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Effect of Using Clove Oil Versus Normal Saline Solution in the Management of Oral Mucositis among Patients Undergoing Chemotherapy

A Thesis Submitted to the College of Nursing Council / University of Kerbala in Partial Fulfillment of the Requirements for the Master's degree in the Nursing Sciences

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سورة النحل الآية (69)

Supervisor Certification

I certify that this thesis, which entitled **(Effect of Using Clove Oil Versus Normal Saline Solution in the Management of Oral Mucositis among Patients Undergoing Chemotherapy)** was prepared under my supervision at the College of Nursing, University of Kerbala in partial fulfillment of the requirements for the degree of master in nursing sciences.

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/ / 2022

Dedication

- ♥ *To those who enlighten the world with their light, my masters: Fatima, her Father, her Husband and her Sons (peace be upon them).*
- ♥ *To my mother for her love, support, and encouragement with love and respect forever.*
- ♥ *To my father's pure soul with honor and pride forever.*
- ♥ *To my brother and sister for their love, support, and encouragement.*
- ♥ *To my love, my dear and my life partner... My husband for his support and encouragement.*
- ♥ *To my dear friends and to all who support me to pursue my study…*

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Abstract

Background: Chemotherapy is determined as the main treatment option for the management of patients with tumors. Patients receive high doses of chemotherapy experience oral mucositis. The present study aims to determine the effect of using clove oil versus normal saline solution in the management of oral mucositis among patients undergoing chemotherapy.

Methodology: A true-experimental design was carried out in Imam Al-Hussein Oncology Center and at oncology wards of Imam Al-Hassan Al-Mujtaba Teaching Hospital. A Systematic random sample consists of 30 patients were selected from patients undergoing chemotherapy and have oral mucositis. The data were collected through the interviewing technique using WHO oral toxicity scale and oral mucositis assessment tool and then analyzed by using the program of SPSS Version 25. Both descriptive and inferential statistical analysis were used to analyze the study results.

Results: The result exposed that 40% of patients had grade II and III oral mucositis at the pre-test period, after seven days of using the clove oil the result shows that 80% of patients are at grade I oral toxicity. Significant statistical difference at p-value of 0.011, 0.042, and 0.000 were reported after seven days of intervention in the levels of oral mucositis between (clove oil and normal saline solution, clove oil and control, and normal saline solution and control) groups respectively.

Conclusions: Mouth care using clove oil gargling procedure is potent in decreasing oral mucositis grade and enhancing the comfort of patients undergoing chemotherapy and it is more effective than normal saline solution gargling procedure in minimizing the severity of oral mucositis.

Recommendations: The study recommended the necessity of using clove oil three times daily as an oral gargle because this can help reduce the overall

burden of oral mucositis complications and the cost of treatment for both patients and hospital.

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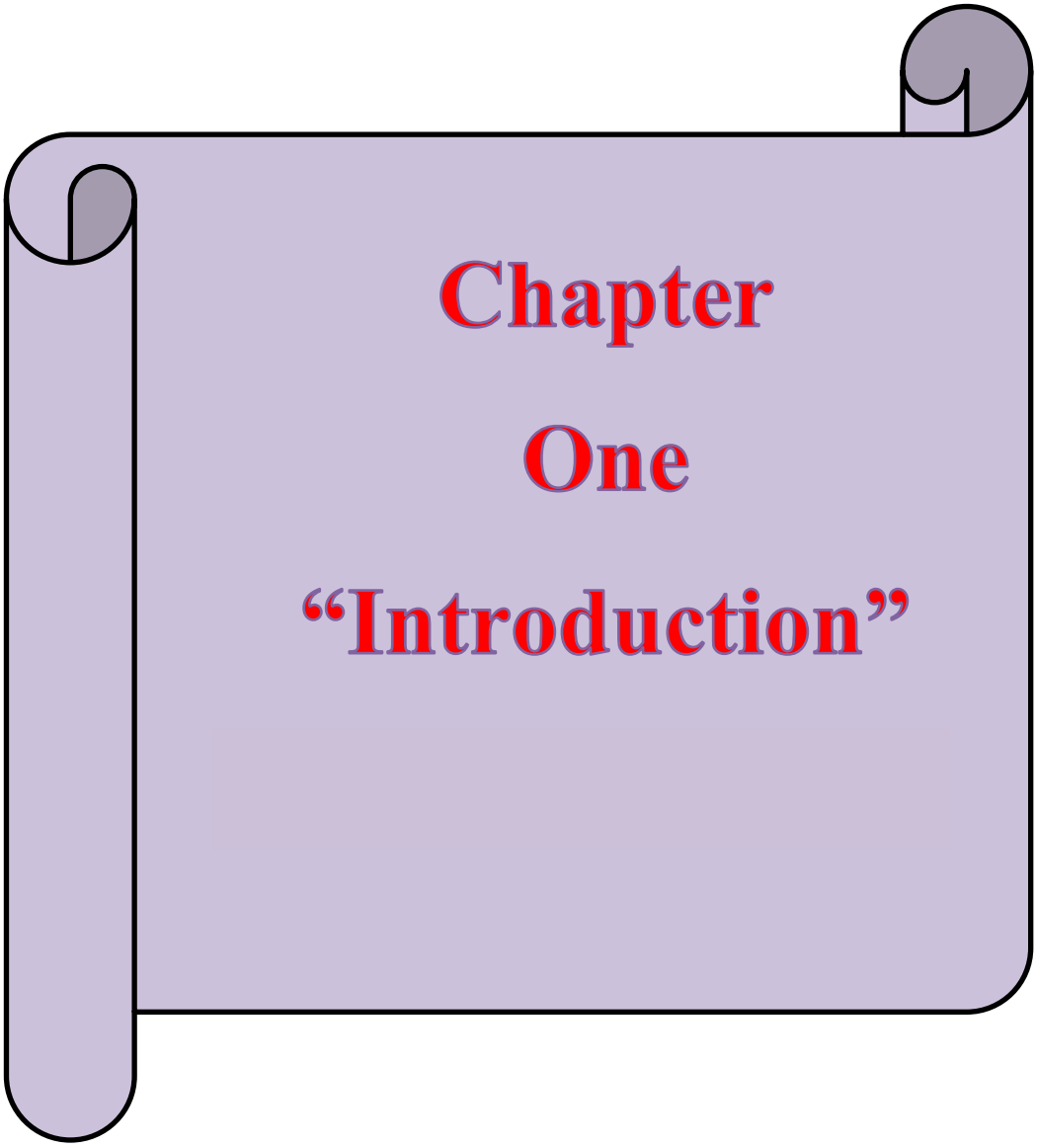
List of Abbreviations and Symbols

Items	Meaning
AV	Aloe Vera
H_1	Alternative Hypothesis
AOX	Antioxidants
BRM	Biological Response Modifiers
CI-NSW	Cancer Institute of New South Wales
CR	Chamomilla Recutita
CT	Chemotherapy
CINV	Chemotherapy Induced Nausea and Vomiting
CIOM	Chemotherapy Induced Oral Mucositis
CEO	Clove Essential Oil
CVR	Content Validity Ratio
CG	Control Group
COX-2	Cyclooxygenase-2
DCS	Daily Comfort Scale

DNA	Deoxyribonucleic Acid
K^{th}	Distance Between Number and Another
EMT	Epithelial Mesenchymal Transition
et al.	Et alia
etc.	Et cetera
FVI	Face Validity Index
f	Frequency
GI	Gastrointestinal
HIPEC	Hyper-Thermic Intraperitoneal Chemotherapy
ITP	Immune Thrombocytopenia
IL-1	Interleukin 1 Beta
IARC	International Agency for Research on Cancer
IPC	Intraperitoneal Chemotherapy
IV	Intravenous
I-FVI	Item Face Validity Index
I-CVI	Item Level Content Validity Index
Sig.	Level of Significance
MH	Marginal Homogeneity Test
MS	Mean of Score
MTX	Methotrexate
NCI-CTC	National Cancer Institute-Common Toxicity Criteria
NSCLC	Non-Small Cell Lung Cancer
NS	Normal Saline
NFKB	Nuclear Factor Kappa-B
H_0	Null Hypothesis
NO.	Number
NE	Number of Experts in Agreement

NRS	Numeric Rating Scale
ANEO	Oral Antineoplastic Drugs
OC	Oral Cryotherapy
OM	Oral Mucositis
OS	Oxidative Stress
PM	Peritoneal Metastases
PIPAC	Pressurized Intraperitoneal Aerosol Chemotherapy
P value	Probability Value
RT	Radiotherapy
RNS	Reactive Nitrogen Species
ROS	Reactive Oxygen Species
RBCs	Red Blood Cells
S-FVI	Scale Face Validity Index
S-CVI/UA	Scale Level Content Validity Index Based on the Universal Agreement
S-CVI/Ave	Scale-Level Content Validity Index Based on an Average Method
NaCl	Sodium Chloride
SD	Standard Deviation
SPSS	Statistical Package for Social Science
SPSS	Statistical Package of Social Sciences
SIM-Card	Subscriber Identity Module Card
For sum	The Cumulative Total Mucositis Assessment Score
ISOO	The International Society of Oral Oncology
MASCC	The Multinational Association for Supportive Care in Cancer
TACE	Trans-Arterial Chemoembolization
TNF	Tumor Necrosis Factor Alpha

UK	United Kingdom
UA	Universal Agreement
WHO	World Health Organization
&	And
$\mathbf{X^2}$	Chi-Square Test
≤	Equal or less than
≥	Equal or more than
t	Independent Sample t Test
$\boldsymbol{\tau}$	Kendal-Taue Test
<	Less than
U	Mann-Whitney Test
>	More than
%	Percent


Chapter
One
“Introduction”

Chapter One

Introduction

1.1. Introduction:

Cancer is considered an important global issue that from which about eight million people die each year. According to the International Agency for Research on Cancer (IARC) reported that 7.6 million worldwide deaths were attributed to cancer. The estimated number of new cases each year is 12.7 million. Only developing nations accounted for 63 percent of cancer-related deaths, suggesting that developing nations have a higher risk of developing the disease (Abbas and Rehman, 2018).

One of the main risks to public health in sophisticated world, as well as increasingly in developing nations, is cancer, it is the second most common cause of mortality in developed nations. Since 1999, cancer has exceeded the cardiovascular diseases as the top cause of death for people below 85 years old when deaths were counted by the age (Motallebnejad, et al., 2008).

The most common methods for the treatment of cancer are chemotherapy (CT) and radiation therapy (RT). These therapies have a number of adverse effects, despite being used to enhance the patient's quality of life. Patients suffer from morbidity and death as a result of severe adverse responses brought on by these treatments. Additionally, they contribute to affected patient's economic status (Naidu, et al., 2004).

Chemotherapy prevents tumor growth by eradicating their capacity to divide and inducing apoptosis. However, because chemotherapy also affects normal cells, there may be side effects such as hair loss, nausea, oral mucositis, exhaustion, and vomiting, depending on the dose (Abbas and Rehman, 2018). One of the most frequent adverse effects of CT is oral mucositis (OM), it is characterized by an inflammation accompanied by pain

and ulcers formation in the oral mucous membrane (Avci and Sari, 2019).

Almost all patients receiving high doses of CT experience chemotherapy-induced oral mucositis (CIOM), which causes the mucosal lining of the mouth to atrophy and break down, resulting in ulcers (Saldanha and Almeida, 2014). Oral mucositis occurs in about 40 percent of patients with cancer who undergoing chemotherapy and this percentage increases to about 90 percent for patients with head and neck cancer who treated with both CT and RT. These patients will enter the hospitals and about 19 percent of them will suffer from delay in antitumor treatment especially for high-degree OM treatment, and this result in decrease quality of life, bad prognosis, and high patient treatment budget (Pulito, et al., 2020).

Fungal infection of the mouth is prevalent in patients undergoing CT. Fungal infection is most commonly related to Candida albicans and Candida glabrata, which is considered the two basic components of oral mycobiota in the human. The production of high levels of phospholipase by Candida albicans oral isolates from patients with cancer who undergoing CT, and it was suggested that this may increase the risk of OM (Sobue, et al., 2018).

Typically, OM appears seven days following CT administration and resolves within 21 days. Pain due to OM is the most frequent side event mentioned by patients undergoing CT. Patients' quality of life is reduced by pain, which also makes it difficult to chew, swallow, and communicate. It also negatively impacts the patient's ability to eat properly, which results in nutritional deficiencies and therefore results in weight loss (Avci and Sari, 2019).

Redness and ulceration of oral mucosa are clinically characteristics of OM. The development of OM occurs on average five to seven days after CT administration, it peaks at 12 days and continue about more five days. Different oral functions are affected as a result of oral mucositis because of severe pain

including speaking, eating, drinking, as well as difficult or impossible sleep leading to prolonged stay in the hospital, need for several medications such as antibiotic and opioid, intravenous nutrition, and increased care costs (Laheij, et al., 2019).

