2001), sesamolin, sesaminol (Kang et al, 1998),

cephalin called lignan and tocopherol (Fukuda, 1990) and sesamin, the major component of antioxidants in sesame oil. Particularly, cephalin has hemostat activity (Beckstrom-Sternberg et al., 1994). This hemostatic property of sesame oil can be beneficial to stop the bleeding from oral mucositis sites in patients with thrombocytopenia induced by myelosuppression.

In a study of antioxidant properties in sesame oil, researchers indicated that sesame oil significantly enhanced the functional activity of vitamin E and serum gamma-tocopherol levels and trapped ROS generated during inflammation in vitro (Cooney et al, 2001). Others have shown that the antioxidant properties of sesame oil significantly inhibit cytokine production of TNF-α, IL-1β, and IL-6 and lipid peroxidation. (Hou et al, 2003; Hsu et al., 2005). Hou and colleagues (2003) reported that sesame oil antioxidants particularly, sesamin and sesamolin significantly reduced p38MAPK signals of the cells through inhibition of nitric oxide (NO) production. Furthermore, it was found that these sesame oil antioxidants are able to inhibit H_2O_2-induced ROS generation (Hou et al, 2003). Therefore, it is believed that sesame oil containing abundant antioxidants may inhibit the MAPK expression, which is thought to mediate the inflammatory responses in various cell types (Chen & Wang, 1999), including oral mucous membrane.

In an experiment at the Maharishi International College in Fairfield, Iowa, students rinsed their mouths with sesame oil, resulting in an 85% reduction in bacteria, which is attributed to cause gingivitis (Stevens et al, 2000). An anecdotal report also indicates that severe oral mucositis was treated using sesame oil before and after

radiation treatments (Rosenfeld, 1996). Although these studies were limited by small sample size and lack of blinding and a control group, the findings support the need to examine the effect of sesame oil on oral mucositis in cancer patients undergoing chemotherapy.

In another, recent clinical trial, sesame oil was found to be highly effective for treating nasal mucosal dryness in 20 cancer patients on radiation therapy (Bjork-Eriksson et al, 2000). Bjork-Eriksson and colleagues (2000) reported that the patients who sprayed sesame oil into each nostril three times a day experienced a significant reduction in dryness of the nasal mucosa. Others also found similar results (Johnson and colleague, 2001). Therefore, it is hypothesized that topical applications of sesame oil reduce or prevent oral mucositis in patients treated with chemotherapy. This effect will be mediated by the mechanism in which antioxidants in sesame oil scavenge the flood of ROS, thus preventing the production of pro-inflammatory cytokines and subsequent tissue injury.

Ⅲ. CONCEPTUAL FRAMEWORK OF THE STUDY

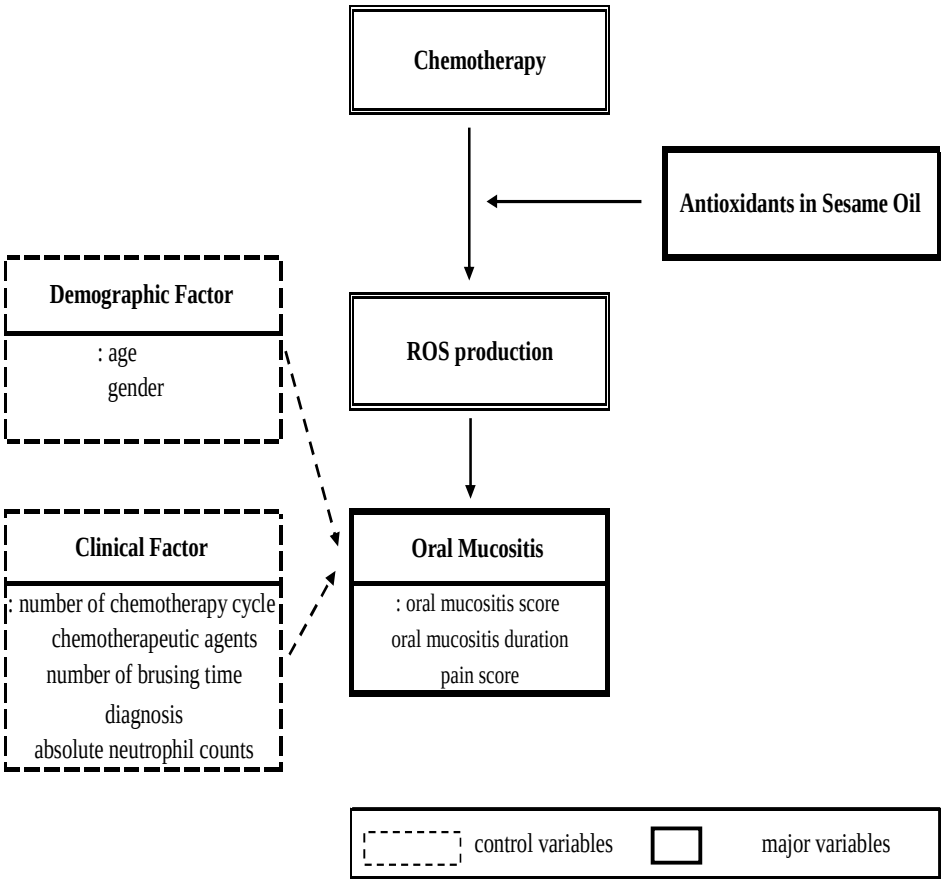
A. Conceptual Framework of the Study

The biological framework of the study is based on previous study and model of signal amplification during mucositis presented by Sonis (2004). The risk factors of oral mucositis induced by chemotherapy are classified into three broad categories; socio-demographic factors and clinical factors and ROS and inflammatory cytokines. Socio-demographic factors are age, gender, education, marriage, and religion. Clinical factors are number of chemotherapy cycle, chemotherapeutic agents, number of times that teeth are brushed, diagnosis, and absolute neutrophil counts. Chemotherapy is an oxidative stress resulting in the production of ROS or free radicals which induce inflammatory cytokines such as NF-kB, TNF-α, IL-1β, MAPK, COX2, and MMP1, 3 causing oral mucositis (Sonis, 2004c).

Based on the above review of the literature, anti-oxidants are known to scavenge these ROS or free radicals, resulting in decreased mucosal injury. The study hypothesized that sesame oil containing abundant antioxidants can scavenge or neutralize ROS or free radical induced by chemotherapy, thus reducing and treating oral mucositis, improving the oral mucositis score, and decreasing pain and the duration of the oral mucositis oral mucositis.

The biological framework of the study is illustrated in Figure 2.

Figure2. Conceptual Framework of the study



B. Research hypotheses

1) The severity of oral mucositis will be lower in participants in the experimental group receiving sesame oil mouth-rinse than those in the control group receiving usual care with chlorhexidine mouth-rinse.

2) The duration of oral mucositis will be shorter in participants in the experimental group receiving sesame oil mouth-rinse than those in the control group receiving usual care with chlorhexidine mouth-rinse.

3) The pain score will be lower for participants in the experimental group receiving sesame oil mouth-rinse than those in the control group receiving usual care with chlorhexidine mouth-rinse.

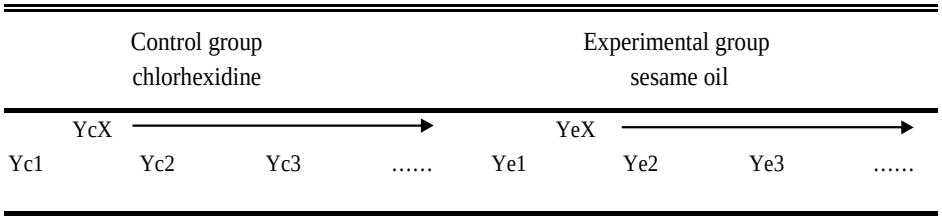
Ⅳ. METHODOLOGY

A. Research Design

The study was a clinical trial with nonequivalent control group non-synchronized design to examine the effect of sesame oil on oral mucositis induced by chemotherapy in patients with hematologic cancer. Using a 2-group, repeated measures design, participants were randomized into the experimental or control group. The control group received the usual care consisted of chlorhexidine gargles 5 times a day, whereas the experimental group received a sesame oil gargle 5 times a day.. Data collection was initiated at the onset of oral mucositis and continued daily until oral mucositis disappeared.

The design of the study is schemed as following:

Figure3. The Schema of the Study design



Yc1 : Pretest of the control group

YcX : The control group receiving chlorhexidine mouth washes 5 times per day after Yc1 until oral mucositis disappeard

Yc2 : 1st posttest of the control group

Yc3 : 2nd posttest of the control group

Yc4… : 3rd posttest of the contro group until oral mucositis disappeard

Ye1 : Pretest of the experimental group

YeX : The experimental group receiving sesame oil mouthwashes 5 times per day after Ye1 until oral mucositis disappeard

Ye2 : 1st posttest of the experimental group

Ye3 : 2nd posttest of the experimental group

Ye4… : 3rd posttest of the experimental group until oral mucositis disappeard

B. Study participants

1. Selection of participants

The participants of the study were 18 patients diagnosed with hematologic cancer, hospitalized in G university hospital in Seoul. The study took place between May 2004 and August 2005. Inclusion criteria were as follows:

a) Patients who had a diagnosis of hematologic cancer

b) Patients who did not have previous oral disease

c) Patients who had no allergy to sesame oil

d) Patients who were 19 years of age or over

e) Patients who were able to read and comprehend Korean

f) Patients who agreed to participate in the study

The reason to restrict the study participants to the above criteria was that types of cancer, cycles of chemotherapy, previous oral diseases, allergy, and age at the time of the study were all found as variables in previous studies, variables which could have a direct or indirect effect on oral mucositis.

2. Sample size

The sample size for the study was calculated based on the Cohen's method with level of significance (α) .05, power .80, and effect size 0.4. It was suggested that 26 subjects were required for each group, and 26 multiplied score 0.23 obtaining from constant R which corresponds when sample size is determined in research comparing mean of repeated measures ANOVA of two independent groups. Twelve participants for the study were calculated as a minimum sample size based on the above method.

Twenty five patients enrolled the study and the 7 participants withdrew from the study. Finally, 28 participants were remained in this study. Although the study sample was large enough to meet proper sample size, the power of the study was low because of the small number of study participants. The reason for the small sample size was due to the difficulty in recruiting study participants because of the high sensitivity of patients with cancer.

The p in the formula indicates a correlation coefficient of various measurement values. Machine and colleagues (1997) suggested 0.6~0.75 as the conservative range and middle value 0.68 was selected as p for this the study. Formula of calculating R is as follows;

$$R = \left(\frac{1 + (\omega - 1)p}{\omega} - \frac{vp^2}{[1 + (v - 1)p]} \right)$$

v : Measurement number of pre-test

ω : measurement number of posttest

C. Research Instruments

1. The severity of oral mucositis

The Oral Assessment Guide (OAG) has been most commonly used for the assessment of oral mucositis. In this study, however, the Oral Assessment Tool (OAT) developed by the London Standing Conference (2002) was used to measure the severity of oral mucositis. The OAT was selected because it is an objective, simple, and reproducible assessment tool and is convenient for use. The OAT consists of 13 items (voice, swallow, mucous membrane, saliva, tongue, lips, gums, teeth/denture, analgesic requirement, complication, self care assessment, taste), and each item is rated as 1=normal findings, 2=mild alterations, and 3=definitely compromised. An overall score is obtained by summing all item scores with a possible score range from 13 to 39. Higher scores indicate greater severity of oral mucositis. The tool takes approximately 3 minutes to complete. Reliability of internal consistency of the OAT consisting 13 items developed by the London Standing Conference (2002) was Cronbach's α = .57. The reason for the low reliability of the instrument is thought to be the small sample size of the study.

2. Measurement of pain

Pain is a subjective feeling experienced by the patient with oral mucositis as measured by a 0-10 Numerical Rating Visual Analogue Scale. Patients were asked to mark the level of pain on the 0-10 pain rating scale, 0 meaning no pain and 10 meaning the worst pain possible. The middle of the scale around 5 is moderate pain. A 2 or 3 would be mild pain, but 7 or higher is severe pain.

3. Measurement of Duration of oral mucositis

Duration of oral mucositis was measured by counting the number of days from the onset of oral mucositis to its resolution.

4. Measurement of Covariates

The major covariates of the study were classified into two categories: general and clinical. Covariates in general category included age, gender, education, marriage, and religion; and covariates in clinical category included the number of chemotherapy cycle, chemotherapeutic agents, the number of times that teeth were brushed, diagnosis, and absolute neutrophil counts.

Age, gender, education, marriage, religion drinking, smoking, preexisting oral disease (bleeding, swelling, bad breath, losing teeth, pus), and the number of

times that teeth were brushed, were collected from self-report questionnaire. Chemotherapy cycle, chemotherapeutic agents, diagnosis, and absolute neutrophil counts were collected from the patient's chart.

Neutrophils are the main white blood cell for fighting or preventing bacterial or fungal infections, and absolute neutrophil counts (ANC) refer to the total number of neutrophils present in the blood. The ANC was calculated by multiplying the total WBC count by the percentage of neutrophils and bands in the CBC and differential test. ANC and other hematological components were measured from the starting point of the study to the end of the study.

D. Process of the Study

1. Obtaining informed consent and a pilot study

Prior to data the conduct of the proposed study, the following procedure was implemented to examine the feasibility of the study.

1) The purpose and plan of the study were explained to two hematological oncologists and they were asked to help select research participants. Permission was obtained from the oncology staff to use sesame oil as an experimental mouth-rinse during the study for cancer patients with oral mucositis.

2) The literature review indicated that sesame oil contains the highest amount of antioxidants when oil is extracted by proper roasting of sesame seeds at a temperature around 190℃. Sesame oil produced by H Company was selected for the study because the H Company is known to produce the highest quality sesame oil as recommended by nutritionists.

3) Fresh sesame oil within 1 month from the date of manufacture was used in the study. Although sesame seeds roasted at over 190℃ (Kim, 1997) produce sterilized sesame oil, only fresh sesame oil was used to ensure the safety of already myelosuppressed patients with cancer who could be vulnerable to infections. A pilot study was done to confirm the safety of the sesame oil. The culture of sesame oil

revealed no bacteria or pathogens, and sesame oil was verified to be aseptic and safe to be used for myelosuppressed patients. Because the container of the sesame oil could also be contaminated, all containers were sterilized with ethylene oxide (EO) gas. Then, a bottle of sesame oil containing 200 ml of sterilized sesame oil was distributed to each study participant.

4) The research protocol was approved by the nursing department of the hospital. Then, the researcher explained the purpose of the study and research process to the head nurses in the wards and asked for cooperation in accessing and recruiting the study participants.

5) Before the pilot study, the study protocol was submitted to the Institutional Review Board (IRB) of the hospital to assure the safety of the study. IRB replied that the study using sesame oil did not need IRB testing because sesame oil is safe and is not a pharmacologic agent. Therefore, the study was approved.

6) A pilot study was conducted and found the existing oral mucositis assessment tool to be very impractical. Hence, an expert panel consisting with 2 oncology staff, 5 junior physicians, the researcher and research assistant discussed the need for a proper oral assessment tool and major measurement variables for the study. Through the discussion, the major measurement variables were defined and the oral assessment tool developed by London Standing Conference work group was selected for the study

2. Experimental Treatment

The total experimental period for each participant was from the onset of oral mucositis to its resolution. Chlorhexidine in the control group and sesame oil in the experimental group were used as mouth-rinse for this study. All study participants gargled for 1 minute, 5 times per day.

To minimize variability among different research members, only one research assistant was engaged for the study. In order to obtain accurate data, the researcher trained the research assistant before the study as follows:

1) The purpose of the study was explained to the research assistant
2) The process of the study including diagnosis each variable and chemotherapy used in the study were explained to the research assistant

3) The researcher demonstrated directly to the research assistant how to use the research tool and gather data from the study participants.

4) The researcher observed the research assistant's use of the tool and gathering of data from the study participants and identified the problems related to data collection and corrected or re-explained the procedure. This process was repeated until data collection between researcher and research assistant was demonstrated to be consistent.

5) Experimental protocol was as follows:

a. The severity of oral mucositis was scored at the beginning of oral mucositis development. After measuring oral mucositis, the study participants in the control group received chlorhexidine as a gargling agent and the study participants in the experimental group received sesame oil as a gargling agent.

b. The study participants were instructed to take 5ml of the gargling agents and gargle for one minute, 5times per day: after waking in the morning, after each meal and before going to bed. This was done daily until the oral mucositis disappeared.

c. The severity of oral mucositis score and pain was measured daily at 10:00 a.m. until all signs of oral mucositis disappeared.

E. Method of Data collection

The data of the study were collected between March 2004 and August 2005. Twenty five patients who met the eligibility criteria and had developed oral mucositis following the administration of chemotherapy participated in the study. The 7 participants withdrew from the study.

Potential study participants meeting the inclusion criteria of the study were identified from the patients' medical records. The research assistant then monitored these patients to determine if they developed oral mucositis with chemotherapy. Patients who developed oral mucositis were asked to participate in the study and consent was obtained when they agreed to do so. Participants were informed that they were free to withdraw from the study at any time. In addition, patients were assured that their refusal to participate or withdrawal from the study would not affect their care in any way.

To avoid potential contamination of the intervention, the study was designed to have sequential data collection. The data were first collected from the control group followed by data collection from the experimental group in the same hospital. The severity of oral mucositis was assessed daily at 10 a.m. using the OAT until resolution of the oral mucositis. Hematological data were collected from patient’s routine blood work

F. Method of data analysis

The data were analyzed using SPSS/WIN 12.0. The specific method of analysis for variables in the study was as follows:

1. Differences in demographic and clinical data between the control and experimental groups were analyzed using t-test and chi-square.
2. Differences between group, main effect of time and the effect of group by time interaction for oral mucositis scores, oral mucositis duration and pain scores were analyzed using Repeated Measures ANOVA
3. Differences in oral mucositis scores and pain scores according to daily time interval between the control and the experimental groups were analyzed using Repeated Measures MANOVA.
4. Reliability of the study instrument (OAT) was analyzed using Cronbach's *a.*

G. Limitations of the study

1) The study was conducted over 2 years, only 25 patients enrolled in the study and only 18 participants were able to finish the study. The reason for the small sample size was the difficulty in recruiting study participants because of the high sensitivity of patients with cancer. Twelve participants for the study were calculated as a minimum sample size based on Cohen's method and sample size formula of Repeated measures ANOVA of independent two groups. Although the study sample was enough to meet proper sample size, the power of the study was low because of the small number of study participants. Therefore, generalization of the study results is limited.

2) The end points of participation in the study were different for each of the study participants, resulting missing values in the statistical analysis. According to the advice of a statistician, missing values were treated by recording the last measured value

Ⅴ. RESEARCH RESULTS

A. General characteristics of the study participants

The characteristics of the study participants are presented in Table 1. There were a total of 18 participants who completed the study, 17 (94.4%) men and 1 (5.6%) women. The control group consisted of 8 (88.9%) men and 1 (11.1%) woman and the experimental group 9 (100%) men. The mean age in the control group was 29±11.24 years and in the experimental group 38±16.96. Bad breath was experienced with stomatitis and 9 (100%) of the control group had experienced bad breath whereas only 2 (22.2%) in the experimental group had the experience. There were no statistically significant differences between the control and experimental groups for gender, age, education, marriage, religion, smoking, drinking, the number of time teeth were brushed and existing stomatitis symptoms such as bleeding, swelling, loose teeth or pus (see Table 1)

Table1. Demographic Characteristics of Subjects in the Control and Experimental Groups

Characteristics	Control N=9 M	Control N=9 SD	Experimental N=9 M	Experimental N=9 SD	t-value	p-value
age	29	11.24	38.78	16.96	-1.44	0.169

Characteristics	N	%	N	%	χ^2	p-value
Gender						
male	8	88.9	9	100	1.06	1.000
female	1	11.1	0	0		
Education						
middle school	0	0	1	11.1		
high school	5	55.6	2	22.2	3.40	0.334
college	4	44.4	5	55.6		
university	0	0	1	11.1		
Marriage						
single	6	66.7	4	44.4	0.90	0.637
married	3	33.3	5	55.6		
Religion						
Protestant						
Christian	3	33.3	1	11.1		
Buddhist	3	33.3	0	0	6.60	0.083
Catholic						
Christian	0	0	1	11.1		
No religion	3	33.3	7	77.8		

Characteristics	N	%	N	%	χ^2	p-value
Smoking						
yes	2	22.2	3	33.3	0.28	1.000
no	7	77.8	6	66.7		
Drinking						
yes	5	55.6	5	55.6	0.00	1.000
no	4	44.4	4	44.4		
Denture						
yes	1	11.1	3	33.3	1.29	0.576
no	8	88.9	6	66.7		
Bleeding						
yes	9	100	7	77.8	2.25	0.470
no	0	0	2	22.2		
Swelling						
yes	7	77.8	3	33.3	3.06	0.153
no	2	22.2	6	66.7		
Bad breath						
yes	9	100	2	22.2	11.45	0.002
no	0	0	7	77.8		
Losing teeth						
yes	5	55.6	3	33.3	0.90	0.637
no	4	44.4	6	66.7		
Pus						
yes	2	22.2	1	11.1	0.40	1.000
no	7	77.8	8	88.9		

B. Comparison of Homogeneity of the Control and the Experimental Groups

1. Clinical characteristics of Participants in the Control and Experimental Groups

The common diagnoses were Acute Lymphoblastic Leukemia (n =11, 61.6%), Acute Myelogenous Leukemia (n =5, 27.8%), and Lymphoma (n = 2, 11.1%) as shown in Table 2, which displays data pertaining to diagnosis of the cancer for participants in the control (n = 9) and experimental (n = 9) groups. There were no significant differences between these two groups relative to the type of diagnosis ($p > 0.05$). The most commonly used chemotherapeutic agent was idarubicin (n = 11, 66.7%) (see Table 3). The most commonly used combination of chemotherapeutic agents was idarubicin, cyclophosphamide and vincristine and 6 of 18 study participants received this combination (Table 2). No significant difference was found between the two groups of the participants with respect to the type of chemotherapy or combination of chemotherapeutic agents ($p > 0.05$). There were also no significant differences between the control and experimental groups on the number of chemotherapy cycles ($p = 0.29$) (see Table 2). Although there was no significant difference in types of chemotherapeutic agents, combination of chemotherapeutic agents or number of chemotherapy cycle, there was a significant difference between the control group and the experimental group relative to days to onset of oral mucositis after chemotherapy ($p = 0.01$) (see Table 2). The days to onset of oral mucositis after chemotherapy in the control group was earlier (5.56±2.7) than the experimental group (10.22±4.09).

Table2. Clinical Characteristics of Subjects in the Control and Experimental Groups

Characteristics	Control N=9		Experimental N=9		t-value	p-value
	M	SD	M	SD		
Number of chemotherapy cycle	2.33	1.94	4.11	4.48	-1.09	0.298
Number of chemotherapy drugs	2.33	0.71	2.56	0.53	-0.76	0.460
Days to onset of oral mucositis after chemotherapy	5.56	2.7	10.22	4.09	-2.86	0.011
Number of times teeth were brushed	3.00	0.5	2.89	0.78	0.36	0.724
Characteristics	N	%	N	%	χ^2	p-value
Diagnosis						
Acute myelogenous leukemia	3	33.3	2	22.2		
Acute lymphoblastic leukemia	5	55.6	6	66.7	0.29	1.000
Lymphoma	1	11.1	1	11.1		
No chemotherapy drugs						
1	1	11.1	0	0		
2	4	44.4	4	44.4	-0.76	0.460
3	4	44.4	5	55.6		
Combination of chemotherapeutic agent						
Indarubicin	1	11.1	0	0		
Indarubicin + Etoposide	2	22.2	1	11.1		
Indarubicin + Cytarabine	0	0	1	11.1		
Indarubicine + Vincristine + Cyclophosphamide	3	33.3	3	33.3	4.33	0.632
Methotrexe + Ifostamide	0	0	1	11.1		
Mitoxan + Cytarabine	2	22.2	1	11.1		
Mitoxan + Cytarabine + Etoposide	1	11.1	1	11.1		
Mitoxan + Cytarabine + Fludarabine	0	0	1	11.1		

Table3. Types of Chemotherapeutic Agents used in the Control and Experimental groups

	Control group		Experimental group		χ^2	p-value
	use	no use	use	no use		
	N (%)	N (%)	N	%		
Vincristine	3 (33.3)	6 (66.7)	3 (33.3)	6 (66.7)	0.000	1.000
Idarubicin	6 (66.7)	3 (33.3)	5 (55.6)	4 (44.4)	0.234	1.000
Cyclophosphamide	3 (33.3)	6 (66.7)	3 (33.3)	6 (66.7)	0.000	1.000
Mitoxantrone	3 (33.3)	6 (66.7)	3 (33.3)	6 (66.7)	0.000	1.000
Cytarabine	3 (33.3)	6 (66.7)	4 (44.4)	5 (55.6)	0.234	1.000
Etoposide	3 (33.3)	6 (66.7)	2 (22.2)	7 (77.8)	0.277	1.000
Fludarabine	0 (0)	9 (100)	1 (11.1)	8 ((88.9)	1.059	1.000
Methotrexate	0 (0)	9 (100)	1 (11.1)	8 (88.9)	1.059	1.000
Ifosfamide	0 (0)	9 (100)	1 (11.1)	8 (88.9)	1.059	1.000

2. Characteristics related to Baseline Variables for Participants in Control and Experimental Groups

Table 4 shows the means and standard deviations for the baseline values of oral mucositis and pain count between participants in the control and experimental groups. Although the baseline mean oral mucositis score of the experimental group (M = 22.67, SD = 3.20) was slightly higher than the control group (M = 20.44, SD = 2.92), the difference was not statistically significant (p = 0.143). Participants in the experimental group also reported a slightly higher pain score at baseline (M = 5.0, SD = 1.87) but this difference was not statistically significant (p = 0.710).

Table4. Baseline Variables for Subjects in the Control and Experimental Groups

Characteristics	Control N=9		Experimental N=9		t-value	p-value
	M	SD	M	SD		
Oral mucositis score	20.44	2.92	22.67	3.2	-1.54	0.143
Pain score	4.67	1.87	5	1.87	-0.38	0.710

In summary, the absence of significant differences for the demographic and clinical characteristics as well as baseline variables indicates that there was a high level of homogeneity between the control and experimental groups in this study.

C. Testing of the study hypotheses

The study hypotheses were tested using a 2-group Repeated Measures ANOVA and MANOVA, thus comparing trends in change between the two groups

1. Hypothesis 1

The 1st hypothesis was "the severity of oral mucositis in patients in the experimental group receiving sesame oil will be lower than those in the control group receiving usual care with chlorhexidine." In Tables 5, 6 and 7, the results are summarized to indicate the comparison between the control and experimental groups.