Many therapeutic agents are available for OM management such as anti-inflammatory agents, benzydamine hydrochloride rinse, and oral decontamination but there is still no actually proven treatment, also many of these agents have side effects and require high cost. As a result, research on naturally occurring medicines is underway to target the therapy in a more economical way and decrease OM morbidity with fewer adverse effects than manufactured pharmaceuticals. Additionally, these herbal agents are widely accessible without a prescription, enabling individuals to take them without any supporting data from science (Nagi, et al., 2018).

The natural products can be given as a food supplement. Thus, they do not cause severe side effects and are well accepted by patients. Furthermore, they can significantly affect different pathways of cellular signaling according to their chemical structure and thus affecting the pathogenesis of OM at several levels, as well as negatively affecting cancer cells activities. Substantially, different herbal or natural compounds have been examined and others are under tests. Oral zinc supplement, glutamine, and vitamin E are examples of the natural products that were tested previously. (Pulito, et al., 2020).

The clove essential oil is utilized in the fragrance and flavoring sectors as well as in the treatment of illness and the promotion of healing through topical application. The United States Food and Drug Administration have classified clove oil as a product that is generally recognized as safe. Numerous pharmacological and biological benefits of clove essential oil include antioxidant, anti-fungicidal, anti-carcinogenic, anesthetic, and antiprotozoal actions (Xu, et al., 2016).

Using salt mouthwash helps reduce discomfort, keep food debris out of the mouth, and preventing infection. The 0.9 percent concentration of normal saline is not irritating and is thought to aid in the development of granulation tissue and accelerate healing. Mouthwash is affordable, dependable, and safe. When we have oral wounds, salt water mouthwash rinses are recommended as a great remedy. The explanation is that salt water not only acts as a natural disinfectant but also reduces tissue edema (Saldanha and Almeida, 2014).

1.2. Importance of the study:

Surgery, CT, and RT are some of the cancer therapies that have altered over the past three decades. Patients receiving cancer treatment frequently face oral side effects (Bolouri, et al., 2015). About 20-40 percent of patients undergoing CT and nearly all patients having head and neck RT experience the development of oral mucositis (Avsi and Sari, 2019).

When desquamation is interrupted, a white patch is the first symptom of OM. After that, erythema appears on the mucosa within a week or two. Throughout treatment, pseudo-membrane production indicates ulceration, which is accompanied by discomfort and tenderness (Bolouri, et al., 2015).

Oral mucositis often shows up clinically as atrophy, edema, erythema, and ulceration. Local causes, such as tooth damage or microbial colonization, may make the situation worse. The patient's quality of life is significantly impacted by OM. One of the main reasons for unanticipated treatment cessation, CT dose minimizations, and modifications in the choice of anti-tumors drugs is severe OM (Ahmed, 2013).

The development of many infections is accelerated by OM, which has a negative effect on both the patients and their family members' quality of life. The most often reported adverse effect of OM is pain, which makes it difficult to talk, swallow, and eat. Patients with OM experience unpleasant, inadequate food and fluid intake, and finally, they frequently become malnourished and

dehydrated. Mucositis-related consequences also lengthen hospital stays, increase cost inpatient care, the need for narcotic painkillers, and the need for parenteral nutrition (Yavuz and Yılmaz, 2015).

Patients with OM take care of their oral hygiene in order to alleviate their pain and suffering. Oral care is the practice of keeping the mouth clean, brushing teeth, and gargling to avoid smells and cavities, maintain the health and hydration of the lips and oral mucosa, maintain oral mucosa, and improve comfort and self-esteem. Baking soda and regular saline are two dental care procedures. The suggested method for oral care is normal saline (Naibaho, et al., 2020).

The essential oil that extracted from the dried flower buds of clove is known as clove oil. Medically, it is significantly used for teeth pain or oral cavity problems, acne, rheumatoid arthritis, scars, different allergic problems, and as an antiseptic in oral cavity infections. Furthermore, the clove oil has inhibitory activity on different infections and pathogens as a result of its antimicrobial properties that were tested through its application to any product, such as food and health products (Wongsawan, et al., 2019).

According to the Ministry of Health/ Environment Annual Statistical Report (2020) reported the higher percentage of patients receiving chemotherapy for cancer in Iraq. It is represented that the malignant neoplasm as the seventh top ten cause of deaths in Iraq with a percentage of 5.8, tenth top ten cause of deaths for males was malignant neoplasms of digestive organs with a percentage of 2.2, and fourth top ten causes of deaths for females was malignant neoplasms with a percentage of 9.2 (Iraqi Ministry of Health/ Environment Annual Statistical Report, 2020).

Therefore, the present study has huge importance because of the large percentage of patients with cancer who requires treatment with CT and/or RT which after that cause and induce different side effects including OM. Also, the

statistical report from Imam Al-Hussein Oncology Center statistical unit confirmed the large number of patients with cancer who received treatment in the center for the last six years as follow: 861 patients in 2015, 1043 patients in 2016, 1213 patients in 2017, 1163 patients in 2018, 1263 patients in 2019, 1294 patients in 2020, and 1325 patients in 2021.

Thus, according to these statistical numbers and according to previous studies that identify the risk of OM on reducing the patients healing process, impairs their ability to adhere to the cancer treatments as a result of mucositis-related pain , and negatively affects the patient's nutritional status and thus leads to deficiency of nutrition and consequent losing weight, therefore it is important to study this problem and investigate the best current evidence-based nursing interventions in order to alleviate the suffering of these patients and enhance their health status.

1.3. Problem statement:

Oral mucositis is a very complex issue that poses a significant risk to the health of the patients. OM causes several problems, such as therapy delays, dose reductions, and even treatment plan termination (Ameen, et al., 2019). The intolerable OM pain severity has been attempted to be reduced using a wide range of therapeutic agents currently available, including oral care, anti-inflammatory agents, local anesthetic agents, oral decontamination, benzydamine hydrochloride rinse, and low-level laser therapy, but there is still no proven effective treatment. Some medications have adverse effects and are more expensive (Nagi, et al., 2018).

Thus, the researcher found that this problem still requires additional studies and focus because if ignoring it, risks of OM will be increased which includes severe pain impairing the patient's ability to eat, swallow, and even speak leading to malnutrition and dehydration. This consequently will lead to increased periods of hospitalization and treatments budget and other burdens

on both patients and health care staff. Therefore, this study may add a new evidence to support the use of clove oil or normal saline solution in the management of OM. Thus, the problem of the present study is directed toward determining the effect of using clove oil versus normal saline solution in the management of OM among patients undergoing CT.

1.4. The present study objectives:

1.4.1. Determine the effect of using clove oil versus normal saline solution in the management of oral mucositis among patients undergoing chemotherapy.

1.4.2. Find out the differences between levels of oral mucositis of patients undergoing chemotherapy with their sociodemographic characteristics and clinical data.

1.5. Research question:

1.5.1. Does clove oil solution enhance the healing levels of oral mucositis among patients undergoing chemotherapy?

1.5.2. Does normal saline solution enhance the healing levels of oral mucositis among patients undergoing chemotherapy?

1.6. Hypotheses:

a. **H_0:** There is no significant effect of clove oil on improving healing levels of oral mucositis.
b. **H_1:** Clove oil has a significant effect on the improvement of oral mucositis healing levels.
c. **H_0:** There is no significant effect of normal saline solution on improving healing levels of oral mucositis.
d. **H_1:** Normal saline solution has a significant effect on the improvement of oral mucositis healing levels.

e. **H_0:** There is no difference between the effect of clove oil and normal saline solution on the improvement of oral mucositis healing levels.
f. **H_1:** There is a significant difference between clove oil and normal saline solution in response to its effect on the improvement of oral mucositis healing levels.

1.7. Definition of the terms:

1.7.1. Clove oil:

1.7.1.a. Theoretical definition:

Is the clove plant's essential oil, which may be obtained from the flower buds, leaves, and stems. Eugenol is the main physiologically active ingredient. An herbicide, fungicide, or insecticide are all properties of clove oil (Baker, et al., 2018).

1.7.1.b. Operational definition:

Is an aromatic oil extracted from cloves that is used topically to treat inflammation of oral mucosa due to its potent antiseptic and analgesic activity. It also has a strong antioxidant, antibacterial, antifungal, and antiviral activities, so it is given for patients with cancer who undergoing CT and experiencing OM.

1.7.2. Normal saline solution:

1.7.2.a. Theoretical definition:

It is the most often used crystalloid and the cornerstone of intravenous solutions used in clinical settings. It can have different concentrations, including 0.9 percent and 0.45 percent (Tonog and Lakhkar, 2019).

1.7.2.b. Operational definition:

Is one of the isotonic solutions that can be used as a mouth rinse due to it is anti-plaque, anti-inflammation properties, and its impact on wound healing in patients with OM who received CT.

1.7.3. Oral mucositis:

1.7.3.a. Theoretical definition:

Is an inflammation of the mucous membrane in the mouth, it is characterized by erythema, edema, mucosal shedding, and ulceration (Laheij, et al., 2019).

1.7.3.b. Operational definition:

Is an ulcerative, and erythematous lesions of the oral mucosa which is most commonly occur as a complication of CT or RT in patients with cancer who undergoing chemotherapy.

1.7.4. Chemotherapy:

1.7.4.a. Theoretical definition:

Is the use of chemical medication to stop cancerous cells or disease-causing pathogens like microorganisms without significantly damaging the host cells. Consequently, CT for cancer and CT for infectious diseases may be roughly categorized as the two types of treatment (Alam, et al., 2018).

1.7.4.b. Operational definition:

Is the administration of specific chemical drugs for destroying the cells of cancer. It is generally working by preventing the cancer cells from multiplication, growth, and division. It is given to the patients with cancer who receiving CT.

Chapter

Two

"Review of Literature"

Chapter Two

Review of Literature

Chapter two presents the review of studies and theories that support the subject of present research.

2.1. Historical overview of chemotherapy:

At the beginning of the 20th century, efforts were made to reduce the number of chemicals that could have an impact on the condition by developing techniques to test compounds using transplantable tumors in rats. However, four World War II-related initiatives and the outcomes of the pharmaceuticals that resulted from them were what gave rise to the national drug development initiative known as the Cancer Chemotherapy National Service Center, which was founded in 1955 (DeVita and Chu, 2008).

The term CT refers to the use of chemicals to suppress cancerous cells or disease-causing pathogens or microorganisms without significantly damaging the host cells. CT for cancer and CT for infectious diseases may thus be generally classified into two groups. The medications that fall under these categories differ from the others in that they often aim to kill or suppress the target organism while having little to no impact on the host cell (Alam, et al.,2018).

Chemotherapy is the use of cytotoxic drugs to treat or prevent suspected metastases as well as to treat or prevent the development of some malignancies, including leukemias, lymphomas, and some solid tumors. Additionally, CT may be used with biotherapy. Every kind of CT has adverse or severe side effects. The usage of medicines affects the kind and intensity of OM (Lemone-Koeplin, et al., 2017).

Chemotherapy is frequently employed and may be administered alone or in conjunction with other medications. It is possible to combine this therapy

with radiation or monoclonal antibody therapy to best meet the demands of each patient's unique condition. Fludarabine and comparable single-agent CT treatments are often well tolerated and simple to administer. Combination CT treatments contain two or more medications and are frequently linked to additional adverse effects (Brady, et al., 2014).

Chemotherapy interferes with cell metabolism and replication at different stages of the cell cycle. It also functions by impeding the cancerous cell's capacity to generate necessary enzymes and molecules. Only some phases of the cell cycle are affected by phase-specific medications, whereas the complete cell cycle is affected by non-phase-specific pharmaceuticals (Lemone-Koeplin, et al., 2017).

Surgery was the first technique used to treat cancer. When Roentgen reported on his discovery of x-rays in 1895, the age of RT officially started. It then quickly gained momentum after Pierre and Marie Curie discovered radium in 1898. Paul Ehrlich was the person who first began a serious effort to create chemicals to treat cancer around the start of the 20^{th} century. The term "chemotherapy" was his invention (DeVita and Rosenberg, 2012).

Traditional CT destroys normal cells that divide quickly, such as those in the gastrointestinal tract, bone marrow, and hair follicles, because all anticancer chemicals used in the treatment are cytotoxic to both cancer and healthy cells. The following adverse effects of CT are frequently reported: OM (inflammation of the entire mucosal lining of oral cavity), alopecia (loss of hair), and myelosuppression (decreased blood cells production, hence also suppression of the body’s immune system) (Alam, et al., 2018).

2.2. Uses of chemotherapy:

2.2.1. Cure specific cancer:

Chemotherapy usage includes treatment of cancer when it is possible, which means that once the cancer is eliminated, it stays gone forever. The

majority of medical professionals only refer to "cure" as a potential or expected outcome of treatment. Therefore, the doctor may refer to treatment as having a probability of curing cancer when it is administered to a patient. Even while many patients with cancer hope for a cure in these circumstances, it does not always happen that way. It sometimes takes years to determine whether a person's cancer has truly been cured (American cancer society, 2019).

2.2.2. Control tumor growth:

Chemotherapy inhibits or retards the cancer cells' rapid cell division and proliferation. However, it can also damage rapidly dividing good cells, such as those that line the mouth and intestines or stimulate the growth of the hair. Side effects might lead to harm the healthy cells. After CT is finished, side symptoms frequently become better or disappear. when CT stops cancer from spreading, slows down the disease's progress, or eradicates the cells of cancer that have already transport to other regions of the body (National Institutes of Health, 2018).