The mean severity score for oral mucositis was 19.37 (±3.79) for the control group and 16.51 (± 4.29) for the experimental group. Even though oral mucositis score for the experimental group was slightly higher than the control group at the baseline (see Table 4), Table 6 indicates that there was a significant difference in oral mucositis score between the two groups ($F = 6.55$, $p = 0.0184$), indicating that the experimental group had significantly lower severity of oral mucositis than the control group. The main effect of time was shown to be significantly different ($F = 8.19$, $p=0.0001$) and the effect of group by time interaction was also statistically different ($F = 4.22$, $p=0.0001$) (see Table 6). According to the daily time intervals for oral mucositis scores, the differences in the oral mucositis scores between the two groups was significantly different from day 9 of the study (see Table 7 and Figure 3).

Therefore, the 1st hypothesis "The severity of oral mucositis in patients in

the experimental group receiving sesame oil will be lower than those in the control group receiving usual care with chlorhexidine" was supported.

Table 5. Mean and Standard Deviation of Oral Mucositis Scores for the Control and Experimental Groups

	Control N=9		Experimental N=9		t-value	p-value
	M	SD	M	SD		
Oral mucositis score	19.37	3.79	16.51	4.29	7.50	0.0001

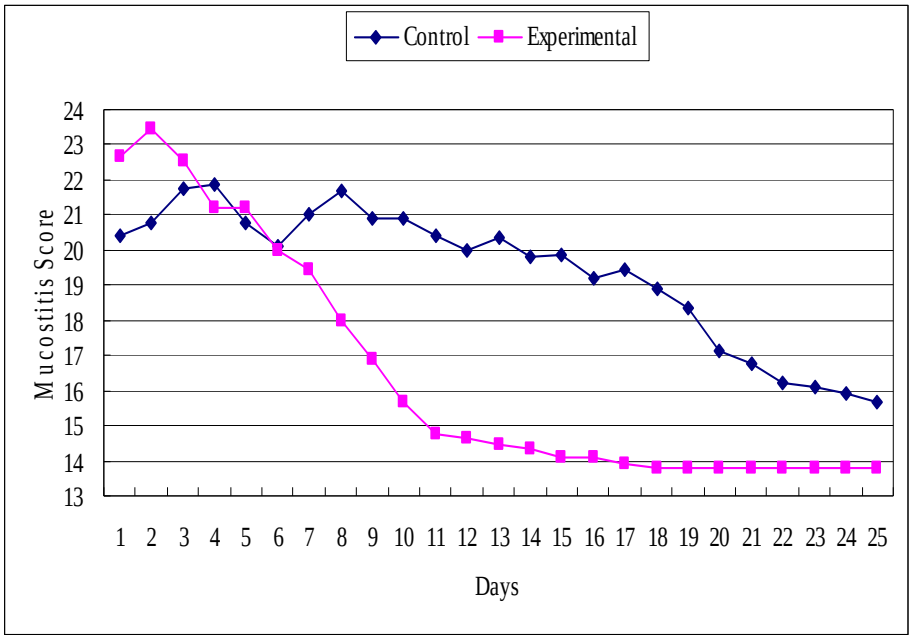
Table 6. Repeated Measure ANOVA of Oral Mucositis score of the control and Experimental groups

	SS	MS	F-value	P-value
Between Subject				
Group	222.48	222.48	6.55	0.0184
Within Subject				
Day	1251.20	52.13	8.19	0.0001
Group*Day	456.24	456.24	4.22	0.0001

Table 7. Repeated measure MANOVA of Mucositis Scores of the Control and Experimental groups from Days 1-25.

	Control N=9		Experimental N=9		F-value	p-value
Days	M	SD	M	SD		
1	20.44	2.92	22.67	3.2	2.37	0.1435
2	20.78	3.63	23.44	3.05	2.85	0.1109
3	21.78	4.06	22.56	3.71	0.18	0.6769
4	21.89	3.98	21.22	4.66	0.05	0.8306
5	20.78	3.87	21.22	4.18	0.05	0.8177
6	20.11	3.33	20.00	3.94	0.00	0.9493
7	21.00	3.97	19.44	3.81	0.72	0.4089
8	21.67	4.69	18.00	3.39	0.61	0.0755
9	20.89	4.17	16.89	2.8	5.71	0.0295
10	20.89	3.86	15.67	2.96	10.40	0.0053
11	20.44	3.88	14.78	2.49	13.62	0.002
12	20.00	3.91	14.67	2.4	12.19	0.003
13	20.33	4.56	14.44	2.35	11.88	0.0033
14	19.78	3.83	14.33	2.12	13.90	0.0018
15	19.89	3.95	14.11	1.76	16.05	0.002
16	19.22	3.53	14.11	1.76	15.11	0.0013
17	19.44	3.21	13.89	1.62	21.55	0.0003
18	18.89	2.89	13.78	1.64	21.27	0.0003
19	18.33	2.24	13.78	1.64	24.27	0.0002
20	17.11	2.03	13.78	1.64	14.69	0.0015
21	16.78	2.17	13.78	1.64	10.96	0.0044
22	16.22	2.28	13.78	1.64	6.82	0.0189
23	16.11	2.32	13.78	1.64	6.08	0.0253
24	15.89	2.15	13.78	1.64	5.49	0.0324
25	15.67	2.35	13.78	1.64	3.92	0.0652

Figure 4. Mean Oral Mucositis Score of the Control and Experimental Groups From Day 1-25 After Onset of Oral Mucositis



2. Hypothesis 2

To examine the 2nd hypothesis “oral mucositis duration in participants in the experimental group receiving sesame oil will be shorter than those in the control group receiving usual care with chlorhexidine”, the number of days was measured from day 1 to the day in which oral mucositis disappeared in each participant in the two groups. Table 8 displays comparison of the duration of oral mucositis in the control and experimental groups

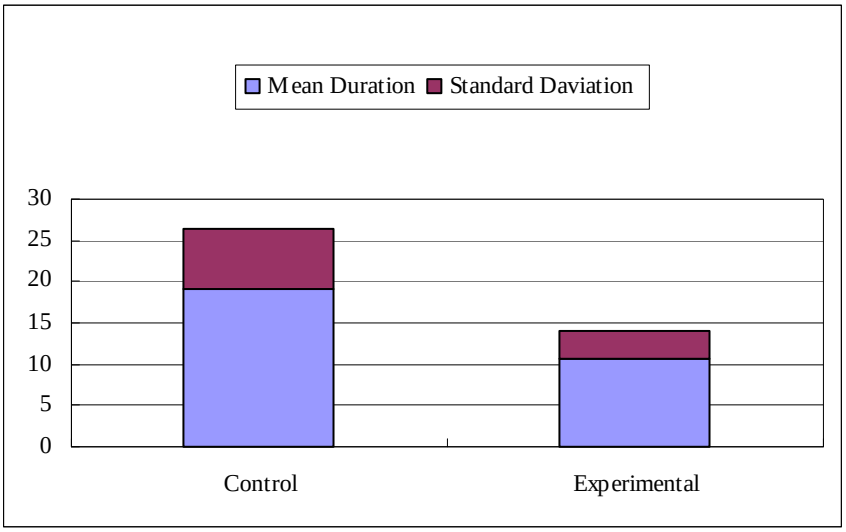
The mean duration of oral mucositis in the control group was 19.11 (±7.20) days and in experimental group treated with sesame oil 10.67 (±3.46) days (see Table 8 and Figure 5). There was a statistically significant difference in the duration of oral mucositis between the two groups ($F = 10.05$, $p = 0.0085$). The longest duration was 25 days and the shortest 8 days in the control group whereas they were 18 days and 6 days respectively in the experimental group.

Therefore, the 2nd hypothesis “oral mucositis duration in participants in the experimental group receiving sesame oil will be shorter than those in the control group receiving usual care with chlorhexidine” was supported.

Table 8. Repeated measure ANOVA of Oral Mucositis Duration of the Control and Experimental Groups

	Control N=9		Experimental N=9		F-value	p-value
	M	SD	M	SD		
Duration	1911	7.20	10.67	3.46	10.05	0.0085

Figure 5. Mean and Standard Deviation of Oral Mucositis Duration



3. Hypothesis 3

To examine the 3rd hypothesis, “The pain score for participants in the experimental group receiving sesame oil will be lowered than those in the control group receiving usual care with chlorhexidine”, the scores for oral pain in the control group receiving usual care and the experimental group receiving sesame oil were measured daily from the time of oral mucositis developed until the oral mucositis disappeared. A numeric pain scale was used.

The mean pain score was 3.3 (±2.42) for the control group and 1.34 (± 2.27) for the experimental group (see Table 9). Table 10 shows that there was a significant difference in pain score between the two groups ($F = 12.77$, $p = 0.018$), indicating that the experimental group had significantly lower pain score than the control group. The main effect of time was shown to be significantly different ($F = 9.12$, $p=0.0001$) and the effect of group by time interaction was also statistically different ($F = 2.19$, $p=0.0055$) (see Table 10). According to the daily time intervals for pain scores, the difference in the pain scores between the two groups was significantly different from day 9 (see Table 11 and Figure 5). Repeated measures MANOVA showed statistically significant difference in oral pain between the two groups and indicated that the oral pain of the experimental group was significantly lower at all time points from day 3 (see Table 11).

Therefore, the 3rd hypothesis, “the pain score for participants in the experimental group receiving sesame oil will be lowered than those in the control group receiving usual care with chlorhexidine” was supported.

Table 9. Mean and Standard deviation of Pain Scores in the Control and Experimental Groups

	Control N=9		Experimental N=9		t-value	p-value
	M	SD	M	SD		
Pain score	3.3	2.42	1.34	2.27	8.87	0.0001

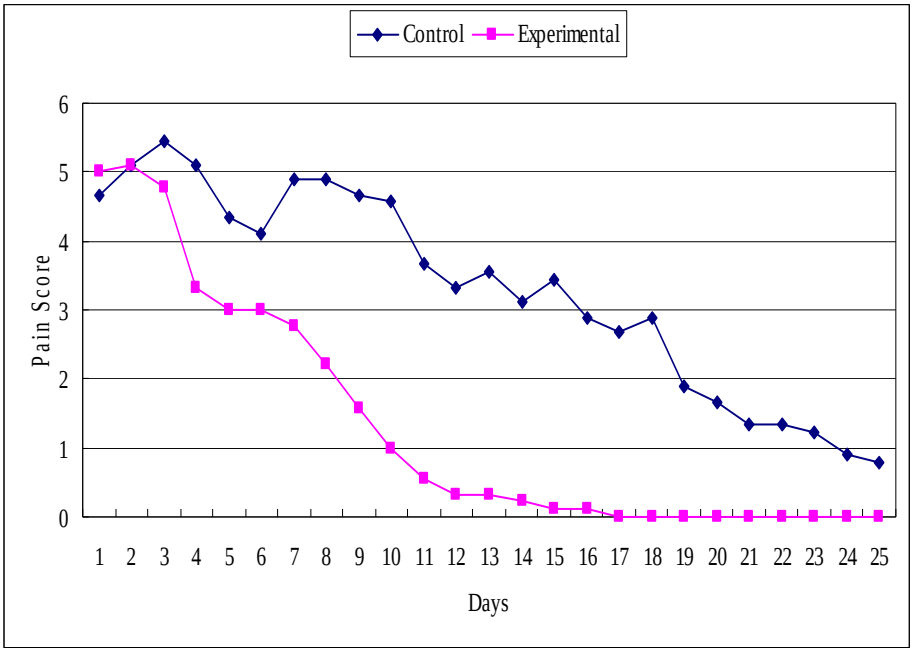
Table 10. Repeated Measure ANOVA of Oral Mucositis score of the control and Experimental groups

	SS	MS	F-value	P-value
Between Subject				
Group	162.81	162.81	12.77	0.0018
Within Subject				
Day	601.26	25.05	9.12	0.0001
Group*Day	102.01	6.00	2.19	0.0055

Table 11. Repeated measure MANOVA of Pain Scores for the Control and Experimental Groups from Days 1-25

	Control N=9		Experimental N=9		F-value	p-value
Days	M	SD	M	SD		
1	4.67	1.87	5.00	1.87	0.14	0.7104
2	5.11	1.76	5.11	1.36	0.00	1.0000
3	5.44	1.59	4.78	2.22	0.54	0.4750
4	5.11	2.20	3.33	2.40	2.68	0.1211
5	4.33	2.45	3.00	2.74	1.19	0.2924
6	4.11	2.32	3.00	2.83	0.83	0.3753
7	4.89	2.47	2.78	3.27	2.39	0.1419
8	4.89	2.76	2.22	2.72	4.18	0.0577
9	4.67	2.78	1.56	1.81	7.90	0.0126
10	4.56	3.13	1.00	1.41	9.66	0.0098
11	3.67	2.06	0.56	1.33	14.45	0.0016
12	3.33	2.24	0.33	1.00	13.50	0.0036
13	3.56	2.40	0.33	1.00	13.79	0.0036
14	3.11	1.97	0.22	0.67	17.45	0.0020
15	3.44	2.88	0.11	0.33	11.92	0.0083
16	2.89	1.83	0.11	0.33	20.00	0.0018
17	2.67	2.00	0.00	0.00	16.00	0.0039
18	2.89	1.54	0.00	0.00	31.81	0.0005
19	1.89	1.05	0.00	0.00	28.90	0.0007
20	1.67	1.22	0.00	0.00	16.67	0.0035
21	1.33	1.22	0.00	0.00	10.67	0.0114
22	1.33	1.22	0.00	0.00	10.67	0.0114
23	1.22	1.20	0.00	0.00	9.31	0.0158
24	0.89	1.27	0.00	0.00	4.41	0.0688
25	0.78	1.30	0.00	0.00	3.21	0.1108

Figure 6. Mean Pain Scores of the Control and Experimental Groups from Day 1-25



Ⅵ. DISCUSSION

This chapter is organized to discuss the findings of 1) reduced severity of oral mucositis, 2) duration of oral mucositis, and 3) reduced intensity of pain. Following the discussion of the study findings, the significance of the study and implication will be discussed.