2.2.3. Shrink tumor before surgery or radiation therapy:

Chemotherapy can be administered either prior to or following other procedures like surgery or RT. Neoadjuvant therapy's goal is to make the cancer smaller before the other treatment, which is typically surgery, to increase the effectiveness of that procedure. The goal of adjuvant therapy, if administered after, is to eradicate any cancer cells that may still exist. Radiation treatment is frequently used with CT to increase its efficacy (Sheard, 2020).

2.2.4. Relieve symptoms:

Cancer, which is the unchecked proliferation of damaged aberrant cells, is treated with CT, commonly known as chemo. Cancer cells are destroyed with CT drugs. If the patient has cancer, the doctor may elect to administer CT to treat the disease's symptoms such as shortness of breath, pain, etc. Early management of treatment side effects or other cancer-related symptom, such as

pain, constipation, nausea, anxiety, etc., can be assisted by the palliative and supportive care program (American University of Beirut, 2019).

2.3. Types of chemotherapy drugs:

2.3.1. Alkylating agents:

One of the first and most widely used anticancer medications is an alkylating agent. Beginning in the early 1940s, their recorded usage in cancer treatment began. The majority of alkylating chemicals are double-edged swords with enormous destructive and healing potential. These medications interfere with Deoxyribonucleic Acid (DNA) to stop the development of cancer cells. They are so named because they may modify negatively charged biological molecules like DNA and proteins by adding alkyl groups. It is among the first class of substances shown to be helpful in CT for cancer. Because of their demonstrated and strong clinical anticancer activity, they continue to be the most crucial elements of contemporary chemotherapeutic regimens (either alone or in conjunction with other medications) (Ralhan and Kaur, 2007).

2.3.2. Nitrosoureas:

Since 1975, nitrosourea anti-neoplasm medications have been widely used to treat (lung, breast, colorectal) cancers, melanoma, brain neoplasms, and Hodgkin's lymphomas. These medicines appeared to be extremely reactive, exhibiting fast transit through the barrier of blood-brain and concurrent rapid breakdown, according to pharmacokinetic investigations. The nitrosoureas ion release has been suggested as the general or popular mechanism of action for this drugs series homogeneity. It has been proposed that the shakiness of nitrosoureas is primarily caused by the nucleophilic attack sensitivity, which results in chloroethyl-carbonium ion offset and alkylation (Schallreuter, et al.,1990).

2.3.3. Anti-metabolites:

A variety of malignancies, including breast and bladder tumors, several acute leukemias, and Non-Hodgkin lymphomas, are treated with methotrexate (MTX), either alone or in combination with other drugs. Pemetrexed, another antifolate, is used in conjunction with cisplatin to treat non-small cell lung cancer (NSCLC), while raltitrexed is an antifolate that can be used to treat colorectal cancer. MTX and the other antimetabolites can induce OM, which can result in mouth ulcers, and stomatitis, which is an inflammation of the mouth. It is believed that 20-60% of people using MTX develop some degree of OM or stomatitis, which is a significant side effect and frequently dose-limiting (Todd, et al., 2018).

2.3.4. Plant alkaloids and natural products:

Alkaloids, which are mostly found in plants and frequently include heterocyclically bonded nitrogen, are organic nitrogenous bases that are produced by the metabolism of amino acids. Their basicity, however, varies significantly due to structural differences, and even neutral alkaloids have been identified. Alkaloids frequently exhibit strong bioactivities, and as a result, it is believed that they are crucial in how plants interact with their surroundings. Throughout human history, cures, poisons, and psychoactive substances have all been made from alkaloids and plant extracts that contain alkaloids (Fester, 2010).

Natural compounds called alkaloids, which contain nitrogen and have intricate and varied structures, may be found in bacteria, fungus, mammals, and plants. Alkaloids are widely distributed, and their diverse range of structural variations make it challenging to classify them. Alkaloids can be categorized for research purposes based on their chemical makeup, biochemical provenance, and/or natural origin. Plant alkaloids have historically been used as disinfectants, anticough, analgesics, and medication for a wide variety of

illnesses in traditional medicine. There are several alkaloids used in pharma science today, including codeine, brucine, morphine, ephedrine, and quinine. Several alkaloids have acted as forms for contemporary drugs (Gutiérrez-Grijalva, et al., 2020).

2.3.5. Anti-tumor antibiotics:

Through their anti-reproduction, anti-epithelial-mesenchymal-transition (EMT), and pro-apoptotic properties many antibiotics have been utilized in the treatment of cancer. However, a growing number of studies have suggested that antibiotics may also contribute to the development of cancer by altering the microbiota of the intestinal tract. This further encourages long-term inflammation, modifies the metabolism of normal tissue, causes genetic toxicity, and impedes the ability of the immune system to respond to malnutrition of bacteria, all of which have a negative impact on cancer treatment. Research has shown that antibiotics can encourage cancer cell death, suppress cancer development, and stop cancer spread. Due to these factors, the antibiotics usage in the treatment of cancer is increasing (Gao, et al., 2020).

2.3.6. Hormonal agents:

The body produces hormones, which are proteins or chemicals that aid in regulating the behavior of specific cell types. For instance, the effective operation of several bodily components depends on sex hormones including progesterone, estrogen, and testosterone. Our bodies also contain several additional hormones, including insulin, cortisol, adrenaline, and thyroid hormones. Hormones are required by some tumors to grow. As a result, therapies that change or block hormones can occasionally aid in reducing the progression of certain tumors. Hormone treatment, hormonal therapy, or endocrine therapy are terms employed to describe the usage of hormones for cancer treatment. The majority of cases of breast and prostate cancers that consider sex hormone-dependent are treated with hormone treatment. A few

other cancers can be treated with hormone therapy (American Cancer Society, 2020).

2.3.7. Biological response modifiers:

Biotherapy is a type of treatment that fortifies the body against some adverse effects of other therapies and leverages the body's own immune system to defend against infection, cancer, and other disorders. Biological response modifiers (BRMs), such as vaccinations, monoclonal antibodies, cytokines, and adjuvants, are used in biotherapy. Biological response modifiers are used in biotherapy (BRMs). BRMs, also known as biologics, are chemicals that alter the activity of one or more immune system components in order to modify the immune system. The words "BRM" and "immunomodulator" are frequently used interchangeably (Kuroki, et al., 2012).

2.4. Methods of chemotherapy administration:

2.4.1. Intravenous (I.V) chemotherapy:

Chemotherapy is frequently administered through injection or infusion. Through a tiny tube known as a catheter that is inserted into a vein, artery, body cavity, or other body component, CT medications are infused into the body during chemo infusions. A chemo medication may occasionally be immediately administered using a syringe. Through a thin, flexible plastic tube known as a catheter, intravenous, or IV chemotherapy is directly injected into the circulation. It is inserted into a vein in the forearm or hand using a needle, and the needle is then discarded, leaving the catheter in its place (The American Cancer Society, 2019).

2.4.2. Oral chemotherapy :

Oral administration of antineoplastic medications (ANEO) has increased during the past ten years, about 25%. Due to its ease and ability to improve quality of life, the oral route of administering antineoplastic therapy is also the choice of both patients and medical professionals. However, one of the biggest

issues facing patients using oral antineoplastic medicines is a lack of adherence. According to the medications used and the measuring techniques used, earlier investigations revealed inconsistent results regarding the adherence rate with ANEO, ranging from 23 to 100 percent (Talens, et al., 2021).

2.4.3. Injected chemotherapy:

Chemotherapy was also administered in both intramuscular and subcutaneous injections. For intramuscular injection, the most suitable needle should be chosen based on the length of the needle needed to enter the muscle (but not any farther) and the bore (which should be as large as possible to minimize the pressure at which the injection is delivered). When administering medications by subcutaneous injection, caution should be given to ensure the smallest acceptable needle is used and positioned appropriately. Apply the injection at a 45-degree angle to the skin's surface using the pinch method. To reduce discomfort, injection locations should be alternated (Ballantine, 2018).

2.4.4. Chemotherapy into the artery:

Many malignant tumors, including those of the liver, pancreas, kidney, lung, cervix, and breast, can be treated preoperatively with intra-arterial CT (with embolization). In fact, after using this technique on the malignancies listed above, improved efficacies were seen. However, primary rectal cancer reports are uncommon. The route of administration of oxaliplatin in rectal cancer is intended to be altered since it is the most popular CT agent for trans-arterial chemoembolization (TACE) in liver cancer (Meng, et al., 2021).

2.4.5. Chemotherapy into the peritoneum or abdomen:

The anticancer efficacy of intraperitoneal chemotherapy (IPC) is considerably limited since the penetration of chemotherapeutic medicines into peritoneal tumor nodules is much below 1 mm. To increase medicine availability within these tumor nodules, several initiatives have been tried. Two physical principles utilized in IPC; hyperthermia and intraperitoneal pressure;

have, to some extent, enhanced medication penetration into tumor tissue. A Peritoneal metastases (PM) treatment based on the idea of hyperthermia is hyper-thermic intraperitoneal chemotherapy (HIPEC) in assistance with cytoreductive operation. On the other hand, a therapy for more advanced PM called pressurized intraperitoneal aerosol chemotherapy (PIPAC) uses the idea of pressure (lau, et al., 2020).

2.4.6. Topical chemotherapy:

In a region where some tumors are present, topical CT is applied directly to the skin. A cream, gel, or ointment can be used for topical CT. Skin-applied CT agents are just as potent as other types of CT. Many are also regarded as dangerous. When using topical CT, make careful to be aware of the safety measures that must be followed when handling, storing, and discarding the tube or container it comes in. Additionally, safety measures must be taken while applying it to the skin, such as donning protective gloves. The type of cancer the patient has, the intended outcomes of the treatment, the medications being used, and how the body reacts to them all determine how frequently the patient receives topical CT and how long the treatment lasts (The American Cancer Society, 2019).

2.5. Side effects of chemotherapy:

2.5.1. Neutropenia (low levels of white blood cells/immune cells):

Immunosuppression is the term for a decreased level of immunity. Some people may develop immunosuppression as a result of specific illnesses, such as cancer, and specific treatments, such as CT and RT. Having a low white blood cell count is the common term for this. A lower than usual level of neutrophils is known as neutropenia (a type of white blood cells). The immune system includes white blood cells. Neutrophils play a critical role in the body's fight against the majority of infections. Neutrophils typically make up the majority of white blood cells. Neutropenia in patients with cancer is typically

brought on by therapy. Doctors use the patient's neutrophil count when assessing the likelihood of infection (The American Cancer Society, 2020).

2.5.2. Anemia (low levels of red blood cells):

Is a disorder in the blood, which is important and vital liquid that veins and arteries carried it. About five to six quarts of blood make up the body, and the heart continually pumps blood throughout it. Blood delivers nourishment, oxygen, and other vital substances. Additionally, it aids in controlling body temperature, fights illness, and eliminates waste. The body does not have enough red blood cells when it has anemia. One of the three primary categories of blood cells is red blood cells (RBCs). Hemoglobin, a protein found in them, transports oxygen throughout the body. The body does not receive all the oxygen it requires when the patient does not have enough RBCs or when the level of hemoglobin in the blood is low (National Institute of Health, 2011).

2.5.3. Thrombocytopenia (low levels of platelets):

Primary immune thrombocytopenia (ITP) is a persistent isolated low platelet count (100*109/L) autoimmune illness brought on by a loss of immunological system homeostasis that tilts the scales in favor of autoimmunity. The pathophysiology of ITP has been much study over the past few years; however, this area is still not fully understood. Another noteworthy aspect of ITP is the variability of individuals' clinical profiles and treatment responses, with only a small percentage of patients being categorized as refractory. This variability is probably caused by the involvement of many pathophysiological contributing processes, each of which affects individuals to varying degrees (Lev, et al., 2020).

2.5.4. Hair Loss:

A fairly frequent clinical problem that is frequently accompanied by considerable emotional anguish is hair loss. Establishing whether the hair density is normal or reduced is the first stage in making the right diagnosis of a

patient with hair loss. The hair loss must next be assessed for severity (pull test) and examined under a microscope to determine if it is occurring during the anagen or telogen phases of the hair cycle. Hair shaft creation and resting alternate, make this a cyclical process (anagen, catagen, and telogen) (Tosti, et al., 2009).

2.5.5. Nausea and vomiting:

Up to 40% of patients with cancer have the crippling side effect of chemotherapy-induced nausea and vomiting (CINV). The most dreaded adverse reactions of CT for patients are nausea and vomiting, which are also the most frequent. CINV is still a problem for many individuals despite the availability of new antiemetic medications. To increase patient comfort and treatment compliance, medical providers should be aware of CINV and be proactive in managing the symptoms. Contrary to what medical practitioners believe, CT side effects are experienced quite differently by patients, leading to ineffective management (Gupta, et al., 2021).

2.5.6. Diarrhea or constipation:

Although cytotoxic side effects are a substantial barrier that significantly hinders the clinical implementation of otherwise promising medicines, CT has significantly increased overall survival in many kinds of cancer. In addition to delaying, adjusting, and stopping therapy, gastrointestinal (GI) adverse reactions such, vomiting, ulcers formation, nausea, decreased or increased bowel movement, and distention in particular have a great negative effect on many cancer patients' quality of life. Additionally, bouts of persistent constipation and diarrhea that occur after treatment among survivors from cancer have been reported to take up ten years after the end of therapy, with rates as high as 49 percent (McQuade, et al., 2016).

2.5.7. Pain:

Pain is an unneeded emotional and sensory experience that is related to, or comes along with present or prospective tissue damage. The most frequent sensation that patients report is pain, and patient worry is a sort of warning indicator. It is a visual and sensory experience that results in emotional distress and hazards associated with worry. The way each person experiences pain is quite unique and might change from time to time even within the same person. Measurement of pain intensity is challenging, as a person's perception of pain is influenced by their emotional state, the circumstances of how they got their pain, and whether they see it as a warning sign (Świeboda, et al., 2013).

2.6. Oral mucositis:

2.6.1. Overview of oral mucositis:

One of the common frequent and dangerous side effects of cancer therapies is OM. Areas of the oral and oropharyngeal mucosa are included in the treatment field in practically all patients who undergo RT. It has only been the last 20 years or so that the intricate pathobiology of OM has completely been understood, despite the introduction of CT in 1940 and its long clinical legacy. Despite having a long clinical history, the complicated pathobiology of OM has only recently been completely understood. Predicting toxicity risk and tailoring toxicity therapies for genetically eligible people is the key problem (Shankar, et al., 2017).

Oral mucositis, also known as stomatitis, is an inflammatory and degenerative illness that affects the lining of the mucous membrane in the oral cavity. It practically constitutes an unavoidable side effect of high dosage RT. The type of cancer being treated will largely determine the oral will be impacted. OM can develop in patients undergoing bone marrow transplants in addition to being brought on by CT and RT (Ahmad, et al., 2019).

Oral mucosa inflammation brought on by RT (found in 80 percent of treated patients), CT (found in 40-80 percent of treated patients), and bone marrow transplantation (found in over 75 percent of patients) was first referred to as "mucositis" in late 1980. The condition was thought to be a symptom of leukopenia . OM is currently regarded as the most significant non-hematological adverse effect of cancer treatment (Chaveli-López and Bagán-Sebastián, 2016).

The status of the oral cavity, dental health, and patient well-being can all be directly impacted by cancer and its therapies, with the potential to result in severe short-term as well as long-term physical, psychological, and social issues. OM can place a considerable strain on an individual's health and place a significant demand on medical resources (Thomson, et al., 2015).

Confluent, profound, and excruciatingly painful ulcerations of the oral mucosa are how OM manifests in its most severe clinical form. OM has a clinical continuum, nevertheless, like most illnesses do. When OM is in its early stages or in its mildest form, it manifests as mucosal erythema and is accompanied by a burning sensation similar to that experienced after being burned by hot food (Shankar, et al, 2017).

Oral mucositis can have such negative effects that CT dosage reductions, radiation breaks, the use of painkillers, hospitalization, and morbidity may be necessary. Most medical experts may not fully understand the clinical implications of OM, however those who report OM do not share this opinion (Vahanwala and Pagare, 2010).

2.6.2. Pathogenesis of oral mucositis:

The development of OM involves many phases. The initial damage caused to cells by RT and CT can occur directly through DNA damage or, more frequently, indirectly through reactive oxygen species. This is known as the initiation phase. This causes a cascade of enzyme and transcription factor

activations that ultimately culminate in the overexpression of genes encoding inflammatory cytokines including tumor necrosis factor alpha (TNF-), interleukin 1 beta (IL-1), and interleukin 6 beta (IL-6) that harm tissue by targeting the submucosa and basal epithelium. The ulceration and subsequent bacterial colonization that follow the ensuing inflammation and tissue damage perpetuate the vicious cycle of inflammatory cytokine-mediated harm. The extracellular matrix signals through the healing process' last stage, causing the mucosal barrier to be restored by epithelial growth (as shown in figure 2-1) (Georgiou, et al., 2012).

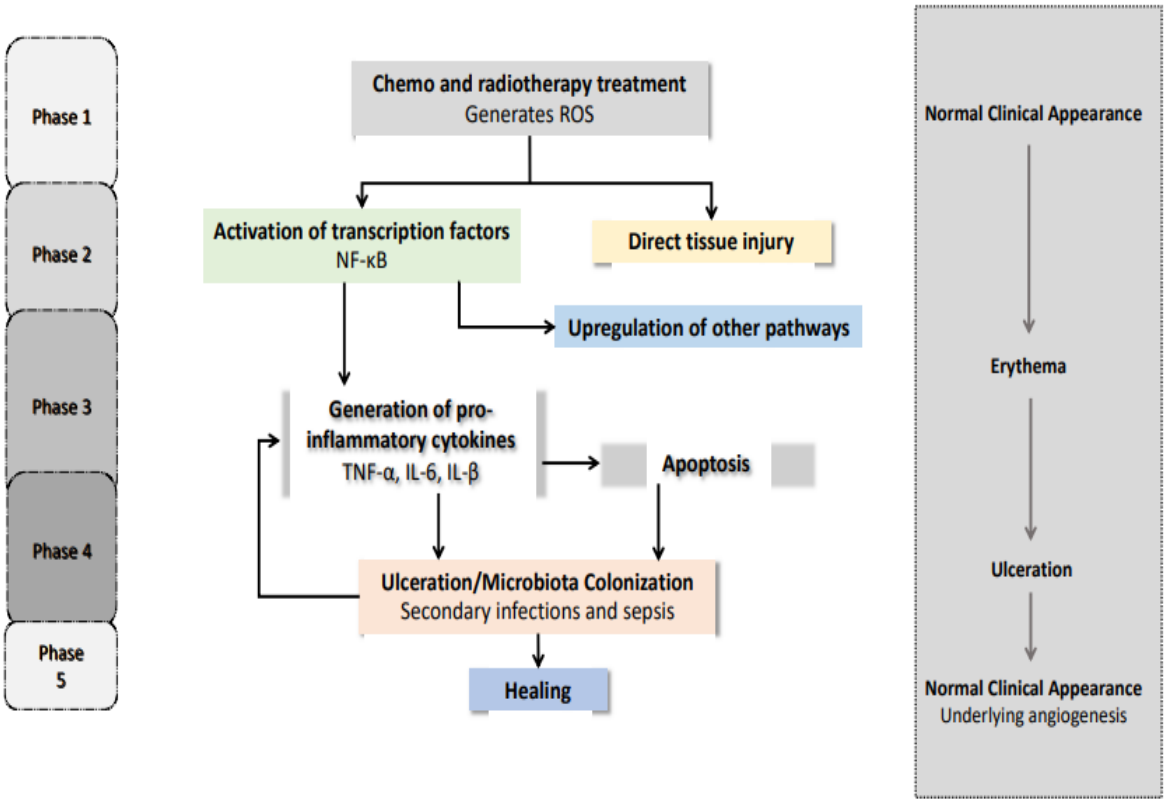


Figure (2-1): (Diagram representing the mucosal cells and clinical manifestations of oral mucositis) (Ferreira, et al., 2022).

2.6.3. Causes of oral mucositis:

The oral mucosal epithelium is destroyed and its growth is suppressed as a result of antineoplastic therapy, such as CT or RT, which is the primary cause of OM. The kind, length, and dosage of the CT being used have a great effect

on the frequency of oral cavity inflammation and the severity of it. This means that the risk of OM is between 60 and 100 percent with bone marrow suppressing (myeloablative) treatment, and approximately 100 percent with CT and RT combined (Alvariño-Martín and Sarrión-Pérez, 2014).

2.6.4. Symptoms of oral mucositis:

Oral mucosal atrophy, swelling, erythema and consequent discomfort, bleeding, ulceration, trouble eating and even swallowing saliva are just a few examples of the symptoms of OM. A patient's nutritional status declines as a result of eating difficulties since less food is consumed. Due to an uncomfortable dry mouth and a change in salivation, this can also have a significant impact on a person's ability to speak. Injuries brought on by bruxism, food, sharpened teeth, and microbes can further exacerbate OM. Additionally, systemic symptoms like fatigue and anorexia as well as psychosocial problems might be exacerbated by the dysphagia, xerostomia, and taste alterations brought on by OM (Ferreira, et al., 2022).

OM is distinguished by an inflammatory and toxic reactions that influence the GI tract outside of the mouth cavity and may clinically begin with edema and redness before developing into painful ulcers coated in fibrinous exudates (pseudo-membrane). The soft palate, jugal mucosa, floor of the mouth, lateral of the tongue, lower lip, and mouth are more commonly influenced, and the sores may be numerous and extensive. This wound exacerbates the risk of serious side effects for the patient, including a higher risk of systemic infections, severe odynophagia, excruciating chewing pain, which frequently necessitates the use of opiates for pain reduction, nutrition by enteral or parenteral way, and therapy interruptions that may shorten the affected persons’ life or cause inflammation of oral cavity. The mucosal lining ulceration offers a good portal of entry for a wide variety of infectious organisms that forms the flora of the

oral cavity, which may cause sepsis and bacteremia, particularly in neutropenic patients (Spindola Antunes, et al., 2014).

2.6.5. Diagnosis of oral mucositis:

Prior to and throughout cancer treatment, it is crucial to accurately examine the oral mucosa. Both OM definition and the accurate, repeatable assessment of the intensity of the condition lack overall uniformity. To evaluate patients' overall oral health and function, a variety of assessment measures have been developed (Napenas, et al., 2007).

The World Health Organization (WHO) and the National Cancer Institute-Common Toxicity Criteria (NCI-CTC) scales are the two rating systems that are most frequently used for both clinical and research reasons. Both ratings take into account the necessity for parenteral nourishment, subjective pain perception, and objective clinical findings. The WHO oral toxicity scale ranges from 0-4 (from the least to the most severity), while the NCI-CTC scale ranges from 1-4 (Napenas, et al., 2007).

In spite of their easy to utilization , both scales have a distinguished disadvantage of being inaccurate in terms of involvement extent (entire buccal mucosa versus isolated patch), causes of objective results (candidiasis or herpes versus CT or RT-induced), and subjective claims (difficulty eating due to dryness versus due to pain) (Napenas, et al., 2007).

2.6.6. Stages of oral mucositis:

The damage to oral mucosal cells brought on by CT and/or RT is what is referred to as the OM starting phase. As soon as the antineoplastic medication is given, this phase starts right away. The second stage-upregulation with messenger generation-involves the cytotoxic impact, which causes DNA damage and reactive oxygen and nitrogen species (ROS and RNS, respectively) production, which kills basal and supra-basal epithelial cells. Transcriptional factor activation causes connective tissue and endothelial damage, restricting

tissue oxygenation and inducing epithelial basal cell death. Tissue damage, apoptosis, enzyme activation, and vascular permeability all contribute to the third phase, signaling and amplification, which amplifies innate immune response molecules as pro-inflammatory cytokines through a positive feedback system, causing more tissue damage. As the mucosa and submucosa's integrity is compromised during the fourth phase of ulceration, clinical indications of OM become evident, necessitating the use of painkillers (Ferreira, et al., 2022).

2.6.7. Management of oral mucositis:

For both preventive effects and treatment of OM, a wide variety of therapies have been explored and tested. The International Society of Oral Oncology (ISOO) and the Multinational Association for Supportive Care in Cancer (MASCC) Mucositis Study Group established practical guidelines for the inhibition and management of OM (Al-Rudayni, et al., 2021).

Oncologists employ a variety of tactics, including as dosage reduction and other therapeutic and preventative measures, to lessen the side effects of anticancer treatment, despite the fact that oral mucositis' complicated biological makeup makes management difficult. For OM brought on by CT, there are several therapeutic options (Chaveli-López and Bagán-Sebastián, 2016).

It is necessary to notify and motivate all patients receiving CT to practice excellent dental hygiene. Prior to starting treatment, patients with cancer of the head and neck and those taking high doses of CT should be referred for a dental evaluation. A nurse or other caregiver can help patients who are unable to do their own dental hygiene. Saline irrigation of the mouth is possible both with and without suction. It is important to promote a balanced diet and enough oral fluid consumption. Look for signs of an oral infection in the patient, and if so, make sure an anti-infective is provided (Thomson, et al., 2015).

2.7. Non-herbal management of oral mucositis:

2.7.1. Cryotherapy (OC):

Oral cryotherapy (oral chilling) is a common method for treating OM since it is low-cost, easy to administer, and unlikely to have any negative side effects. The treatment is putting any kind of ice in the mouth, including chips, cubes, and ice-cold water, either before or during CT administration. A blood perfusion minimization to the tissues of oral mucosa as a result of localized temperature reduction in the oral cavity will result in blood vessels constriction of oral mucous membrane, which will lower the circulating cytotoxic chemicals concentrations in the oral mucous membrane. Additionally, oral chilling can slow down the metabolism of oral epithelium, which may help to lessen the likelihood of inflammation (Al-Rudayni, et al., 2021).