A. The effects of sesame oil on oral mucositis

The findings of the study demonstrate a significantly lower severity of oral mucositis over time in participants who gargled with sesame oil, compared with those who used chlorhexidine as the usual care. The significant group difference in the severity of oral mucositis started to emerge on day 9 and continued until day 24. These findings are consistent with previous finding indicating that antioxidants alleviate chemotherapy-induced oral mucositis by scavenging and neutralizing ROS (Coklin, 2002). Although ROS was not directly measured in this study, given the abundance of antioxidants in sesame oil, it is likely that the antioxidant property of sesame oil is the reason for the significant reduction in the severity of oral mucositis. These findings suggest that sesame oil is more effective to manage oral mucositis than the conventional treatment with chlorhexidine in patients who undergo chemotherapy for cancer.

The observation that erythema was prominent on the right and left buccal

mucosa, the floor of the mouth and soft palate is in agreement with previous work (McGuire et al., 1993). Additional erythema observed in the upper and lower labial mucosa is consistent with the recent work of McGuire et al. (1998) and Kolbinson et al. (1988). These findings may be related to the fact that these anatomical areas are composed of nonkeratinized mucosa and therefore more susceptible to high-dose chemotherapy directly and potential trauma indirectly. In this study, erythema in the mucous membrane was observed first and thus, the study findings support previous studies (McGuire et al., 1993).

The mean days to the onset of oral mucositis after chemotherapy for both groups together was 7.89 (±4.12): It was 5.56 (±2.69) for the control group and 10.22 (±4.08) for the experimental group. The study findings coincide with previous studies that physical symptoms of oral mucositis generally begin 5 to 10 days following the initiation of chemotherapy and lasts 7 to 14 days (Harris & Knobf, 2004; Woo, 2003). In this study, the mean duration of oral mucositis for the participants in both groups together was 14.89 (±6.99): It was 19.11 (±2.69) in the control group and 10.67 (±3.46) in the experimental group. The study findings support a previous report by Woo (2003) in which the whole process of oral mucositis lasted 2 to 3 weeks in more than 90% of the patients (Woo, 2003). However, participants in the experimental group recovered from the oral mucositis about 9 days earlier than those in the control group ($p = 0.0085$), and thus participants in the experimental group experienced a significantly shorter duration of oral mucositis compared to those in the control group. A shorter duration of oral mucositis, in turn,

may improve the sense of well-being in these patients with hematologic cancer and may shorten the number of days of hospitalization, reducing the health care cost.

Oral mucositis is also known to be complicated by the indirect effects of chemotherapy-induced neutropenia and thrombocytopenia on the oral mucosa in immunosuppressed patients (Gordon et al, 1994; Fall-Dickson, 2000), and is resolved with neutrophil recovery (Woo, 2003). The baseline data in this study showed that the absolute neutrophil count in the experimental group was significantly lower than the control group (see Appendix 8). However, it was increased significantly at day 7 in the experimental group, whereas it decreased steadily in the control group (see Appendix 8). Moreover, oral mucositis scores began to decrease significantly from day 9 in the experimental group (see Table 7 and Figure 4). A significant, positive relationship was found between the severity of oral mucositis and absolute neutrophil count ($p = 0.0001$). (see Appendix 15). Therefore, the study findings are consistent with previous studies that oral mucositis resolved as neutrophil count recovered (Woo, 2003). Furthermore, the study findings seem to support the literature of Oriental Medicine that sesame oil increases the effectiveness of the immune system as the experimental group swallowed sesame oil following the mouth-rinses.

In this study, the location of the ulcerative oral legions, which had the greatest involvement such as the buccal and labial mucosa and the tongue elicited the highest levels of pain. Initially the pain was described as a burning sensation but then progressed to a continuous tender, sharp, aching feeling. In general, the pattern of oral pain approximately parallels the pattern of oral mucositis development. The oral

mucositis scores and the pain scores between two groups, significantly decreased from day 9 (see Table 7 and 11) and there was a significant, positive relationship found between oral mucositis severity and acute oral pain intensity in additional analysis ($p = 0.0001$) (see Appendix 15). The same pattern was shown in both groups. Moreover, the study results demonstrated a significant reduction in analgesic consumption for relief of oral pain in the experimental group ($p = 0.025$), which was found in an additional analysis to confirm the effect of sesame oil on pain scores. (see Appendix 9). There was a significant, positive relationship found between the severity of oral mucositis and analgesic consumption ($p = 0.0001$) (see Appendix 15). The study findings are in agreement with the results of previous studies that oral mucositis leads to extra uses of analgesics and significantly more days of hospitalization per cycle, thus resulting in an undesirable economical burden (Elting et al, 2002; Magne et al, 2001; Sonis et al, 2001; Marcy et al, 2000; Bensadoun et al, 1998). In fact, Sonis and colleagues (2001) found that hospital charges exceeded $40,000 per patient for patients with oral mucositis.

In this study, pain scores were relatively low compared with the scores of oral mucositis in patients of both groups. This discrepancy between the severity of oral mucositis and pain rating in the study can be explained by the use of analgesics by patients. Patients continued to use analgesics during the study, causing a downward bias in pain score relative to severity of actual oral mucositis. It was found that 15 out of 18 study participants indeed used analgesics for pain relief during the study. In order to minimize the influence by the analgesic effect, pain needs to be

assessed prior to the administration of pain medication in future studies.

Although pain causes a suffering acute oral pain related to inflammation in the oral cavity also has an adaptive, protective function. The increased pain sensitivity fosters both recuperation and repair through minimizing further injury by attempting to avoid all contact rather than just preventing contact with the noxious stimuli (Woolf, 1995). This protective increased sensitivity also leads patients with acute oral pain to minimize normal functions such as swallowing, talking, and mouth breathing. Oral care protocols often recommend the use of viscous lidocaine before meals to decrease the pain experienced with chewing and swallowing. However, it is also important to remember that the patient may inadvertently cause trauma to oral cavity membranes or /and aspiration which could be life-threatening event if these membranes are totally numb from the effects of a topical anesthetic.

Correlations between decreased saliva and oral mucositis-related acute pain, acute oral pain with swallowing, and affective pain and sensory pain with swallowing have important clinical significance as well. The lubricating function of saliva allows the movement of oral tissues against one another and facilitates the process of swallowing. Chemotherapy is known to decrease saliva production, resulting in xerostomia, a dryness of the mouth related to lack of normal secretion (Lloid, 1995). Moreover, a decrease in the amount of saliva may increase mucosal irritation and lead to difficulties in swallowing, eating, and speech, as well as increasing the risk of trauma and infection (Lloid, 1995). A statistically significant positive correlation was found between the severity of oral mucositis and amount of saliva ($P = 0.0001$) (see

Appendix 14) and both the saliva score and oral mucositis score of the experimental group were lower than that of the control group in this study. Based on the study findings, it is suggested first, that sesame oil having mild acidity acts on bactericidal activity and second, that the savory flavor of sesame oil induces an increased salivary production as it stimulates the sense of smell and therefore, both the saliva and oral mucositis score in the experimental group were lowered. Moreover, it can be assumed that increased saliva and the sesame oil itself both act as lubricating agents. On the contrary, chlorhexidine containing alcohol is thought to dry the oral tissues and alter the oral flora (Parulekar et al, 1998; Rosenberg, 1990), thus leading to increased severity of oral mucositis. From the findings of this study, it can be concluded that sesame oil not only helps to ease oral discomfort, but also buffers the hyperacidity that occurs with xerostomia induced by chemotherapy. Therefore, it is suggested that sesame oil can be considered as a lubricating agent in patients with hematological cancer who have oral mucositis.

One of the necessary conditions of effective gargling agents is that they do not to provoke any discomfort to vulnerable cancer patients. Foote and colleagues (2001) reported discomfort with chlorhexidine mouth-rinse which has been widely used for relieving chemotherapy induced oral mucositis. In this study, 100% of patients in the control group experienced discomfort following chlorhexidine mouth-rinses, reporting burning sensation (66.7%), nausea (55.6%), vomiting (33.3%), bitter taste (22.2%) , but only 55.5% of patients in the experimental group reported discomfort associated with sesame oil mouth-rinses. The symptoms of discomfort

were sensation of abdominal discomfort (33.3%), and not refreshing (22.2 %) (see Appendix 11). There was a statistically significant difference in discomfort symptoms between the control and experimental groups ($p = 0.0019$) (see Appendix 10). The study findings support the previous work of Fernandes-Naglik et al. (2001) and Foote et al. (1994) who reported that patients who received chlorhexidine mouth rinses complained of discomfort. Patients in the control group did not report any merits to gargling with chlorhexidine whereas patients in the experimental group reported softening (66.7%), pain relief (66.7%), quenching of thirst (11.1%), and disappearance of bitter taste (11.1%) as merits of gargling with sesame oil (see Appendix 13). There was a statistically significant difference in gargling merits between the control and experimental groups ($p = 0.0054$) (see Appendix 12). Prior to this study, it was speculated that the smell of sesame oil might provoke nausea and vomiting. However, the findings of the study do not support this speculation. Kostler and his colleagues (2001) pointed out a need for non-pharmacological interventions for minimizing physical discomfort in patients with oral mucositis, and the use of sesame oil seems to be advantageous for this purpose.

In summary, the results of this clinical trial indicate the superior effects of sesame oil mouth-rinse on severity, duration of oral mucositis and pain intensity induced by chemotherapy in patients with hematologic cancer . These results are consistent with previous reports that antioxidants scavenge ROS or free radical which induce oral mucositis in cancer patients (Coklin, 2002) and that sesame oil alleviated oral mucositis (Rosenfeld, 1996). Furthermore, it reveals that a mouth-rinse of sesame

oil containing abundant antioxidants induces less discomfort than usual care with chlorhexidine. Sesame oil seems to be highly beneficial as a gargling agent for managing oral mucositis in patients with cancer.

The study is the first clinical trial to examine the effect of sesame oil on oral mucositis based on the connection between antioxidants in sesame oil and the biological process of oral mucositis. Therefore, further replication studies are needed.

B. Significance of the study

The significance of the study was the examination of the effect of sesame oil on oral mucositis induced by chemotherapy in hematological cancer patients and investigating the rational for a sesame oil mouthwash. Specifically, in this study, the biological process and time of onset of oral mucositis following chemotherapy in hematological cancer patients were reviewed and contribution to evidence-based nursing knowledge was made as a clinical trial was used. The study is also significant in that it reinforces nursing practice as connecting theory and research. From the perspective of nursing research, the significance is that in the study a problem in clinical practice was the phenomenon under study and thus offers academic stimulation for the discipline of nursing by showing the process of examining the phenomenon through research. From the perspective of nursing practice, the study results show that sesame oil could be offered as a nursing intervention in practice. It also provides a rational for using the intervention, sesame oil mouth-rinse, as beneficial to patients with oral mucositis induced by chemotherapy. Sesame oil mouthwash decreases the duration of oral mucositis and hospitalization days as well as the patient's economic and suffering burden and thus the importance of the nurses' role can be shown in the team approach in clinical practice. From the perspective of nursing education, the significance is in the need educate student nurses or /and new nurses about sesame oil mouthwash as a nursing technique for patients who have

problem with oral mucositis and student nurses or/ and new nurses who have this education can apply it as a nursing intervention to resolve a health problem within the frame of the nursing process.

Expected effects and practical applications are as follows:

1. Expected effect

1) The study findings can explain scientifically and systematically to nurses who care for cancer patients the rational for using sesame oil as a nursing intervention and offering sesame oil mouthwash could be included as an effective and acceptable oral care protocol to alleviate and prevent oral mucositis.

2) Sesame oil mouthwash, as an intervention to alleviate and prevent of oral mucositis improves the sense of well-being and quality of life which would decrease with oral pain and also reduces the economic burden by reducing extra consumption of analgesic and the period of hospitalization. Thus, it contributes to efficient hospital administration by increasing the availability of beds.

2. Practical Application

1) Sesame oil examined could use as a direct nursing intervention to facilitate recovery from oral mucositis in hematological cancer patients.

2) Sesame oil could be used at home without a physician's order as a non-pharmacological intervention for oral mucositis in hematologic cancer patients who are discharged from hospital after cessation of chemotherapy.

3) Sesame oil could be used as a direct nursing intervention to facilitate recovery of oral mucositis in cancer patients receiving chemotherapy.

4) Sesame oil could be used as a direct nursing intervention to relieve oral mucositis induced by drug intoxication of Gramoxone which produces ROS and results in severe oral mucositis

Ⅶ. CONCLUSION AND RECOMMENDATIONS

A. Conclusion

The study was a clinical trial with nonequivalent control group non-synchronized design to examine the effect of sesame oil on oral mucositis induced by chemotherapy in patients with hematologic cancer.

The data for the study were collected between March 2004 and August 2005 with 18 patients who met eligibility criteria. The participants in the study were diagnosed with hematologic cancer, hospitalized in G university hospital in Seoul and had developed oral mucositis following the administration of chemotherapy. Study participants in the control group received the usual care which consisted of chlorhexidine gargles 5 times a day, whereas study participants in the experimental group received sesame oil gargles 5 times a day. Data collection was initiated at the onset of oral mucositis and assessed daily at 10 a.m. using the OAT until the resolution of oral mucositis.