2.7.2. Growth factors:

Growth factors are proteins that promote cellular division, growth, and proliferation. Target cell membranes include particular receptors that growth factors and cytokines bind to. Growth factors are crucial because they may influence a wide range of cellular functions that are crucial for the regeneration of tissues. The usage of growth factors can also help patients' bodies recover themselves more quickly. This class of medications appears to be the one attracting the most attention at the moment. The timing, dose, concentration, length of contact, or drug release in the oral environment all have a significant impact on the effectiveness of growth factors. In hematological tumors receiving high-dose CT and total body radiation prior to hematopoietic stem cell transplantation, growth factors are currently advised in the prevention of OM (Soni, et al., 2019).

2.7.3. Anti-inflammatory agents:

In radiation and CIOM, inflammation is thought to be a significant tissue response. TNF and IL-1, in particular, have been thought to take a crucial part

in the pathogenicity of OM. Studies have indicated that after cytotoxic CT, levels of nuclear factor kappa-B (NFkB) and cyclooxygenase-2 (COX-2) were considerably higher in the oral mucosa. As may be seen in the earlier MASCC/ISOO guideline papers on anti-inflammation medicines, suppression of these has therefore been addressed in controlling tumor therapy-induced OM. Anti-inflammatory drugs are used in the inhibition and management of OM according to the complete modernization of the MASCC/ISOO practical guidelines for OM (Ariyawardana, et al., 2019).

2.7.4. Antioxidants:

Radiotherapists, oncology specialist, , and other healthcare staff with an interest in this area have placed a high priority on research into the advantages and disadvantages of using antioxidants (AOX) drugs during antineoplastic therapy. The researchers discovered 280 studies, including observational studies and randomized clinical trials. After reviewing these researches, the scientists concluded that AOX supplementation decreased side effects and safeguarded healthy tissues. In patients with cancer, the drop in the levels of AOX and rise in oxidative stress (OS) can be seen even before the initiation of oncological treatment. Patients with cancer of the tongue and have plasma lipid peroxides levels, which are known signs of OS, were greatly increased in patients having cancer when compared with the patients of the controls (de Freitas Cuba, et al., 2015).

2.7.5. Normal saline solution mouth rinse:

Mild to moderate OM discomfort can be relieved with regular saline or sodium bicarbonate treatments. These mouthwashes with soda and salt are secure, affordable, and efficient in managing OM. Additionally, patients can prepare a home version of these treatments using 1 teaspoonful of food salt and 1 teaspoonful of baking soda in 1 teaspoonful of water. As often as every four hours can be spent using these mouthwashes. However, despite their

widespread use, therefore called magical oral rinses (which typically contain combinations of local analgesic, anti-histamines, and/or steroids) are not standard regarding the ingredients or ratios component and not more effective than normal rinses in decreasing the pain of OM (Brown and Gupta, 2020).

There are several studies that looked at how normal saline mouthwash affects OM prevention in a range of treatment groups. Results were contradictory and evidence levels were different. The majority of studies combined normal saline with additional therapies. Due to few and/or incompatible data, it is not possible to establish guidelines for the usage of normal saline mouth rinsing in the inhibition or management of OM in any group. The expert agreed that ordinary solution is a risk-free, smooth wash that can be beneficial for maintaining the hygiene of the oral cavity and patient's comfort (McGuire, et al., 2013).

Clinical practice guidelines for radiation-induced oral mucositis include oral rinse as one of the oral care procedures (OM). Typical saline mouthwashes maintain the wound's bed moisture and absorb drainage 4-6 times each day. A number of studies have demonstrated the efficacy of medicated mouth rinses in reducing the signs and symptoms of OM. The agent for moist dressings was suggested during the oral care skills session to be normal saline (0.9 percent). By helping to maintain a moist wound surface, wet dressings assist hemostasis to promote an ideal healing environment. The saline-wetted dressing will absorb or eliminate exudates, lessen discomfort, and increase safety (Huang, et al., 2018).

2.8. Herbal management of oral mucositis:

2.8.1. Effect of Aloe vera on oral mucositis:

Aloe vera (AV) is frequently used to treat a variety of skin conditions, including dermatitis brought on by radiation exposure and dry, burnt skin. It has been documented in the literature for more than 70 years that aloe vera may be

used to treat irritating contact dermatitis. According to certain studies, aloe vera can help prevent and heal OM and ulcers brought on by radiation. Aloe vera improved wound healing, according to preclinical studies, by decreasing platelet association and vasoconstriction at the site of the wound, boosting collagen production and oxygenation of the wound, removing free roots, metalloproteinase and collagenase inhibition, and macrophages stimulation. Additionally, through inhibiting cyclooxygenase, AV has many anti-inflammation characteristics (Aghamohamamdi and Hosseinimehr, 2016).

The Liliacea family includes AV (Aloe barbadensis Miller). As a natural medication, it is frequently utilized. By promoting oxygenation of the tissue, free roots removing, and collagen synthesis promotion, it can improve the healing process of the wound. It also inhibits the generation of free radicals and has antibacterial and antioxidant effects. Additionally, several studies have demonstrated the effectiveness of using AV topically to prevent OM brought by RT or CT. These investigations demonstrated that AV may be used to prevent CIOM since it can block the pathogenic mechanism of OM, is easily available, and is inexpensive (Alkhouli, et al., 2021).

2.8.2. Effect of Turmeric on oral mucositis:

Turmeric (Curcuma longa), a rhizomatous plant frequently used as a culinary spice and traditionally employed as a therapy for a number of ailments in eastern medicine, has been the topic of update researches in the recent years. Turmeric and curcumin, a polyphenol derived from the rhizome, have been shown to have anti-oxidation, analgesic, anti-inflammation, antiseptic, antibacterial, and anticarcinogenic properties. When administered as a cavity sealant, subgingival irrigator, tooth pain reliever, and therapy for aphthous and potentially cancerous lesions, turmeric's effects on the oral cavity showed promise (Normando, et al., 2019).

In south and southeast tropical Asia, the perennial herbal product turmeric (Curcuma longa), which is one of the ginger's family member, is greatly farmed. The most beneficial portion of the plant for both culinary and medicinal uses is the rhizome, commonly known as the "root" of this particular plant. Curcumin, which accounts for 2-5% of the spice turmeric, is the most active ingredient. Additionally, it has been claimed to have strong antioxidant properties and to provide both in-vivo and in-vitro radiation protection (Mansourian, et al., 2015).

2.8.3. Effect of chamomile on oral mucositis:

The chamomile plant, Chamomilla Recutita (CR), is native to Europe and has adapted to various areas of Asia and Latin America. It is commonly farmed all over the world. It is particularly prominent in the South and Southeast of Brazil and has been utilized for therapeutic reasons for many years. According to several research, patients who are taking CT and receiving RT for cancer of the head and neck as well as candidates for hematopoietic stem cell transplantation utilized mouthwashes containing chamomile extract with a concentration of one percent. Benefits were discovered, including decreased OM occurrence and severity, decreased discomfort, and xerostomia. As part of the pre-transplant regimen, participants in these trials underwent substantial doses of CT (da Silva, et al., 2021).

The plant chamomile (Chamomilla Recutita) is known for its ability to reduce inflammation. It has long been used to treat a variety of skin and mucosal inflammatory diseases. The anti-inflammatory, antifungal, and antibacterial components of chamomile extract include chamazulene, bisabolol oxides, alpha-bisabolol, spiroethers, and flavonoids. An in vitro preclinical investigation showed that chamomile has anti-inflammatory properties, which it does through inhibiting cyclooxygenase-2. In several clinical investigations,

chamomile extract was examined for toxicity and proved to be fully safe for mucosal surfaces (Elhadad, et al., 2022).

2.8.4. Effect of clove oil on oral mucositis:

Clove essential oil (CEO) (as shown in figure 2-2) is used topically for a number of health benefits. Eugenia caryophyllata Thunb [Myrtaceae] its bactericidal effects, fungicidal effects, antioxidation, anti-viral, anti-inflammation, and anti-neoplasm activities have been examined in scientific research using a range of model organisms. At concentrations as low as 0.03 percent, eugenol, the primary active ingredient in clove essential oil, showed cytotoxicity toward human fibroblasts and endothelial cells (Han and Parker, 2017).

Due to its strong analgesic and antibacterial properties, clove oil is a well-known treatment for toothaches. Additionally, it possesses potent antiviral and antioxidant properties. Clove oil's primary ingredient is eugenol (Devkota and Adhikari- Devkota, 2020).

Many cases of CIOM were treated with an herbal mouth rinses-based on clove oil. Several studies have found that the chemicals in herbal mouth rinses-based on clove oil had anti-inflammation characteristics in both setting of working within or outside the living organism (Kong, et al., 2016).

Figure (2-2): (clove oil)

Among the different fruits, vegetables, and edible plants, clove buds (Syzygium aromaticum L.) (as shown in figure 2-3), a common household spice, are one of the greatest sources of antioxidant polyphenols. Preclinical research on Clovinol has already shown that it has both anti-inflammatory and anti-ulcerogenic properties, and that it also significantly increases the levels of stomach mucus and antioxidant defense enzymes. Additionally, repeated doses of acute (28 days), chronic (90 days) (Mammen, et al., 2018).

Figure (2-3): (clove buds) (Britannica, 2022)

The biological effects of clove oil include antiseptic, aphrodisiac, antiviral, antifungal, insecticide, antioxidant, and antibacterial activity against microorganisms. Additionally, clove oil has many other uses, including the treatment of bronchitis, cough, fever, and sore throats. Asthma and other allergy conditions have reportedly been treated with Syzygium aromaticum when taken orally. The high eugenol concentration of clove bud oil contributed to its antibacterial properties. Water distillation, steam distillation, and Soxhlet extraction are three methods for obtaining essential oils. Although it is not costly, this procedure can result in chemicals that are hydrolyzed, thermally degraded, or water-soluble (Sulistyoningrum, et al., 2017).

Clove oil was used to treat irritation of the stomach, difficulty digestion, vomiting, nausea, and abdominal distention and has aromatic, stimulating, and carminative qualities. Phenylpropanoids, sesquiterpenoids, tannins, and triterpenoids are the primary chemical components of cloves. Clove extracts have demonstrated a range of biological actions, including fungicidal effects, bactericidal effects, antitumor, antioxidation, antiviruses, and anticonvulsant characteristics. One of the most often utilized processed products of clove is CEO. It has a long history of usage as an analgesic and antiseptic in dental treatment to treat toothaches. Rubefacient, carminative, and antispasmodic properties are all present in clove oil. The oil has a distinctive flavor and taste, and it is a light-yellow liquid. Eugenol is the essential compound of clove oil. Eugenol content in clove oil has been shown to differ from about 45 percent to almost 90 percent in varied studies (Devkota and Adhikari-Devkota, 2020).

Clove buds must be extracted in order to acquire the essential oil, which has a therapeutic effect. Numerous studies have investigated the medical uses of clove, including its use in dental care and effectiveness against numerous different bacteria, including Eschericia coli, as well as its antifungal, anticarcinogenic, antiallergic, and antimutagenic properties. Eugenol is

essentially the main chemical in clove oil. Eugenol has antioxidant and insecticidal properties that are beneficial (Ratri, et al., 2020).

One may consider clove to be the most effective antioxidant there is. One drop of clove oil may have about 400 times more antioxidant potential per unit than blueberries or wolfberries. The therapeutic properties of clove are strong, and it has a long tradition and history. Benefits of clove are for mental, emotional, and physical health. Clove has anti-inflammatory, anesthetic, pain-relieving, antiviral, antifungal, antiviral, antimicrobial, anti-diabetic, antithrombotic, and antibacterial effects. One of mother nature's most potent antiseptics is cloves. The primary ingredient responsible for the therapeutic benefits of clove buds is eugenol (Nivetha, et al., 2014).

2.9. Theoretical framework:

Parker and Smith, (2010) described the theory that fall with the present thesis topic which is (Hall's Care, Cure, and Core Model). Three aspects were enumerated by Hall and these aspects including the person as patient: the person, the body, and the illness. She was representing these three aspects as crossed circles of care, core, and cure that affect each other. Everyone in the health professions either neglects or takes into consideration any or all of these, but each profession, to be a profession, must have an exclusive area of expertness with which it practices, creates new practices, new theories, and introduces newcomers to its practice.

September 21, 1906 was the date of born of theorist Lydia Eloise Williams Hall in New York City. Hall's father was a general practice doctor and she was the first child of her family and was named after her maternal grandmother. Hall's family travel to York, Pennsylvania at a young age. In 1927, Lydia Hall completed the diploma degree in nursing from Hospital School of Nursing in York. After that she got a Bachelor degree of science in public health nursing from the Teacher's College at Columbia University in

New York in 1932 because of her feeling that she needs more education. Also, many years later in practical work, she continued her learning and got a degree of master in the sciences in teaching of natural life from Columbia University in 1942. Finally, she completed all requirements of doctorate degree except the dissertation (Gonzalo, 2019).