The data were analyzed using SPSS/WIN 12.0. Differences in demographic and clinical data between the control and the experimental group were analyzed using t-test and chi-square. Differences in between group, main effect of time and the effect of group by time interaction for oral mucositis score, duration of oral mucositis, and pain were analyzed using Repeated ANOVA . Differences in the oral mucositis scores, oral mucositis duration and pain scores according to daily time interval between the

control and experimental group were analyzed using MANOVA. The specific study results are as follows:

1) The 1st hypothesis was “the severity of oral mucositis in patients in the experimental group receiving sesame oil will be lower than those in the control group receiving usual care with chlorhexidine”. There was a statistically significant difference in oral mucositis scores according to groups ($F = 6.55$, $p = 0.0184$). The main effect of time ($F = 8.19$, $p = 0.0001$) and the effect of group by time interaction ($F = 4.22$, $p=0.0001$) was statistically different. The oral mucositis according to daily time intervals between the control and experimental group was significantly different from day 9. Therefore, the 1st hypothesis was supported.

2) The 2nd hypothesis was “oral mucositis duration in participants in the experimental group receiving sesame oil will be shorter than those in the control group receiving usual care with chlorhexidine”. The mean duration of oral mucositis in the control group was 19.11 ($\pm$7.20) and in experimental group treated with sesame oil 10.67 ($\pm$3.46). There was a statistically significant difference in the duration of oral mucositis between the two groups ($F = 10.05$, $p = 0.0085$). The longest duration was 25 days and the shortest 8 days in the control group whereas they were 18 days and 6 days respectively in the experimental group. Therefore, the 3rd hypothesis was supported.

3) The 3rd hypothesis was “The pain score for participants in the experimental group receiving sesame oil will be lowered than those in the control group receiving usual care with chlorhexidine”. The mean pain score was 3.3 (±2.42) for the control group and 1.34 (± 2.27) for the experimental group. There was a statistically significant difference in pain score according to groups (F= 12.77, p = 0.018). The main effect of time (F = 9.12, p = 0.0001) and the effect of group by time interaction (F = 2.19, p=0.0055) was statistically different. The pain scores according to the daily time interval between the control and experimental group was significantly different from day 9. Therefore, the 3rd hypothesis was supported.

In conclusion, the findings of the study demonstrate that mouth-rinse of sesame oil, containing abundant antioxidants, is more effective than the current usual care with chlorhexidine in reducing the severity, duration, and pain of chemotherapy-induced oral mucositis in patients with hematologic cancer.

B. Recommendations

Based on the study results, further study is suggested as follow:

1. Repeated study is needed which there is a large enough sample size to statistically validate using sesame oil as nursing intervention for patients with oral mucositis induced by chemotherapy.

2. Study is needed to further identify scientifically the effect of sesame oil on oral mucositis induced by chemotherapy particularly wit regard to mucosal biology and mucosal immunology.

3. Further study of prophylactic use for sesame oil in patients who undergo chemotherapy for cancer is needed.

4. Further study using sesame oil as a nursing intervention in patients with oral mucositis induced by other disease is needed.

REFERENCES

Abe S., Hirakawa Y. & Takagi S. (2001). Roasting effects on fatty acid distributions of triacylglycerols and phospholipids in sesame (sesame indicum) seeds. Journal of the Science of Food and Agriculture, 81 : 620-626.

Adelstein D.J., Kalish L.A. Adams G.L. Wagner H., Oken M.M, Remick S.C., Mansour E.G. & Haselow R.E. (1993). Concurrent radiation and chemotherapy for locally unresectable squamous cell head and neck cancer : an eastern cooperative oncology group pilot study. Journal of Clinical Oncology, 11 : 2136-2142.

Ambrus J.L., Ambrus C.L., mink I.B. (1975). Causes of death in cancer patients. Journal of Medicine, 6 : 40-42.

American Cancer Society (2005). Cancer Facts and Figures. http://www.cancer.org/docroot/stt/stt_0.asp.

Annussek G. (2001). Sesame oil. In Gale encyclopedia of alternative medicine. Gale Group and Looksmart.

Awidi A., Homsi U., Kakail R.I., Mubarak A., Hanssa A., Kelta M., Martinez P., Sulaiti S., Al Qady A., Jamhoury A., Daniel M., Charles C., Ambrose A & El-Aloosy A.S. (2001). Double-blind, place-controlled cross-over study of oral philocarpine for the prevention of chemotherapy-induced oral mucositis in adult patients with cancer. European Journal of Cancer, 37 : 2010-2014.

Baker D.G. (1982). The radiobiological basis for the tissue reactions in the oral cavity following therapeutic X-irradiation. Archives of Otolaryngology 108 : 21-24.

Bamba S., Andoh A., Yasui H., Araki Y., Bamba T. & Fujiyama Y. (2003). Matrix metallopropeinase-3 secretion from human colonic subepithelial myofibroblasts : Role of interleukin-17. Journal of Gastroenterology, 38 : 548-554.

Barasch A. & Peterson D.E. (2003). Risk factors for ulcerative oral mucositis in cancer patients : Unanswered questions. Oral Oncology, 39 : 91-100.

Barkvoll P. & Attramadal A. (1989). Effect of nystatin and chlorhexidine digluconate on candida albicances. Oral Surgery, Oral Medicine, Oral Pathology, 67 : 279-281.

Beck S.L. (1999). Mucositis. In Yabro C.H., Frogge M.H. & Goodman M. (2nd ed), Cancer Symptom Management, Jones and Bartlett Publishers, Boston.

Beckstrom-Sternberg S.M., duke J.A. & Wain K.K. (1994). “The phytochemical database” ars-genome from roots of *Sesamum indicum*. Bioscience, Biotechnology and Biochemistry, 64 : 873-874.

Bensadoun R.J., Marcy P.Y &Demard F. (2001). Chemotherapy- and radiotherapy-induced mucositis in head and neck cancer patients : New trends in pathophysiology, prevention and treatment. European Archives of Otorhinolaryngology, 258 : 481-487.

Bensadoun R.J., Franquin J.C., Ciais G., Darcourt V., Schubert M.M., Viot M., Djou J.,

Tardieu C., Benezery K., Nguyen T.D., Laudoyer Y., Dassonville O., Poissonnet G., Vallicioni J., Thyss A., Hamdi M., Chauvel P. & Demard F. (1999). Low-energy He/Ne laser in the prevention of radiation induced-mucositis. A multi center phaseⅢ randomized study in patients with head and neck cancer. Supportive Cancer Care. 7: 244-252.

Biork-Eriksson T., Gunnarsson M., Holmstrom M., Nordqvist A. & Petruson B. (2000). Fewer problems with dry nasal mucous membranes following local use of sesame oil. Rhinology, 38 : 200-203.

Biron P., Sebban C., Gourmet R., Chvetzoff G., Philip I & Blay J.Y. (2000). Research controversies in management of oral mucositis. Support Care Cancer, 8: 68-71.

Borbasi S., Cameron K., Quested B., Oliver L & Evans D. (2002). More than a sore mouth : patients' experience of oral mucositis. Oncology Nursing Forum, 29 (7) : 1051-1057.

Borowski B., Benhamou E., Pico J.L., Laplanche A., Margainaud J.P. & Hayat M. (1994). Prevention of oral mucositis in patients treated with high dose chemotherapy and bone marrow transplantation : A randomized controlled trial comparing to protocols of dental care. Oral Oncology, 30 : 93-97.

Bourhis J., De Crevoisier R., Abdulkarim B., Deutsch E., Lusinchi A., Luboinski B., Wibault P. & Eschwege F. (2000). A randomized study of very accelerated radiotherapy with and without amifostine in head and neck quamous cell carcinoma. International Journal of Radiation Oncology, Biology, Physics,

46 : 1105-1108.

Byrnes S. (2005). Staying on top of oxidative stress. http://www.sumeria.net/health/os.html

Carl W. & Emrich L.S. (1991). Management of oral mucositis during local radiation and systemic chemotherapy : A study of 98 patients. Journal of Prosthetic Dentistry, 66 : 361-369.

Chavali S.R., Utsunomiya T. & Forse R.A. (2001). Increased survival after cecal ligation and puncture in mice consuming diets enriched with sesame seed oil, Critical Care Medicine, 29 : 140-143.

Chi K.H., Chen C.H., Chan W.K., Chow K.C., Chen s.y., Yen S.H., Chao J.Y. & Chen K.Y. (1995). Effect of granulocyte-macrophage colony stimulating factor on oral mucositis in head and neck cancer patients after cisplatin, fluorouracil, and leucovorin chemotherapy. Journal of Clinical Oncology, 13 : 2620-2628.

Chiara S., Nobile M.T., Vincenti M Gozza A., Pastrone I., Ross M. & Rosso R. (2000). Sucralfate in the treatment of chemotherapy-induced stomatitis : A double-blind placebo-controlled pilot study. Anticancer Research, 21 : 3707-3710.

Coklin K.A. (2002). Dietary polyunsaturated fatty acids : impact on cancer chemotherapy and radiation. Alternative Medicine Review, 7(1) : 4-21.

Coklin K.A. (2000). Dietary antioxidants during cancer chemotherapy : Impact on chemotherapeutic effectiveness and development of side effects. Nutrition and Cancer, 37 (1) : 1-18.

Cooney R.V., Custer L.J., Okinaka L. & Franke A.A. (2001). Effects of dietary

sesame seeds on plasma tocopherol levels. Nutrition and Cancer, 39 (1) : 66-71.

Crawford J., Holzer H., Stoller R., Jensen O, Lyman G., Tabbara I., Kris M., Grous J., Picozzi V. & Rausch G.. (1991). Reduction by granulocyte colony-stimulating factor of fever and neutropenia induced by chemotherapy in patients with small cell lung cancer, New England Journal of Medicine, 325 : 164-170.

Daeffler R. (1981). Oral hygiene measures for patients with cancer: Cancer Nursing, 4 : 29-35.

Dazzi ., Cariello A., Giovanis P., Monti M., Vertogen B., Leoni M., Tienghi A., Turch D., Rosti G., Nanni O., Rondoni C. & Marangolo M. (2003). Prophylaxis with GM-CSF mouthwashes does not reduce frequency and duration of severe oral mucositis in patients with solid tumors undergoning high-dose chemotherapy with autologous peripheral blood stem cell transplantation rescue : A double blind, randomized, placebo-controlled study. Annals of Oncology, 14 : 559-563.

De Conno F., Ripamonti ., Sbanotto A. & Ventafridda V. (1989). Oral complications in patients with advanced cancer. Journal of Palliative Care, 5(1) : 7-15.

Denham J.W. & Hauer-Jensen M. (2002). The radiotherapeutic injury-a complex “wound”. Radiotherapr & Oncology, 63 : 129-145.

Derizen S., Bodey G.P., & Brown L.R. (1974). Opportunistic gram-negative bacillary infections in leukemia; Oral manifestations during myelosuppression.

Postgraduate Medicine, 55 : 133-137.

Derizen S., Daly T., Drane J. & Brown L. (1977). Oral complications of cancer radiotherapy. Postgraduate Medicine, 61 : 448-453.

Driezen S. (1978). Stomatotoxic manifestations of cancer chemotherapy. Journal of Prosthetic Dentistry, 40 : 650.

Driezen S. (1990). Description and incidence of oral complication. Consensus Development Conference on Oral complications of Cancer Therapies : Diagnosis, Prevention, and Treatment. National Cancer Institute Monographes, 9 : 11-16.

Elting L.S., Cooksley C., Chambers M., Cantor S.B., Manzullo E. & Rubenstein E.B. (2003). The burdens of cancer therapy. Cancer, 98 (7) : 1531-1539.

Epstein J.B., Tsang A.H.F., Warkentin D. & Ship J.A. (2002). The role of salivary function in modulating chemotherapy-induced oropharyngeal mucositis : A review of the literature. Oral Surgery, Oral Medicine, Oral Pathology, 94 (1) : 39-44.

Epstein J.B., Vickas L., Spinelli J. & Reece D. (1992). Efficacy of chlorhexidine and nystatin rinses in prevention of oral complications in leukemia and bone marrow transplantation : Oral Surgery, Oral Medicine, Oral Pathology, 73 : 682-689.

Fall-Dickson J.M. (2000). Stomatitis-related acute oral pain experience of breast cancer autotransplant patients. A Doctoral Dissertation of Jones Hopkins University, Balyimore, Maryland.

Ferretti G.A., Raybould T.P., Brown A.T., Macdonald J.S., Greewood M., Maruyama Y., Geil J., Lillich T.T & Ash R.C. (1990). Chlorhexidine prophylaxis for chemotherapy- and radiotherapy induced-stomatitis : A randomized-double blind trial. Oral Surgery, Oral Medicine, Oral Pathology, 69 : 331-338.

Ferretti G.A., Ash R.C., Brown A.T., Parr M.D., Romond E.H. & Lillich T.T. (1988). Control of oral mucositis and candidiasis in marrow transplantation : A prospective, double-blind trial of chlorhexidine digluconate oral rinse. Bone Marrow Transplant, 3 : 483-493.

Foote RL, Loprinzi CL, Frank AR, O'Fallon JR, Gulavita S, Tewkif HH, Ryan MA, Earle JM. & Novotny P (1994). Randomized trial of a chlorhexidine mouthwash for the alleviation of radiation induced mucositis. Journal of Clinical Oncology 12: 2630-2633.

Fu K.K., Pajak T.F., Trotti A., Jones C.U., Spencer S.A., Phillips T.L., Garden A.S., Ridge J.A., Cooper J.S. & Ang K.K. (2000). A radiation therapy oncology group (RTOG) phase Ⅲ randomized study to compare hyperfractionation and two variants of acetated fractionation to standard fractionation radiotherapy for head and neck squamous cell carcinomas : First report of RTOG 9003. International Journal of Radiation Oncology, Biology, Physics, 48 : 7-16.

Fu K.K., Pajak T.F., Marcial V.A., Ortiz H.G., Rotman M., Asbell S.O., Coia L.R., Vora N.L., Byhardt R., Rubin P., Sorgen S.D., Cox J.D. & Stetz J. (1995). Late effects of hyperfractionated radiotherapy for advanced head and neck

cancer : Long-term follow up results of RTOG 83-13. International Journal of Radiation Oncology, Biology, Physics, 32 : 577-588.