According to Hall, pathology and therapy are the purview of medicine. Psychiatry, social work, and the ministry are just a few of the professions that, in Hall's opinion, have gravely ignored the realm of the person. She perceived nursing's area of competence to be the body as a whole, as well as being impacted by the other two domains. Hall made it very apparent that the primary goal of nursing is to provide private body care. This is recognized by the public as entirely related to nursing, as she thought. A skilled nurse will be able to adapt the patient's care based on the pathology and the therapy while taking into account their individual requirements and personalities. Hall developed her definition of nursing as having three components based on her understanding of the patient, and she distinguished between the areas that fall within the exclusive purview of nursing and those that are participated by other health care professions (Parker and Smith, 2010).

2.9.1. Hall’s three aspects of nursing:

Parker and Smith, (2010) reported that the three aspects of Hall’s model are including the Care, Cure, and Core. The cure circle is the biggest during the acute care stage. The care circle predominates during the assessment and follow-up step. The Care, Core, and Cure Model is Hall's conceptualization of nursing (Figure 2-4).

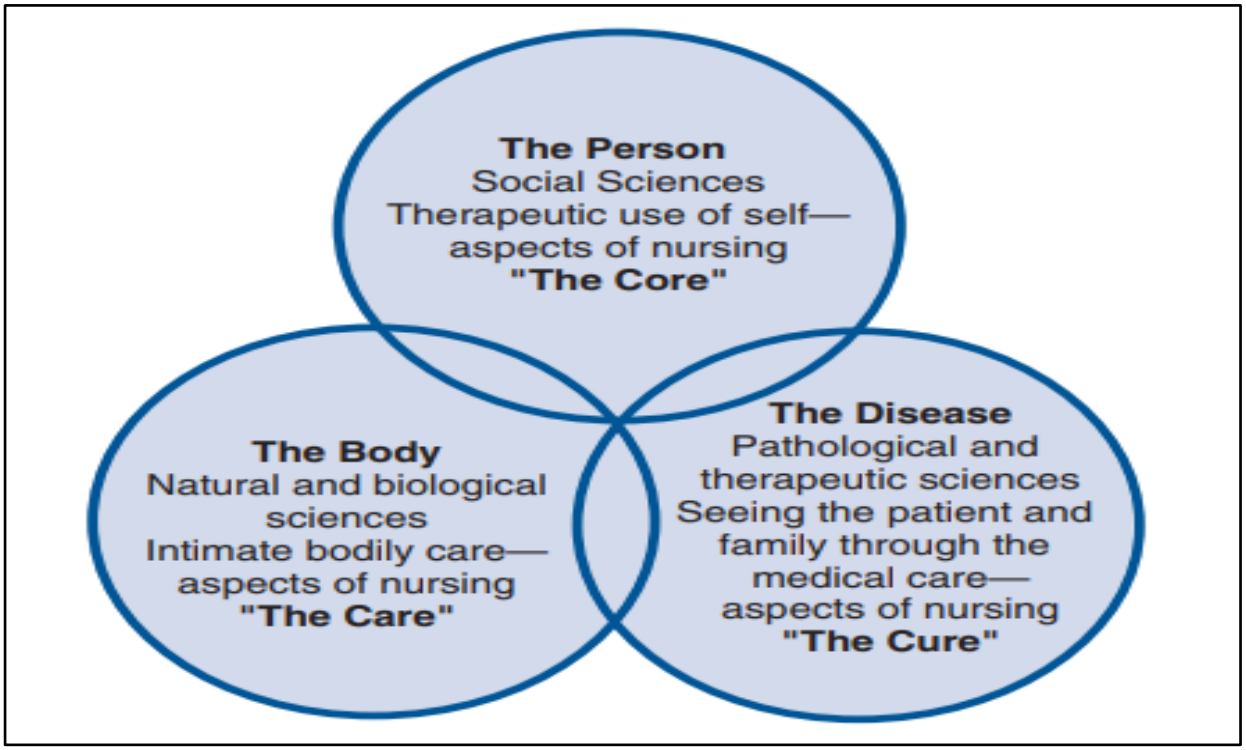


Figure (2-4): (Hall's Care, Cure, and Core Model) (Parker and Smith, 2010).

Care:

The care represents patients' bodies and reflects the aspect of nursing that involves physical care. It is associated with nurses' role in providing comprehensive care, which encompasses attitudes and actions, such as providing for patients' physical and psychological needs, being attentive, getting to know the patient, taking time, being firm, showing respect and providing the extra touch. It also defines the role of professional nurses to support basic daily human needs such as eating, bathing and elimination (Sumarno, 2019).

Cure:

The "cure" is the name given to the second stage of the nursing process, which is partake with medicine. According to Hall (1958), this medical side of nursing profession can be understood as either the nurse aiding the physician by doing medical functions/ tasks or as the nurse providing the patient with comfort and nurturing care throughout his or her medical, surgical, and rehabilitative

treatment. Hall believed that the nursing profession was taking on an increasing amount of the medical components of care while handing off the nurturing aspect of nursing to less qualified individuals (Parker and Smith, 2010).

Core:

It is the patients who receive nursing care. This dimension consists of goals; reflecting feelings and values; that have been set by the patient, rather than by any other person involved in the care process. By using effective communication, nurses are encouraged to recognize patients' goals, including social, biological, spiritual and psychological elements. The core also refers to the emotional, spiritual and intellectual needs of the patient, which are associated with family and the community (Sumarno, 2019).

2.9.2. Assumptions of Hall's Care, Cure, and Core theory:

According to Priyadarshini, (2021) represents that the major assumptions of this model are as follow:

1. The patient has the source for the energy and motivation necessary for health and healing not the team of the healthcare.
2. The nursing three aspects should be showed as having interrelated functions and not as independent working.
3. Finally, depending on the patient's progress course, the three aspects of nursing interact, and the size of the circles that representing them change.

2.9.3. The practical application of theory in the present study:

- **Care:** The researcher assisted the patients to manage OM through implementing mouth care interventional protocol using either clove oil or normal saline solution gargling procedures for seven days to help in improving OM level and reducing oral toxicity grade.
- **Cure:** The researcher solved the patients' problems including level of OM and grade of oral toxicity through the application of an interventional

protocol for mouth care using clove oil and normal saline solution gargling procedures. Thus, degree of oral toxicity was decreased and level of OM was relieved and enhanced.

- **Core:** The patients that diagnosed with cancer who undergoing CT and were confirmed to have OM as a severe adverse effect of CT administration.

2.10. Previous studies:

First study: Gupta and Prakash, (2021) performed a study in India to do a comparison study of clove oil and clove extract on the micro-biota of oral cavity causing dental caries and also to evaluate the fungicidal activity. The antimicrobial properties of clove oil and clove extract was evaluated against Halobacterium sp., Lactobacillus sp., Pseudomonas sp., Micrococcus sp. and Streptococcus mutans (main causative bacteria of dental plaque) by the paper disc diffusion method. For each extract three replicate experiences were conducted against each organism. The fugicidal activity of clove oil and extract was also evaluated against seven fungal species (Aspergillus niger, A. fumigatus, Aspergillus sp., Alternaria sp., Rhizomucor sp., Rhizopus sp. and Penicillium sp.) by agar disc diffusion method. Clove oil offers strong bactericidal activity against oral cavity microorganisms. The highest inhibition zone of diameter was seen by clove oil as compared to clove extract against the test fungal species. The clove oil has the potential to be used as a normal bactericidal agent for oral cavity microorganisms. The clove oil was potent against both Gram positive and Gram-negative bacteria.

Second study: Naibaho et al., (2020) performed a study in Indonesia to determine the effects of oral care using normal saline solution and baking soda regarding pain and comfort in patients with OM who undergoing CT. This is a quasi-experiment pre-posttest design with a control group. Pain measurement was performed using the Numeric Rating Scale (NRS) while the

comfort measurement was done by using the Daily Comfort Scale (DCS). The technique of sampling that was used is consecutive sampling. The sample was 40 divided into two groups. the results of this study used the Paired sample t-test in the intervention group pre and post management revealed a great difference in the comfort and intensity of pain. In the control group there were also great differences in the comfort and intensity of pain. Based on the Independent t-test, there was a great difference in pain and comfort after gargling using normal saline solution. The findings of this study showed that gargling using normal saline solution is potent in decreasing OM pain and enhancing the comfort of patients undergoing CT.

Third study: Kong, et al., (2016) performed a study in Republic of Korea to assess the effects and safety of herbal mouthwash-based on clove oil in enhancing radiation-induced OM in patients with cancer of the head and neck. Fourteen patients were involved in this study and randomized to either an interventional group or a control group. The patients of the interventional group rinsed their oral cavity with herbal mouthwash-based on clove oil during RT, while the patients of the control group rinsed with clear water. The evaluation of patients' pain within the RT field was assessed with a 10 cm visual analog scale every day, and the weight of the body was also checked every week from the beginning of RT to eight weeks after its completion. The use of herbal mouthwash-based on clove oil decreased the duration of grade 2 OM compared with clear water. The use of herbal mouthwash-based on clove oil also decreased the incidence of grade 3 OM, and minimized the duration of grade 3 OM. In addition, herbal mouthwash-based on clove oil delayed the time to onset of OM. This single blind randomized study revealed that herbal mouthwash-based on clove oil can have a possibly beneficial influences on decreasing or preventing radiation-induced OM in patients with cancer of the head and neck.

Fourth study: Agrawal, et al., (2014) performed a study in India to investigate that plant or natural product medicine is becoming more and more general as a safe and potent means of management for many various medical conditions. Plants are often preferable because they are natural and do not leave harmful chemicals in the body. The clove oil antimicrobial activity proposes its usage as an assistance to oral cavity therapy. Oral intake of clove oil inhibits the overgrowth of C. albicans in the GI tract including the oral cavity. It acts as an antioxidant and anti-inflammation agent at low concentration, whereas at higher concentrations it acts as a pro-oxidant resulting from the promoted generation of tissue destroying free roots. Clove oil assists in the minimization of amount of plaque deposition on oral hard tissues. Clove oil is a medicinally essential herbal medication, reported to have a wide variety of various actions like antioxidation, fungicidal, antiviral, antibacterial effects, anti-inflammation, antithrombic, antipyretic, anesthetic, anticonvulsant, antimycotic, insecticidal, antimutagenic, antiulcerogenic. The oil is used for managing a different health problem including pain of the teeth, indigestion, cough, asthma, pain in the head, stress, and blood problems. There is a wide scope for researchers to develop potent and effective formulations using clove oil.

Fifth study: McGuire, et al., (2013) performed a study to investigate research in essential oral care interventions to update evidence-based practical guidelines for inhibition and managing OM in patients with cancer undergoing RT or CT. An available studies systematic review was conducted by the essential mouth care part of the OM study group of MASCC/ISOO. Seven interventions including: oral care protocols, dental care, normal saline solution, sodium bicarbonate, mixed medication mouth-rinse, chlorhexidine, and calcium phosphate were assessed. Fifty-two generalized papers were investigated by treatment population (RT, CT, and hematopoietic stem cell transplant) and by whether the management aimed to inhibit or manage OM. The evidence for

essential mouth care interventions encourages the utilization of mouth care protocols in patients receiving RT and/or CT. Nine studies were located that investigated the impact of normal saline solution mouth-rinses on inhibition of OM across different treatments. Many studies used normal saline solution in conjunction with other medications, and studies using normal saline solution alone did not show obvious benefit. Therefore, normal saline is un-hurt soft rinse that can be beneficial for oral cavity hygiene maintenance and comfort of the patients.

2.11. Literature synthesis:

From reviewing the previous studies, it is evidenced that OM management can be successful and effective when using herbal and natural product like clove oil. It was found that clove oil has a strong antiseptic, antifungal, antibacterial, antioxidant, and antiviral properties which make it effective in minimizing the intensity of OM and enhancing OM level when it used regularly as an oral care protocol in patients with cancer who receiving CT or RT. Also, from this studies revision, it was found that normal saline solution is effective in improving OM level and provide comfort for patient who suffer from OM when it used as mouthwash. Furthermore, both clove oil and normal saline solution are cost-effective and can be used by patients topically and safely compared with other medications used for OM management.

Chapter Three "Materials and Methods"

Chapter Three

Materials and Methods

Chapter three represents the form of research design, selection of samples, construction of interventional protocol, construct research instrument, pilot study, and methods that used in data collection and analysis.

3.1. The study design:

A true-experimental design was used in the present study. It was used to identify the effect of using clove oil versus normal saline solution in the management of OM in patients with cancer undergoing CT. This study was initiated from 20th October 2021 to 20th August 2022.

3.2. Administrative arrangements:

In order to initiate the present study in a formal manner, an official request must be submitted to the official authorities concerned in this field. Therefore, a formal administrative request had been submitted to College of Nursing, University of Kerbala, Imam Al-Hussein Oncology Center, and Imam Al-Hassan Al-Mujtaba teaching hospital. These official permissions were obtained as follow:

A. Official permission from Nursing College Council/University of Kerbala at (30 December 2021) (Appendix A-I).
B. Official permission from Iraqi Ministry of Health/ Training and Human Development Center/ Kerbala Health Department at (10th February 2022) (Appendix A-II).
C. Official permission from Iraqi Ministry of Health/ Kerbala Health Department/ Imam Al-Hussein Oncology Center and Imam Al-Hassan AL-Mujtaba teaching hospital at (21 November 2021) and (10th February 2022) (Appendix A-III).