Fukuda Y. (1990). Food chemical studies on the antioxidants in sesame seed. 37 : 484-492. Garbrilove J.L., Jakubowski A., Scher H., Sternberg C., Wong G., Grous J., Yagoda A., Fain K., Moore M.A.S., Clarkson B., Oettgen H.F., Alton K., Welte K. & Souza L. (1988). Effect of granulocyte colony-stimulating factor on neutropenia and associated morbidity due to chemotherapy for transitional cell carcinoma of the urothelium. New England Journal of Medicine, 318 : 1414-1422.

Gonzalez-Barca E., Fernandez-Sevilla A. & Carratal J. (1996). Prospective study of 288 episodes of bacteremia in neutropenic cancer patients in a single institution. European Journal of Clinical Microbiology & Infectious Diseases, 15 : 291-196.

Gordon B., Spadinger A., Hodges E. Ruby E., Stanley R. & Coccia P. (1994). Effect of granulocytemacrophage colony stimulating factor on oral mucositis after hematopoietic stem-cell transplantation. Journal of Clinical Oncology, 12 : 1917-1922.

Hallahan D.E., Haimovitz-Friedman A., Kufe D.W., Fuks Z. & Weichselbaum R.R. (1993). The role of cytokines in radiation oncology. Important Advances in Oncology, 71-80

Harris D.J. & Tish Knobf M. (2004). Assessing and managing chemotherapy-induced mucositis pain. Clinical Journal of Oncology Nursing, 8 (6) : 622-628.

Homles S (1991). Theoral complications of specific anticancer therapy. International Journal of Nursing Study 28(4) : 343-360.

Horiot J.C., Bontemps P., Van Den Bogaert W., Fur R.L., van den Weijngaert D., Bolla M., Bernier J., Lusinchi A., Stuschke M., Lopez-Torrecilla J., Begg A.C., Pierart M. & Collette L. (1997). Accelerated fractionation (AF) improves loco-regional control in the radiotherapy of advanced head and neck cancers. Results of the EORTC 22851 randomized trial. Radiotherapy & Oncology, 44 : 111-121.

Horiot J.C., Le Fur R., Nguren T., Chenal C., Schraub S., Alfonsi S., Gardani G., Van Den Bogaert W., Dancyzak S., Bolla M., Van Glabbeke M. & DePauw M. (1992). Hyperfractionation versus conventional fractionation in oropharyngeal carcinoma : final analysis of a randomized trial of the EORTC cooperarive group of radiotherapy. Radiotherapy & Oncology, 25 : 231-241.

Hou R.C., chen H., Tzen J.T.C. & Jeng K.G. (2003). Effect of sesame antioxidants on LPS-induced NO production by BV2 microglial cells. Neuroimmunology, 14 (14) : 1815-1819.

http://kr.dic.yahoo.com/search/ene/search.html?prop=ene&p=duration

Hur J. (2002). Donguibogam. pp 1800-1801. Buinbooks, Seoul, Korea.

Inagki J., Rodriguez V. & Bodey G..P. (1974). Causes of death in cancer patients. Cancer, 33 : 568-573.

Ishii E., Yamada S., Higuchi S., Honjo T., Igarashi H. & Kanemitsu S., Kai T. & Ueda

K. (1989). Oral mucositis and salivary methotrexate concentration in intermediate-dose methotrexate therapy for children with acute lymphoblastic leukemia. Medicinal & Pediatric Oncology, 17 : 429-432.

Iwamoto R.R. (1996). Alterations in Oral status. A comprehensive Textbook (2nd ed, pp 944-962). Philadelphia, W.B. Saunders.

Jensen S.B., Pedersen A.M., Reibel J. & Nauntofte B. (2003). Xerostomia and hypofunction of the salivary glands in cancer therapy. Supportive Cancer Care, 11 : 207-225.

Jung J.W. (1994). Oral discomfort in gynecological cancer patients undergoing chemotherapy. Master's thesis of Yonsei University, Seoul, Korea.

Johnson J., Bratt B.M., Michel-Barron O., Glennow C. & Petruson B. (2001). Pure sesame oil vs isotonic solution chloride solution as treatment for dry nasal mucosa. Archives Otolaryngol Head Neck Surg, 127 : 1353-1356.

Kaanders J.H., van der Kogel A.J. & Ang K.K. (1998). Altered fractionation: Limited by mucosal reactions? Radiotherapy & Oncology, 50 : 247-260.

Kaanders J.H., van Uaal W.A., Hongonraad W.J. & van der Kagel A.J. (1992). Accelerated fractionation radiotherapy for laryngeal cancer, acute and late toxicity. International Journal of Radiation Oncology, Biology, Physics, 24 : 497-503.

Kang M.H., Katsuzaki H. & Osawa T. (1998). Inhibition of 2, 2'-Azobis (2, 4-dimethylvaleronitrile)-induced lipid peroxidation by sesaminols. Lipids, 33 : 1031-1036.

Kannan V., Bapsy P.P., Anantha N., Doval D.C., Vaithianathan H., Banumathy G., Reddy K.B., Kumaraswamy S.V. & Shenoy A.M. (1997). Efficacy and safety of granulocyte macrophage-colony stimulating factor (GM-CSF) on the frequency and severity of radiation mucositis in patients with head and neck carcinoma. International Journal of Radiation Oncology, Biology, Physics, 37 : 1005-1010.

Karthaus M., Rosenthal C. & Ganser A. (1999). Prophylaxis and treatment of chemo- and radiotherapy-induced oral mucositis – are new strategies? Bone Marrow Transplantation, 24 : 1095-1108.

Karthaus M., Rosenthal C., Huebner G.., Paul H., Elser C., Hertenstein B., Krauter J., Scharmann T., Geissler R.G., Heil G. & Gauser A. (1998). Effect of topical oral G-CSF on oral mucositis : A randomized placebo-controlled trial . Bone Marrow Transplantation, 22 : 781-785.

Katano M., Nkamura M., Matsuo T., Iyama A. & Hsatsugu T. (1995). Effect of granulocyte colony-stimulating factor on chemotherapy-induced oral mucositis. Surgery Today, 25 : 202-206.

Kim H. (1997). Studies on the physicochemical characteristics of sesame with roasting temperature and volatile flavor compounds of sesame oil. Doctoral Dissertation of Korea University, Seoul, Korea/

Klastersky J., Danteau D. & Vernest A. (1972). Causes of death in patients with cancer. European Journal of Cancer, 8 : 149-154.

Kolbinson D.A., Schubert M.M., Flournoy N. & Truelove E.L. (1988). Early oral

changes following bone marrow transplantation. Oral Surgery, Oral Medicine, Oral Pathology, 66 : 130-138.

Kostler W.J., Hejna M., Wenzel C. & Zielinski C.C. (2001). Oral mucositis complicating chemotherapy and / or radiotherapy : options for prevention and treatment. CA. Cancer Journal for Clinicians, 51 (5) : 290-315.

Koukourakis M.I., Kyrias G., Kakolysis S., Kouroussis C., Frangiadaki C., Giatromanolaki A., Retails G.. & Georgoulias V. (2000). Subcutaneous administration of amifostine during fractionated radiotherapy : A randomized phase Ⅱ study. Journal of Clinical Oncology, 18 : 2226-2233.

Legha S.S., Wang Y.M., Mackay B., Ewer M., Hortobagyi G.N. (1982). Clinical and pharmacologic investigation of the effects of a-tocopherol on adriamycin cardiotoxicity. Annals of New York Academy of Science, 393 : 411-418.

Legros M., Fleury J., Bay J.O., Choufi B., Basile M., Condat P., Glenat C., Communal Y., Tavernier F., Bons J.M., Chollet P., Plagne R. & Chassagne J. (1997). RhGM-CSF vs placebo following rhGM-CSF mobilized PBPC transplantation : A phaseⅢ double-blind randomized trial. Bone Marrow Transplantation, 19 : 209-213.

Lenzhofer R., Ganzinger U., Rameis H. & Moser K., Acute cardiac toxicity in patients after doxorubicin treatment and the effect of combined tocopherol and nifedifine pretreatment. Journal of Cancer Research & Clinical Oncology, 106 : 143-147.

Lioid M.E. (1995). Oral medicine concerns of the BMT patients. In M.B. Whedon &

P.C. Buchsel (Eds), Bone Marrow Transplantation : Administrative and clinical strategies, pp 257-281. Bostone, Jones & Bartlett.

Loprinzi C.L., Ghosh C., Camoriano J., Solan J., Steen P.D., Michalak J.C., Schaefer P.L., Novotny P.J., Gerstnet J.B., White D.F., Hatfield A.K. & Quella S.K. (1997). PhaseⅢ controlled evaluation of sucralfate to alleviate stomatitis in patients receiving fluorouracil-based chemotherapy. Journal of Clinical Oncology, 15 : 1235-1238.

Machine D., Campbell M.J., Fayers P.M. & Pinol A.P.Y. (1997). Sample size table for clinical studies (2nd eds). Blackwell Science, Australia.

Macmillan C.H., Carrick K., Bradley J. & Morgan D.L. (1991). Concomitant chemo-radiotherapy for advanced carcinoma of the head and neck. British Journal of Radiology, 64 : 941-946.

Magne N., Marcy P.Y., Foa C., Falewee M.N., Schneider M., Demard F. & Bensadoun R.J. (2001). Comparison between nasogastric tube feeding and percutaneous fluoroscopic gastrotomy in advanced head and neck cancer patients. European Archives of Otorhinolaryngology, 258 : 89-92.

Marcy P.Y., Magne N., Bensadoun R.J., Bleuse A., Falewee M.N., Viot M. & Bruneton J.N. (2000). Systematic percutaneous fluoroscopic gastrotomy for concomitant radiochemotherapy of advanced head and neck cancer : optimization of therapy. Support Cancer Care, 8: 410-413.

McElroy T.H. (1984). Infection in the patient receiving chemotherapy for cancer : Oral complications. Journal of American Dental Association, 109 : 454-456.

McGaw W.T. & Belch A (1985). Oral complications of acute leukemia : Prophylactic impact of a chlorhexidine mouth rinse regimen. Oral Surgery, Oral Medicine, Oral Pathology, 60 : 275-280.

McGuire D., Altomonte V., Peterson D.E., Wingard J., Jones R. & Grochow L. (1993). Patterns of mucositis and pain in patients receiving chemotherapy and bone marrow transplantation. Oncology Nursing Forum, 20 : 1493 –1501.

McGuire D., Yeager K.A., Dudley W.N., Peterson D.E., Owen D.C., Lin L.S. & Wingard J.R. (1998). Acute oral pain and mucositis in bone marrow transplant and leukemia patients: Data from pilot study. Cancer Nursing, 21 : 385-393.

Morris J.B. (2002). Food, industrial, nutraceutical, and pharmaceutical uses of sesame genetic resources. Trends in New Crops and New Uses, 153-156.

National Institute of Nursing Research Priority Expert Panel on Symptom Management (1989). Consensus statement : Oral complications of cancer therapies. National Cancer Institute Monographs, 9: 3-8.

National Institute of Nursing Research. (2006). Strategic Plan for the 21st Century. Announcement on the World Wide Web (1-12). Bethesda, MD: National Institute of Nursing Research. Retrieved January, 2005 from the World Wide Web: http://www.nih.gov/ninr/strategicplan.htm.

National Statistic Office (2005). Moratality and causes of death in Korea. http://kosis.nso.go.kr:7001/ups/chapterRetrieve.jsp?pubcode=MA&seq=46&pub=3

Nemunaitis J., Rosenfeld C.S., Ash R., Freedman M.H., Deeg H.J., Ammelbaum F., Singer J.W., Flomenberg N., Dalton W., Elfenbein G.J., Rifkin R., Rudin A., Agosti J., Hayes F.A., Holcenberg J. & Shadduck P.K. (1995). PhaseⅢ randomized double blind placebo controlled trial of rh GM-CSF following allogenic bone marrow transplant. Bone Marrow Transplant, 15 : 949-954.

Oliff A., Bleyer W.A. & Poplack D.G.. Methotrexate induced-oral mucositis and salivary methotrexate concentration. Cancer Chemoptherapy & Pharmacology, 30 : 215-218.

Parulekar W., Mackenzie R., Bjarnason G. & Jordan R.C.K. (1998). Scoring oral mucositis. Oral Oncology, 34 : 63-71.

Peterman A., Cella D., Glandon G., Dobrez D. & Yount S. (2001). Oral mucositis in head and neck cancer : economic and quality of life outcomes. Journal of the National Cancer Institute Monographs, 29 : 45-51.

Peterson D.E. & Schubert M.M. (1977). Oral toxicity. In Perry MC (ed) : The chemotherapy source book (2^{nd}), Williams & Wilkins, pp. 571-594.

Peterson D.E. & Sonis S.T. (1982). Oral complications of cancer chemotherapy: present status and future studies. Cancer Treatment Reports, 66: 1251-1256.

Pfeiffer P., Madsen E.L., Hansen O. & May O. (1990). Effect of prophylactic sucralfate suspension on stomatitis induced by cancer chemotherapy : A randomized, double-blind cross over study. Acta Oncologica, 29 : 171-173.

Raber Durlacher J.E., Abraham L., van Leevwen E.F., Lustig K.H. & van Winkelhof A.J. (1989). The prevention of oral complications in bone marrow

transplantations by means of oral hygiene and dental intervention. Netherlands Journal of Medicine, 39 : 98-108.

Rahn R., Adamietz I.A., Boettcher H.D., Schaefer V., Reimerk K. & Fleischer W. (1997). Povidone-iodine to prevent mucositis in patients during antineoplastic radiochemotherapy. Dermatology, 195 : 57-61.

Raybould T.P., Carpenter A.D., Ferretti G.A., Brown A.T., Lillich T.T. & Henslee J. (1994). Emergence of gram-negative bacilli in the mouths of bone marrow transplant recipients using chlorhexidine mouthrinse. Oncology Nursing Forum, 21 : 691-696.

Rosenberg S.M. (1990). Oral care of chemotherapy patients. Dental Clinics of North America, 34(2) : 239-250.

Rosenfeld I. (1996). Dr. Rosenfeld's Guide to Alternative Medicine. Gimm-Young Publishers, Korea. Rutkauskas J. & Davis J (1993). Effects of chlorhexidine during immunosuppressive chemotherapy.

Apreliminary report. Oral Surgery, Oral Medicine, Oral Pathology, 76 : 441-447.

See-Lasley K. (1982). Cancer chemotherapy (antineoplastic agents). In Han A.B., Barkin R.L. & Oestreich S.J.K 15TH eds), Pharmacology in Nursing, pp807-818.

Sesaki M., Kashima M., Ito T., Watanabe A., Izumiyama N., Sono M., Kagaya M., Shioya T. & Miura M. (2000). Differential regulation and chemotaxis of human lung fibroblasts by PDGF, interleukin-1β and TNF-α. Mediators of

Inflammation, 9 : 155-160.

Shenep J.L., Kalwinsky D.K., Hutson P.R., Georgge S.L., Dodge R.K., Blankenship K.R. & Thornton D. (1988). Efficacy of sucrafate suspension in prevention and treament of chemotherapy-induced mucositis. Journal of pediatrics, 113 : 758-763.

Slavik M., Wu J. & Riley C. (1993). Salivary excretion of anticancer drugs. Annals of New York Academy of Science, 694 : 319.

Sonis S.T. (2004[a]). Pathophysiology of mucositis. Seminars in Oncology Nursing, 20 (1) : 11-15.

Sonis S.T. (2004[b]). Pathophysiology of mucositis. Nature Reviews Cancer, 4 (4) : 277-284.

Sonis S.T., Elting L.S., Keefe D. Peterson D.E., Schubert M., Hauer-Jensen M., Bekele B.N., Raber-Durlacher J., Donnelly J.P. & Rubenstein E.B. (2004). Perspectives on cancer therapy-induced mucosal injury : Pathogenesis, measurement, epidemiology, and consequences for patients. Cancer, 100 (9) : 1995-2025.

Sonis S.T. (2004[c]). The pathology of mucositis. Natural News Cancer, 4 : 277-283.

Sonis S.T. (2002). The biologic role of nuclear factor-kB in disease and its potential involvement in mucosal injury associated with antineoplastic therapy. Crit Rev Oral Biol Med, 19 : 300-309.

Sonis S.T., Oster G., Fuchs H., et al (2001). Oral mucositis and the clinical and economic outcomes of hematopoietic stem-cell transplantation. Journal of

Clinical Oncology, 19 : 2201-2205.

Sonis S.T. (1998). Mucositis as a biological process : a new hypothesis for the development of chemotherapy-induced stomatotoxicity. Oral Oncology, 34 : 39-43.

Sonis A.L & Sonis S.T. (1979). Oral complications of cancer therapy in pediatric patients. Journal of Pedodontics, 3 : 12-16.

Sonis S.T., Sonis A.L. & Lieberman A. (1978). Oral complications in patients receiving treatment for malignancy other than the head and neck. Journal of American Dental Associaiton, 97 : 476-482.

Sonis S.t & Clark J. (1991). Prevention and management of oral mucositis induced by antineoplastic therapy. Oncology, 5 : 11-18.

Spielberger R.T. (2005). Kepivance ™ : Breakthrough for oral mucositis associated with myeloablative hematopoietic stem cell transplantation. http://www.ibmtr.org/newsletter/newsletters/vol11jan_p01a.html.

Spijkervet F.K., van Saene H.K., Panders A.K., Vermey A., van Saene J.J., Mehta D.M. & fiddler V. (1989). Effect of chlorhexidine rinsing on the oropharyngeal ecology in patients with head and neck cancer who have irradiation mucositis. Oral Surgery, Oral Medicine, Oral Pathology, 67 : 154-161.

Sprinzl G.M., Galvan O., de VTIES a., Ulmer H., Gunkel A.R., Lukas P. & Thumfart A.R. (2003). Local apllication of granulocyte-macrophage colony stimulating factor (GM-CSF) for the treatment of oral mucositis. European

Journal of Cancer, 37 : 2003-2009.

Squier C.A. (1990). Mucosal alterations. Consensus Development Conference on Oral complications of Cancer Therapies : Diagnosis, Prevention, and Treatment. National Cancer Institute Monographes, 9 : 169-172.

Stevens M.M., Campbell J., Smith D.E, How M. Benton S. & Bumpurs P. ( ). The effects of a sesame oil mouthrinse on the number of oral bacteria colony types. In Private company report.

Svojanovsky S.R., Egodage K.L., Wu J., Slavik M & Wilson G.S. (1999). High sensitivity ELISA determination of taxol in various human biological fluids. Journal of Pharmaceutical and Biomedical Analysis, 20 : 549-555.

Symonds R.P. (1998). Treatment-induced mucositis : An old problem with new remedies. British Journal of Cancer, 77 : 1689-1695.

Taylor S.G. IV, Murthy A.K., Vannetzel J.M., Colin P., Dray M., Caldarelli D.D., Shott S., Vokes E., Showel J.L., Huchinson J.C., Witt T.R., Griem K.L., Hartsell W.F., Kies M.S., Mittal B., Rebischung J.L., Coupez D.J., Desphieux j.l., bobbin S. & LePajolec C. (1994). Randomized comparison of neoadjuvant cisplantin and fluorouracil infucsion followed by radiation versus concomitant treatment in advanced head and neck cancer. Journal of Clinical Oncology, 12 : 385-395.

Tombes M.B. & Gallucci B. (1993). The effects of hydrogen peroxide rinses on the normal oral mucosa. Nursing Research, 42 (6) : 332-337.

Trotii A. (2000). Toxicity in head and neck cancer : a review of trends and issues.

International Journal of Radiation Oncology, Biology, Physics, 47 : 1-12.

Valcarcel D., Sanz M.A., Sureda A., Sala M., Munoz L., Subira M., Laborda R., Clopes A. & Sierra J. (2002). Mouth-washings with recombinant human granulocyte-machrophage colony stimulating factor (rhGM-CSF) do not improve grade Ⅲ-Ⅳ oropharyngeal mucositis (OM) in patients with hamatological malignancies undergoing srem cell transplantation. results of a randomized double-blind placebo-controlled study. Bone Marrow Transplantation, 29 : 783-787.

Vokes E.E., Kies M.S., Haraf D.J., Stenson K., List M., Humerickhouse R., Dolan M.E., Pelzer H., Sulzen L., Witt M.E., Hsich Y.C., Mittal B.B. & Weishselbaum R.R. (2000). Concomitant chemotherapy as primary therapy for locoregionally advanced head and neck cancer. Journal of clinical Oncology, 18 : 1652-1661.

Wadleigh R.G., Redman R.S., Graham M.L., Krasnow S.H., Anderson A. & Cohen M.H. (1992). Vitamin E in the treatment of chemotherapy-induced mucositis. American Journal of Medicine, 92 : 481-484.

Wardley A.M., Jayson G.C., Swindell R. Morgenstern G.R., Chang J., bloor R., Fraser C.J. & Scarffe J.H. (2000). Prospective evaluation of oral mucositis in patients receiving myeloblative conditioning regimens and heamatopoietic progenitor rescue. British Journal of Heamatology, 110 : 292-299.

Wagner W., Prott F.J. & Schonekas K.G. (1998). Amifostine : A radioprotector in locally advanced head and neck tumors. Oncology Reports, 5 : 1255-1257.

Wahlin Y.B. (1989). Effects of chlorhexidine mouth rise on oral health in patients with acute leukemia. Oral Surgery, Oral Medicine, Oral Pathology, 68 : 279-287.

Weisdorf D.J., Bostrom B., Raether D. Mattingly M., Walker P., Pihlstrom B., Ferrieri P., Haake R., Goldman A. & Woods W. (1989). Oropharyngeal mucositis complication bone marrow transplantation : prognostic factors and the effect of chlorhexidine mouth rinse. Bone Marrow Transplantation, 4 : 89-95.

Weitzman S.A., Lorrel B., Carey R.W., Kaufman S. & Stossel T.P. (1980). Prospective study of tocopherol prophylaxsis for anthracycline cardiac toxicity. Current Therapeutic Research, 28 : 682-686.

Wesselborg S., Bauer M.K.A., Vogt M., Schmitz M.L. & Schule-Osthoff. K. (1997). Activation of transcription factor NF-kappa B and P-38 mitogen-activated protein kinase is mediated by distinct and separate stress effector pathways. Journal of biological Chemistry, 272 : 12422-12429.

Wojtaszek C. (2000). Management of chemotherapy induced stomatitis. Clinical Journal of Oncology Nursing, 4(6) : 263-270.

Woo S.B. (2003). Chemotherapy induced oral mucositis. http://www.emedicine.com/derm/topic682.htm

Woolf C.J. (1995) : Generation of acute pain : Central mechanisms. British Medical Bulletin, 47 : 523-533.

Woo S.B., Sonis S.T., Mnopoli M.M. & Sonis A.L. (1993). A longitudinal study of oral ulcerative nmucositis in bone marrow transplant recipients. Cancer, 72 :

1612-1617.

Wright W., Haller J. & Pizzo P. (1985). An oral disease prevention program for patients receiving radiation and chemotherapy. Journal of American Dental Association, 110 : 43-47.

APPENDIX

<Appendix 1> 연구참여 동의서

협조해주시는 모든 분에게 감사를 드립니다.

안녕하십니까?

저는 항산화물질을 다량 함유한 참기름 함수가 화학요법을 받는 암환자의 구내염에 대한 효과를 파악하여 향후 구내염 관리에 도움이 되고자 하는 연구를 진행하고 있습니다. 귀하와 같이 화학요법을 받으시는 대부분의 환자분들께서 치료과정 중에 많은 어려움을 겪으실 뿐만 아니라 퇴원 후에도 구내염이 발생하기 때문에 효과적인 도움을 드리지 못하고 있는 실정입니다. 따라서 화학요법으로 인한 구내염을 해결해드리기 위해 구내염의 정도와 증상에 대하여 여쭙고자 하오니 성심껏 응답해 주시기를 부탁드립니다.

다음의 설문내용은 치료과정 중에 계시는 많은 암환자의 간호에 큰 도움이 될 것이며, 연구목적으로만 사용되고 또한 응답내용은 비밀이 보장될 것을 약속드립니다.

협조해주셔서 대단히 감사합니다.

2004 년 4 월

연구자 문선숙 올림

<Appendix 2> 일반적인 정보

다음은 귀하의 일반적 사항에 대한 질문입니다. 해당란에 0표 해주십시오.

1. 이름

2. 성별

3. 연령

4. 귀하의 교육 수준은 어떠하십니까?

① 중졸이하 ② 고졸 ③ 대졸 ④ 대졸이상

5. 귀하의 결혼상태는 어떠하십니까?

① 미혼 ② 기혼 ③ 이혼 ④ 사별

6. 귀하의 종교는 무엇입니까?

① 기독교 ② 불교 ③ 천주교 ④ 종교없음

7. 평소의 흡연 유무

예 아니오

8. 평소의 음주 유무

예 아니오

9. 의치나 틀니가 있으십니까?

예 아니오

10. 다음과 같은 잇몸 증상 중 경험하셨던 갓에 0 표 해주십시오.

출혈이 있었다.

잇몸이 부었다

입안에서 냄새가 났다.

치아가 흔들렸다.

고름이 나왔다.

11. 평소 피곤하거나 힘들 때 입술이나 입안이 헐고 물집이 생기는 등의 문제를 자주 겪으십니까?

예 아니오

12. 함암화학요법 후 구내염을 경험한 적이 있습니까?

예 아니오

“예”라면 몇 번째 치료였습니까?

13. 하루 양치질은 몇 번하십니까?