D. Official permission for safety usage of clove oil liquid on human being from Iraqi Ministry of Health/ Registered Health Products at (30 November 2014) (Appendix A-IV).

3.3. Ethical considerations:

Before conducting the study, the researcher obtained the approval for the ethical committee in Collage of Nursing agreement to conduct the present study (Appendix B-I). Permission was obtained from Imam Al-Hussein Oncology Center and Imam Al-Hassan Al-Mujtaba teaching hospital, then completely explaining the study details to all patients and after that obtaining verbal and written consent from them (Appendix B-II).

3.4. Setting of the study:

The study was conducted at Imam Al-Hussein Oncology Center which is located in Kerbala Holy City and was established in 2015 and the capacity of it includes about more than 80 beds. The center includes 11 specialized oncologist, 35 pharmacists with good experience in their field, 40 nursing staff, and 15 health staff. Furthermore, the center receives its patients from inside and outside Kerbala Holy City, with a daily rate of no less than 250 patients received CT in the center. Moreover, this study was conducted in the oncology wards of Imam Al-Hassan Al-Mujtaba teaching hospital which is also located in Kerbala Governorate and was established in 2020 and the capacity of it includes 492 beds. This hospital has received more than 50,000 patients since its establishment until today, also it consists of two oncology consultant clinics, nuclear medicine clinic, and CT and RT wards for patients with cancer.

3.5. Sample size:

The selected sample size was 30 patients divided into three groups. There were 10 patients each for the control and the two experimental groups. The sample was selected in systematic random sampling method. A list was arranged for all members' inclusion population. The process involved choosing

each individual to list, using a randomly selected starting point that was number two. The number and size of elements in the population were determined by the required sample. Then, the size of the population was divided through the desired size of the sample, k was given to the size of the distance between the selected items from the list. The size of access population was N = 72 and the required sample size is n = 30, the value of k will be: according to the following equation K= 72÷30= 2.4 ≈ 2. Thus k = 2, that means of every 2nd person in the list was including in the sample. The equation was calculated according to Gray, et al., (2016). Also, the researcher was excluded from selecting the elements of the sample to prevent the occurrence of any bias during the selection process and to give strength to the research, thus the task of selection was assigned to another person.

3.6. Sample of the study:

A probability (Systematic random) sample consists of 30 patients selected from patients with cancer who are undergoing CT and was confirmed by the researcher with OM and who were treated in Imam Al-Hussein Oncology Center and oncology wards of Imam Al-Hassan Al-Mujtaba teaching hospital in Kerbala Governorate. A ten patients were enrolled as a control group, ten patients were assigned to the experimental group by using clove oil and ten patients were assigned to the experimental group by using normal saline solution. The two study groups participants were exposed to an interventional protocol (applying clove oil for seven days and applying normal saline solution in the same time). The randomized distribution of study samples was achieved by using a randomized list to ensure an equitable distribution of eligible patients in each of the study groups. The allocation was performed by a strange examiner to ensure bias absence in the distribution.

The selection criteria of sampling method were established as follow:

3.6.1. Inclusion criteria of the sample:

1. Male and female patients with a medical diagnosis of cancer that are confirmed by researcher to have OM as a result of CT in the oncology units.
2. Patients with oral cavity swabs reveal positive bacterial or fungal infection related to OM.
3. Patients who accept to participate and willing to follow the treatment until the end of the study.
4. Patients with all levels of education.
5. Patients with age (18 to 60) years old.

3.6.2. Exclusion criteria of the sample:

1. Patients who was refused participate in the study.
2. Patients who was not continuing CT.
3. Participants of the pilot study.
4. Patients who was not continuing the intervention protocol because of death.
5. Poor mouth hygiene patients or those with unhealed wounds in the oral cavity or oropharynx, who their swabs reveal no infection related to oral mucositis.

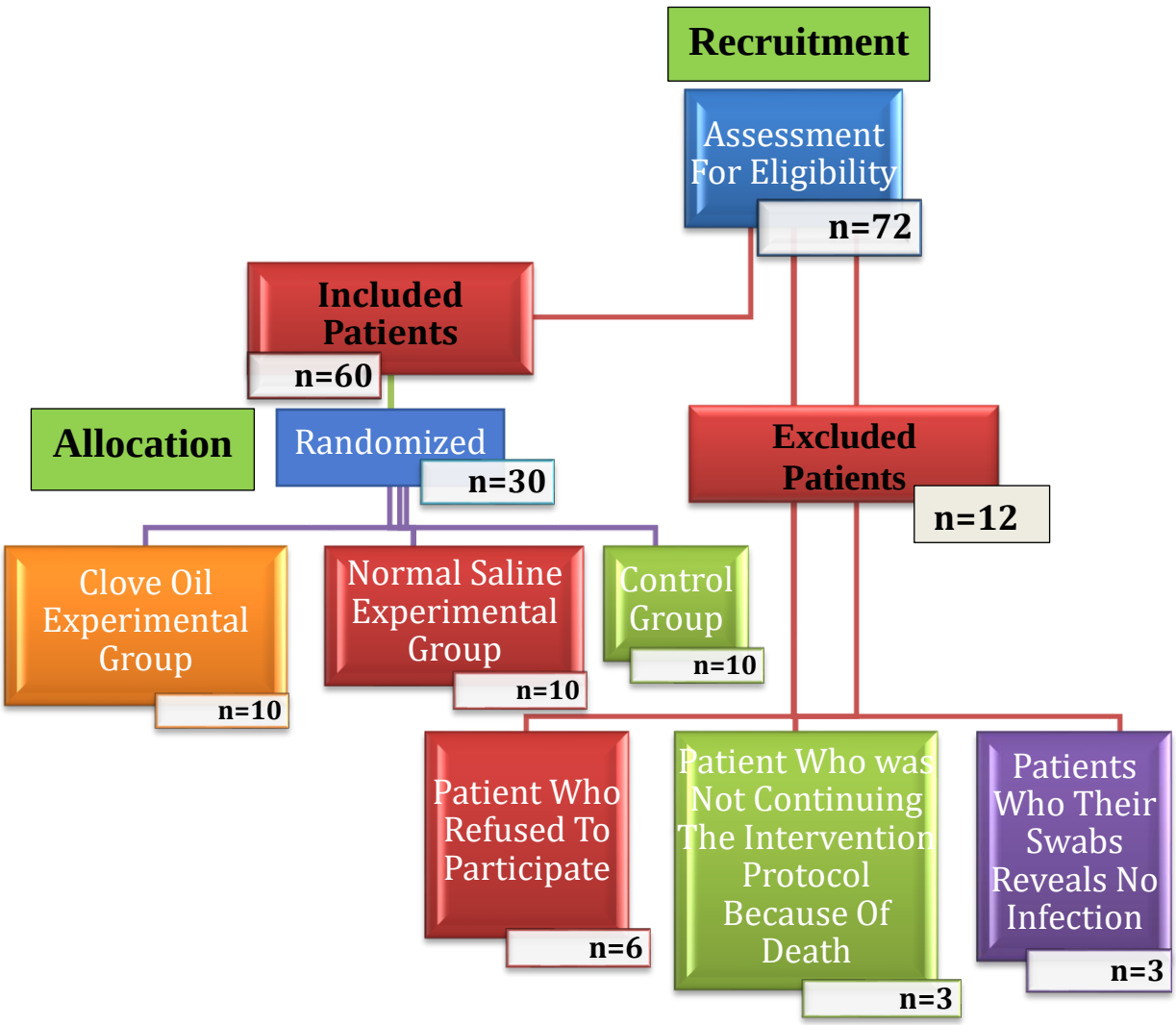


Figure (3-1): (Flowchart of the randomized controlled trial & eligibility criteria)

3.7. Steps of the study:

This study is done according to following steps:

3.7.1. Interventional protocol:

This interventional protocol was made after reviewing scientific references and previous studies, in addition to the researcher's experience in the direction of caring for patients with OM patients undergoing CT. This interventional protocol is designed to include how to relieve the severity and

facilitate the healing process of OM by using clove oil and otherwise using normal saline solution to perform the same purpose. Therefore, this interventional protocol includes two basic procedures (clove oil and normal saline solution), as the patients were divided into two interventional groups, the first measurement was made for each of them, and then they were subjected to the intervention for seven days, and then the second measurement was made to determine the effect of the interventional protocol towards levels and stage of OM.

3.7.2. Preparation of swabs and cultivation procedure:

Oral swab was taken from all patients in each of the three groups (clove oil group, normal saline solution group, and control group) before starting interventional protocol in order to confirm OM by the presence of bacterial or fungal infection that related to it (Appendix C-I).

Taking into consideration that the financial cost of oral cavity swabs materials and swabs cultivation in the laboratory were fully tolerated by the researchers in order to reduce the financial burdens that may negatively affect patients or they cannot afford it.

The swabs were taken by the researchers according to a standardized procedure. Swabs were collected by a cotton roll, placed in the mouth at the orifices of the major glands and was removed after that. Simply, after mouthwash with water the swabs were collected at the temperature of the room and at least three hours after the last meal and the patients were advised to prevent drinking one hour before taking oral swabs (Navazesh, 1993). It was taken with the assistance and direction of the specialized microbiologist supervisor (Appendix C-II) and was sent to the laboratory where it underwent the following standardized steps (Liofilchem, 2015) :

1. 32,5 gm of Sabouraud Dextrose Agar (SDA) medium in one litter of distilled water was suspend.

2. After that, it was heated with multiple excitation and was boiled for full one minute to melt the medium completely.
3. It was placed in Autoclave for complete (15) minutes and at 121 ° C.
4. It was cooled to (45 to 50)°C and put into petri-dishes or tubes.
5. Cultivation was carried out on a bacterial medium.
6. Incubation for 24 hours at a temperature of 27-28 C^{o}, where the emergence of yeasts on the plates was observed.
7. Microscopic examination of dishes using an oil lens. It was viewed first with a lens of (X40) and then (X100) for the purpose of magnification.

Finally, the results of the oral cavity swabs appears after 24 hours from sending it to the laboratory, the samples with positive swabs results indicate the presence of infection by the bacteria or fungi related to OM, and the samples with negative swabs results indicate that there was no infections by bacteria or fungi related to OM (Appendix C-III).

3.7.3. The study instrument:

An instrument was conducted to determine the effects of the management of OM using clove oil versus normal saline solution on patients undergoing CT through data collection, which contain three parts as follow:

3.7.3.1. First part (Socio-demographic characteristics and clinical data):

It is concerned with the patient's socio-demographic data that include (age, gender, social status, level of education, smoking history, chronic diseases, medication used for chronic diseases, period of treating with CT) (Appendix D-I).

3.7.3.2. Second part (Word Health Organization Oral Toxicity Scale):

This part is concerned with Oral Toxicity Scale which is developed by the World Health Organization (WHO), (1979). It contain (5) stages of OM which include stage (0) have described as (no symptoms and diet is normal), stage (1) described as (soreness with/without erythema and solid diet possible),

stage (2) described as (erythema and ulcers , soft or liquid diet possible), stage (3) described as (confluent ulcerations with/ without exudates , liquids only), and finally stage (4) described as (deep ulcerations and/or necrosis and oral alimentation impossible) and this last stage was considered life-threatening (Appendix D-II).

3.7.3.3. Third part (Oral Mucositis Assessment Tool):

This part is concerned with Oral Mucositis Assessment Tool which is constructed by Cancer Institute of New South Wales (CI-NSW), (2019) and manipulated by the researcher according to the experts' opinion. It includes 13 domains each of them contains three items as a scoring levels in which the sum of the final scores ranged from: minor inflammation (13-20), moderate inflammation (21-26), and severe inflammation (27-39). These 13 domains include: voice, swallow, mucous membranes, saliva, tongue, lips, gums, teeth/dentures, ability to maintain nutrition, analgesic requirements, evidence of infection, taste, and self-care assessment (Appendix D-III).

3.8. Testing the validity and reliability for instrument:

3.8.1.The study instrument validation:

The term validity indicates how does the collected information cover the real examination's area. Measuring what the instrument intended to measure is basically the meaning of validity. The four main kinds of validity include: (face, content, construct, and criterion) validity (Taherdoost, 2016).

The interventional protocol and the study instrument underwent series of revisions and modifications and was achieved by 15 experts from different scientific branches (Appendix J-I), each of those experts had greater than ten years of experience in their field of specialty. The researcher proposed each expert member to review the study instrument for content, simplicity, relevance, style, and suitability. Each expert revised the instrument in terms of the scientific content, sequence of information and its competence to perform the

purpose of collecting the sample. So, the modification was made to the instrument according to experts' recommendation.