연구간호사 기재사항

14. 진단명

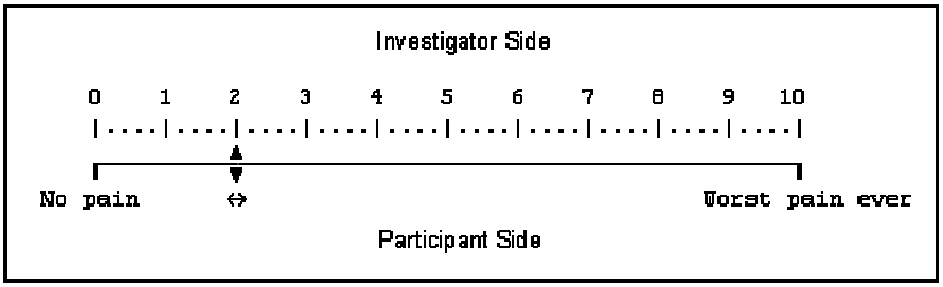
15. 화학요법 횟수

16. 항암제 종류

17. 총투여 용량

18. absolute neutrophil counts

<**Appendix 3**> 통증척도 (Pain Scale)



항암화학요법										
VAS	일	일	일	일	일	일	일	일	일	일
VAS	일	일	일	일	일	일	일	일	일	일

<Appendix 4> 임상검사 및 이상 반응

항목 / 날짜	일	일	일	일	일	일	일	일	일	일
WBC										
Hemoglobin										
Platelet										
Lymphocytes										
neutrophil										
ANC										
ESR										
Albumin										
이상반응										
함수제 종류										
진통제 종류										
진통제 투여량										

<**Appendix 5**> Oral Assessment Tool

Date							
Days post Chemo							
Voice : Converse with patient	1. Normal 2. Deeper/raspy 3. Difficulty						
Swallow : Observation	1. Normal 2. Pain on swallowing 3. Unable to swallow						
Mucous Membrane : Observe appearance with pen torch	1. Pink and moist 2. Reddened /coated 3. Ulceration's+/-bleeding						
Saliva : Touch center of tongue and floor of mouth with spatula	1. Watery 2. Thick/ropy 3. Absent						
Tongue : Feel and observe with a pen torch	1. Pink and moist 2. Coated/shiny+/-reddened 3. Blistered/cracked						
Lips : Feel and observe	1. Smooth, pink and moist 2. Dry/cracked 3. Bleeding/ulcerated						
Gums : Gently press with tip of tongue depressor. Use pen torch	1. Pink and firm 2. Edematous+/-redness 3. Spontaneous bleeding						

Teeth/Dentures : Observe appearance with pen torch	1. Clean, no debris 2. Localized plaque, debris 3. Generalized plaque debris						
Nutritional status : Ask patient	1. Normal 2. Soft diet 3. Fluids only/NBM						
Analgesic requirement	1. None 2. Topical analgesia 3. Systemic analgesia						
Complications : Observation with pen torch	1. No evidence 2. Hemorrhagic mucositis 3. Infection (viral/fungal)						
Self Care assessment :	1. Performs oral care by self 2. Needs encouragement and education 3. Refuse/unable to perform oral care						
Taste : Ask patient	1. Normal 2. Impaired/changed 3. No taste						
Total assessment score							

<Appendix 6> Mean and standard deviation of ANC of the Control and Experimental Groups

	Control N=9		Experimental N=9		t-value	p-value
	M	SD	M	SD		
Oral mucositis score	761.81	1314.0	2662.3	4007.5	-6.76	0.0001

<Appendix 7> Repeated measures ANOVA of ANC of the Control and Experimental Groups

	SS	MS	F-value	P-value
Between Subject				
Group	24859939.00	24859939.00	4.40	0.0462
Within Subject				
Day	53731226.00	2238801.00	1.24	0.2109
Group*Day	100066988.00	5886293.00	3.26	0.0001

<Appendix 8> Repeated measure ANOVA of ANC of the Control and Experimental Groups from Days 1-25

	Control N=9		Experimental N=9		F-value	p-value
Days	M	SD	M	SD		
1	2167.80	3358.20	13.11	9.52	3.70	0.0722
2	1345.20	1963.00	51.22	95.76	3.90	0.0657
3	1134.60	1682.80	89.22	186.48	3.43	0.0825
4	661.00	1042.30	181.56	349.93	1.71	0.2093
5	610.56	979.38	473.44	872.52	1.10	0.7579
6	1152.60	2574.10	981.44	1809.20	0.03	0.8724
7	249.56	723.25	2283.10	4790.00	1.59	0.2260
8	259.78	720.22	2725.00	4999.10	2.14	0.1625
9	581.00	1021.10	2965.80	4791.20	2.13	0.1635
10	516.67	903.51	3343.10	4631.60	3.23	0.0913
11	310.89	724.02	3405.80	4570.20	4.03	0.0620
12	298.44	714.53	3501.10	4504.60	4.44	0.0513
13	328.78	726.82	3611.90	4435.30	4.80	0.0436
14	363.56	758.46	3875.30	4374.70	5.63	0.0305
15	364.22	758.27	3705.30	4397.60	5.04	0.0392
16	374.22	752.90	3576.00	4454.00	4.52	0.0493
17	397.56	741.52	3525.60	4485.40	4.26	0.0556
18	475.56	725.74	3531.20	4481.60	4.08	0.0606
19	750.11	924.43	3531.20	4481.60	3.32	0.0870
20	930.22	829.56	3531.20	4481.60	2.92	0.1070
21	965.89	942.93	3531.20	4481.60	2.82	0.1123
22	1195.30	1248.10	3531.20	4481.60	2.27	0.1515
23	1024.30	861.43	3531.20	4481.60	2.72	0.1189
24	1370.60	1407.80	3531.20	4481.60	1.90	0.1866
25	1217.00	1227.20	3531.20	4481.60	2.23	0.1546

<Appendix 9> Mean and standard deviation of Analgesic consumption of the Control and Experimental Groups

	Control N=9		Experimental N=9		t-value	p-value
	M	SD	M	SD		
Analgesic consumption	2.11	1.17	0.89	0.93	2.46	0.0257

<Appendix 10> Mean and Standard Deviation of Discomfort Symptoms of the Control and Experimental Groups

	Control N=9		Experimental N=9		t-value	p-value
	M	SD	M	SD		
Discomfort symptoms	1.78	0.83	0.56	0.53	3.72	0.0019

<Appendix 11> Frequency Distribution of Discomfort Symptoms of the Control and Experimental Groups

Discomfort symptons	Control N=9		Experimental N=9		χ^2	p-value
	N	%	N	%		
Nausea	5	55.6	0	0.0	6.923	0.029*
Vomiting	3	33.3	0	0.0	3.600	0.206
Bursing sensation	6	667.0	0	0.0	9.000	0.009*
Bitter taste	2	22.2	0	0.0	2.250	0.471
Sesation of abdominal discomfort	0	0.0	3	33.3	3.600	0.206
Nofreshing	0	0.0	2	22.2	2.250	0.471

<Appendix 12> Mean and Standard Deviation of Gargling Merits of the Control and Experimental Groups

	Control N=9		Experimental N=9		t-value	p-value
	M	SD	M	SD		
Gargling merits	0	0	1.56	1.24	-3.78	0.0054

<Appendix 13> Frequency Distribution of Gargling Merit of the Control and Experimental Groups

Pleasant symptoms	Control N=9		Experimental N=9		χ^2	p-value
	N	%	N=9	%		
Refreshing	0	0.0	0	o	-	-
Softening	0	0.0	6	66.7	9.000	0.009*
Dequenched thirst	0	0.0	1	11.1	1.059	1.000
Pain relieving	0	0.0	6	66.7	9.000	0.009*
Disappearing bitter taste	0	0.0	1	11.1	1.059	1.000

<Appendix 14> Mean and Standard Deviation of 13 criteria of OAT of the Control group and Experimental groups

	Control group		Experimental group		t-value	p-value
	M	SD	M	SD		
Voice	1.02	0.13	1.05	0.23	-2.04	0.0419
Swallow	1.18	0.41	1.08	0.27	0.12	0.0019
Mucous Membrane	1.74	0.81	1.61	0.86	1.63	0.1038
Saliva	1.07	0.26	1.05	0.22	0.99	0.3221
Tongue	1.36	0.50	1.15	0.39	6.48	0.0001
Lips	1.64	0.58	1.16	0.45	9.61	0.0001
Gums	1.74	0.79	1.42	0.73	4.39	0.0001
Teeth/Denture	1.65	0.54	1.50	0.70	2.56	0.0108
Nutritional Status	1.62	0.75	1.24	0.44	6.71	0.0001
Analgesic requirement	2.04	1.00	1.37	0.76	8.00	0.0001
Complications	1.33	0.52	1.32	0.50	0.28	0.7814
Self Care	1.30	0.72	1.04	0.25	5.27	0.0001
Taste	1.64	0.72	1.53	0.71	1.58	0.1149

<Appendix 15> Correlation coefficient

	Correlation coefficient	P-value
Oral mucositis & Pain	0.70613	0.0001
Oral mucositis & ANC	-0.44039	0.0001
Oral mucositis & Analgesic consumption	0.46668	0.0001
Oral mucositis & Saliva	0.30917	0.0001

<Appendix 16> Result of Sesame Oil Culture

1. Gram Positive Cocci

1) Staphylococcus like

- Staphylococcus aureus
- Coagulase negative staphylococci
- Staphylococcus epidermidis
- Staphylococcus saprophyticus
- Gemella morbillorum

2) Streptococcus

- α-hemolytic Streptococcus
- Streptococcus pneumoniae
- Streptococcus anginosus group
- Streptococcus agalactiae
- Streptococcus pyogenes
- Group C, E, F, G Streptococcus
- Viridans Streptococcus

3) Enterococcus

- Enterococcus faecalis
- Enterococcus faecium
- Enterococcus avium
- Enterococcus casseliflavus
- Enterococcus flavescens
- Enterococcus mundtii
- Enterococcus durans
- Enterococcus raffinosus
- Enterococcus spp.

4) Other

- Aerocossus
- Leuconostoc
- Macrococcus
- Micrococcus
- Pediococcus
- Stomatococcus

2. Gram Positive Rod

- Coryneform gram-positive rods
- Corynebacterium spp.
- Corynebacterium diphtheriae
- Mixed gram-positive cocci
- Bacillus cereus
- Bacillus cereus group
- Listeria spp.
- Listeria monocytogenes

- Bacillus spp.
- Bacillus anthracis
- Erysipelothrix spp.
- Erysipelothrix rhusiopathiae

3. Gram Negative

1) Gram Negative Fermenter

- Citrobacter freundii
- Escherichia coli
- Enterobacter aerogenes
- Enterobacter agglomerans group
- Enterobacter asburiae
- Enterobacter cloacae
- Klebsiella peumoniae
- Klebsiella pneumo subsp ozaenae
- Morganella morganil
- Proteus mirabilis
- Proteus penneri
- Proteus vulgaris
- Providencia rettgeri
- Providencia stuartii
- Salmonella serogroup B, C, D, E
- Salmonella serotype typhi
- Serratia marcescens

2) Gram Negative Nonfermenter

- Acinetobacter
- Acinetobacter baumannii
- Acinetobacter calcoaceticus
- Acinetobacter Iwoffii
- Alcaligenes faecalis
- Achromobacter xylosoxidans subsp
- Brevundimonas diminuta
- Burkholderia cepacia
- Chryseobacterium Meningosepticu
- Myroides odoratimimus/odoratus
- Pseudomonas aeruginosa
- Pseudomonas fluorescens
- Pseudomonas pseudoalcaligenes
- Shewanella putrefaciens
- Sphingomonas paucimobilis
- Stenotrophomonas maltophilia

3) Other

- Aeromonas hydrophila
- Haemophilus influenza

4. Gram Negative Cocci

- Neisseria gonorrhoeae
- Neisseria meningitides
- Neisseria spp.
- Branhamella spp.
- Moraxella spp.
- Moraxella catarrhalis
- Enteric gram-negative rod
- Non-glucose fermenting, gram-negative rod
- Non-lactose fermenting, gram-negative rod
- Multiple bacterial morphotypes
- Mixed gram-negative rod

Result : No Growth at 4 Days

초록

항암화학요법 암환자의 구내염에 대한 참기름 함수 효과

문 선 숙
간 호 과
대 학 원
연세대학교

본 연구는 혈액암환자에서 화학요법에 의해 초래된 구내염에 다량의 항산화물질을 함유한 참기름 함수의 효과를 시험하기 위한 비동등성대조군 시차설계를 기초로한 임상실험연구이다.

자료수집 기간은 2004년 3월부터 2005년 10월까지였고, 연구대상은 서울시에 위치한 G 대학병원 혈액암병동에 입원한 환자로 본 연구의 대상기준에 부합되는 환자 18명을 대상으로 하였다. 구내염이 발생되면 OAT와 통증척도를 이용하여 구매염정도 통증을 사정한 다음, 실험군에게는 참기름 5ml를, 대조군에게는 클로르헥시딘 5ml를 1일 5회 1분간 함수하도록 한 후 구내염이 사라질 때까지 매일 아침 10시에 구내염정도와 통증을 사정하였다. 수집된 자료는 SPSS/WIN 12.0을 이용하여 두 그룹의 인구학적 임상적 차이는 t-test와 chi제곱으로분석하였고, 두 그룹의 구내염 점수, 구내염기간 그리고 통증정도와 변화추세는 Repeated ANOVA로 분석하였다.

본연구에서 가설검증 결과는 다음과 같다.

1. 제1가설 : “참기름을 제공받는 실험군의 구내염 점수가 클로르헥시딘을 제공받는 대조군의 구내염점수보다 낮을 것이다”는 실험군의 구내염 점수가 대조군보다 통계적으로 유의하게 낮았고 (p=0.0001), 구내염의 변화추세 검증을 위한 분석에서도 두 그룹의 구내염회복 추세에 유의한 차이를 보여 (F=4.22, p=0.0001) 지지되었다.

2. 제2가설 : “참기름을 제공받는 실험군의 구내염 기간이 클로르헥시딘을 제공받는 대조군의 구내염 기간보다 더 짧을 것이다”는 실험군의 구내염 기간이 대조군보다 통계적으로 유의한 것으로 나타나 (F=10.05, p=0.0085) 지지되었다. 대조군의 구내염 기간은 19.11(±7.20) 이었고, 실험군은 10.67(±3.46)으로 나타났다.

3. 제3가설 : “참기름을 제공받는 실험군의 통증점수가 클로르헥시딘을 제공받는 대조군의 통증점수 보다 낮을 것이다”는 실험군의 통증 점수가 대조군보다 통계적으로 유의하게 낮았고 (p=0.0001), 통증의 변화추세 검증을 위한 분석에서도 두 그룹의 통증회복 추세에 유의한 차이를 보여 (F=12.77, p=0.0018) 지지되었다.

결론적으로, 다량의 항산화물질을 함유한 참기름 함수는 항암화학요법으로 인해 발생하는 구내염의 심각성, 기간, 통증에 기존의 chlorhexidine 함수보다 더 효과적인 것으로 나타났다.