3.8.2. The content validation:

It is defined as the questionnaire elements' relation and representation of the aimed construct for the purpose of special evaluation (Yusoff, 2019). The researcher performed content validation and content validity index depending on this reference. Both World Health Organization (WHO) Oral Toxicity Scale and Oral Mucositis Assessment Tool was translated to Arabic language by back Brisilin's back translation model. The steps that were taken for applying content validity process according to the following:

1) Preparing the validation from the experts' review that was had the understanding about the process and the clear expectations.
2) The researcher distributed questioner to five experts that are greater than ten years of profession experience in the field of specialty, these experts are (1) expert from college of nursing/ University of Baghdad, (1) expert from college of nursing/ University of Kerbala, (2) experts from college of nursing/ University of Kufa, and (1) expert from College of Nursing/ Al-Safwa University College.
3) Content validity was conducted by face to face through researcher meeting with experts and by sent form of the questionnaire to the experts online.
4) Reviewing items was clearly provided to the experts and they were giving score for each item and also provided comments on some items and all comments was taken in consideration by the researcher. The scores provided through the experts on each the independent item based on relevant scales.
5) Finally, calculate the content validity index (CVI).

Oral Mucositis Assessment Tool: Number of experts was five. Experts in agreement for each question were (5,5,5,5,5,5,5,5,5,5,5,5,5,5). Universal agreement (UA) for each item was (1,1,1,1,1,1,1,1,1,1,1,1,1 and 1). I-CVR (Item Level Content Validity Index) for each item was (1,1,1,1,1,1,1,1,1,1,1,1,1 and 1). S-CVI\ Ave (The Scales\Levels of Content Validation Index (CVI) Based on an Average Method) of this scale was (1) and this value acceptable for CVI. The term of S-CVI\UA was explained as ("Scale-Level Content Validity Index Based on the Universal Agreement) Method" and it was (1) (Yusoff, 2019). The average of proportions of all items were judged as relevant across five experts were (1) (Appendix J-II).

3.8.3. Face validity:

It is the extent to which respondents of the test represents the content of an instrument and its items as related to the area in which the instrument is being used. Also, face validity as defined by other researchers refers to the extent of raters' judgement about the items of an evaluation instrument whether it is appropriate to the aimed construct and evaluation objectives or not. The face validity raters involved: the person who really take the test, the users who are nonprofessional and working with the test results, and the general population (Yusoff, 2019).

There are six steps of response validity process as follow:

1) The first step was preparing responses steps of validity form to that the raters, who had an understanding for this process and the clear expectations.
2) The researcher distributed questionnaire to ten experts that are have ten years of professional experience in their fields or more, these experts are (3) from faculty members of College of Nursing \University of Baghdad, (2) from faculty members of College of Nursing \University of Kerbala, (2) experts from Kerbala Health Department / Imam Al-Hussein Oncology

Center , (1) expert from the college of nursing/ University of Warith Al-Anbiyaa, (1) expert from College of Nursing/ University of Al-Ameed, and (1) expert from faculty members of Al-Zahrawi University College.

3) The process of response validity done by face to face or by online assessment method.
4) In this step, domain of items was sent to panel of the raters. Reviewers were asked to review these items before submitting the score for it. Reviewers are encouraged for providing a written comment for improving an understanding and clarity of each item.
5) After completing review of each item, the reviewers were asked for providing the scores for all items. Then the researcher was received scores responses from the reviewers.
6) There were two forms of Face Validity Index (FVI), I-FVI for the items and S-FVI for the scale and items Proportion of scale that complete comprehension scales and a clarity of three or four by all reviewers (S-FVI /UA). In this last step the Face Validity Index (FVI) was calculated:

Oral Mucositis Assessment Tool: Number of raters was (10). Raters in agreement for each question were (8, 10, 10, 9, 10, 8, 10, 8, 9, 9, 8, 7, and 8). Universal agreement (UA) for each item was (0, 1, 1, 1, 1, 1, 1, 0, 1, 0, 0, 1, and 1). I- FVI (Item Face Validity Index) for each item was (0.8, 1, 1, 1, 1, 1, 1, 0.8, 1, 0.9, 0.8, 1, and1). S-FVI\Aveof this scale was (0.94) and this value was acceptable for FVI (Yusoff, 2019). S-FVI\UA was (0.9). Proportion average of the item's judgement as comprehension and the clarity across the ten experts was (0.93) (Appendix J-III).

3.9. Clove oil experimental group:

This group consists of 10 patients who were treated at Imam Al-Hussein Oncology Center. Before starting clove oil interventional protocol, a detailed medical history and oral cavity history was obtained from each patient and oral

swab was taken from patient's oral cavity and sent to the laboratory for culturing to confirm that there is bacterial or fungal infection related to OM. The researcher took 15 to 20 minutes to conduct the interview, collect comprehensive data, and take an oral swab from each patient.

3.9.1. Clove oil gargling procedure and usage instructions:

The gargling procedure using clove oil was considered as in-house-adopted protocol and all patients in this group were instructed to adhere to the correct method of the steps of the interventional protocol using clove oil, as well as to adhere to the list of instructions attached with the steps, in order to make the interventional protocol successful. The gargling procedure was prepared according to a standardized method and was administered as a topical method to the mouth and in similar amount, dosage form and duration for all patients in this group and under the supervision of the researcher and the supervisor oncologist.

The recommended dose of clove oil that used in the present study was based on those generally used in obtainable experiences, or on clinical practice. But, with herbal natural products it is usually not obvious what the standard doses are needed to the potency and safety equilibrium, and the preparation of these natural herb products may vary from one manufacturer to another.

3.9.2. Clove oil gargling steps:

Nivetha, et al., (2014) and Basch, et al., (2008) were reported that the using of clove oil for human being should be according to the following steps:

1. Put two to three drops of clove oil into the small single-use container.
2. Add one-fourth to one-half small spoon (teaspoonful) of olive oil to the container.
3. Mix these oils using disposable spoon.
4. Put a single-use cotton swab into the oil mixture until it is saturated.

5. Place the cotton swab saturated with oil on the painful and inflamed areas of the mouth for 10 seconds, be sure not swallow this oil.
6. Once the oil has applied to all the inflamed and painful areas of the mouth, gargle with about 20 to 30 ml of distilled water using a disposable cup for 30 seconds and then spit out it.
7. Repeat these steps three times daily after each meal.

The steps of the interventional protocol were firstly applied by researcher in front of the patients and their relatives, in order to practically teach them how to apply the correct steps and to ensure that no errors will be occur in the steps when the patients starting mouth care using the clove oil (Appendix-E).

3.9.3. Instructions to be adhered:

1. This group was instructed to avoid any drugs or mouth-rinse solutions for OM.
2. All patients were advised to perform better oral hygiene and to clean their teeth three times per day with a smooth toothbrush (after every meal). They were also advised to replace their toothbrush regularly to minimize the risk of infection.
3. All patients were advised to maintain adequate oral fluid intake and diet and received pretreatment dietary counseling which include avoid mouth irritants like alcohol and tobacco, spicy foods and coarse or crispy foods because they may destroy the lining of the mucous membrane or gums which may exacerbate the problem.
4. Avoid eating, drinking, or smoking for at least 30 minutes after using the gargling procedure.
5. Use lip moisturizer to prevent dry lips and keep them moisturized.

3.9.4. Clove oil group materials:

The budget of the materials that used for clove oil experimental group

were fully tolerated by the researcher to avoid the financial burden on the patients and it includes the following materials:

1. 12 boxes of clove oil , each box contain 30 ml of the oil.
2. 24 boxes of olive oil, each box contain 80 ml of the oil.
3. 350 single-used small plastic containers.
4. 350 single-used small micropipettes.
5. 12 boxes of cotton swabs, each box contain 100 pieces.
6. 12 boxes of distilled water bottles, each box contain 12 bottles.
7. 12 boxes of single-use cups, each box contain 100 cups.
8. A list of clove oil gargling procedure usage steps and the instructions that should be followed was printed for each patient (Appendix-F).

Each patient was provided with 1 box of clove oil 30 ml, 2 box of olive oil 80 ml, 30 single-use small plastic containers, 30 single-use small micropipettes, 1 box of cotton swabs, 1 box of distilled water bottles contain 12 bottles, and a box of single-use cups which contain 100 cups.

3.10. Normal saline solution experimental group:

Also like previously mentioned in clove oil experimental group, normal saline solution group was undergoing the same details, so that this group consists of 10 patients who were treated at Imam Al-Hussein Oncology Center. Before starting normal saline solution interventional protocol, detailed medical history and oral cavity history was obtained from each patient and oral swab was taken from patient's oral cavity and sent to the laboratory for culturing to confirm that there is bacterial or fungal infection related to OM. The researcher took 15 to 20 minutes to conduct the interview, collected comprehensive data, and took an oral swab from every patient. Also, all patients were assigned to a completely oral cavity assessment to determine any problems not related to OM.

3.10.1. Normal saline solution gargling procedure and usage instructions:

Also, the gargling procedure of normal saline solution was considered as in-house-adopted protocol and all patients in this group were instructed to adhere to the correct method of the steps of the interventional protocol using normal saline solution, as well as to adhere to the list of instructions attached with the steps, in order to make the interventional protocol successful. The gargling procedure was prepared according to a standardized method and was administered as a mouth rinsing and in similar amount, dosage form and duration for all patients in this group and under the supervision of the researcher and the supervisor oncologist.

Patients who randomized to the normal saline experimental group were used normal saline solution (NaCl 0.9% water solution) for oral rinsing. The recommended dose of normal saline solution that used in the present study was based on those generally used in obtainable experiences, or on clinical practice.

3.10.2. Normal saline solution gargling steps:

Bhatt, et al., (2010) stated that normal saline dose which is accepted and required for mouthwash was 30 ml and the researcher instruct the patients to adhere to the gargling procedure according to the following steps:

1. Using the syringe, pull 30 ml of normal saline solution.
2. Emptying the normal saline solution into a single-use cup.
3. Gargling with the normal saline solution for 30 seconds. Be sure that the solution reaches the entire oral cavity, inflamed, and painful areas in the mouth.
4. Spitting out the normal saline solution after the time allotted for gargling is complete.
5. Repeating these steps three times daily after each meal.

3.10.3. Instructions to be adhered:

1. This group was instructed to avoid any drugs or mouth-rinse solutions for

OM.

2. All patients were advised to perform better oral hygiene and to clean their teeth three times per day with a smooth toothbrush (after every meal). They were also advised to replace their toothbrush regularly to minimize the risk of infection.
3. All patients were advised to maintain adequate oral fluid intake and diet and received pretreatment dietary counseling which include avoid mouth irritants like alcohol and tobacco, spicy foods and coarse or crispy foods because they may destroy the lining of the mucous membrane or gums which may exacerbate the problem.
4. Avoid eating, drinking, or smoking for at least 30 minutes after using the gargling procedure.
5. Use lip moisturizer to prevent dry lips and keep them moisturized.

3.10.4. Normal saline solution group materials:

Like the clove oil experimental group which was previously mentioned, the budget of the materials that used for normal saline solution experimental group were fully tolerated by the researcher to avoid the financial burden on the patients and it includes the following materials:

1. 24 bottles of normal saline solution (NaCl 0.9%), each bottle contain 500 ml.
2. 12 boxes of single-use cups, each box contain 100 cups.
3. 3 boxes of single-use syringes sized 50 ml; each box contains 100 syringes.
4. A list of normal saline solution gargling procedure usage steps and the instructions that should be followed was printed for each patient (Appendix-G).

Each patient was provided with 2 bottles of normal saline solution (NaCl

0.9%), 30 single-use syringes sized 50 ml, and a box of single-use cups which contain 100 cups.

3.11. Patients' follow up method:

During the period of both clove oil interventional protocol and normal saline solution interventional protocol, which consist of seven days, the researcher was followed up the patients three times per day and reminded them to adhere to the steps of the interventional protocol for both clove oil and normal saline solution and to the instructions attached to the protocol, this was done through phone by establishing communication groups through social media sites, which include (WhatsApp and Telegram) and were named as clove oil experimental group and normal saline solution experimental group. Also, patients having no social media sites were followed up using the telephonic (SIM-Card) communication (Appendix-H). During this follow up, the researcher was monitored the progress of the OM level and the effect of clove oil interventional protocol and the extent of patient's response to it (Appendix-I).

3.12. Control group:

This group consists of 10 patients who were treated at oncology wards of Imam Al-Hassan Al-Mujtaba teaching hospital and were not undergone any interventional protocol for OM. The researcher collected the same details as in the previously mentioned two experimental groups, detailed medical history and oral cavity history was obtained from each patient and oral swab was taken from patient's oral cavity and sent to the laboratory for culturing to confirm that there is bacterial or fungal infection related to OM. The researcher took 15 to 20 minutes to conduct the interview, collect comprehensive data, and take an oral swab from every patient. Also, all patients were assigned to completely oral cavity assessment to determine any problems not related to OM. All patients were clinically assessed at two detached time intervals: firstly, when

interviewing the patients and the second time after seven days from the first measurement.

3.13. Pilot study:

A Pilot study was applied to six patients who had the same criteria of the study sample and treated in Imam Al-Hussein Oncology Center and in oncology wards of Imam Al-Hassan Al-Mujtaba teaching hospital in Kerbala Governorate. The pilot study samples were divided into two samples of an experimental group by using clove oil, two samples of experimental group by using normal saline solution, and two samples of control group. It was conducted for the period of 3rd January 2022 to 15th January 2022. It was selected by systematic random sampling method. Pilot study sample was isolated from the main study sample.

Firstly, pre-test was made to the patients through the instrument to assess for the severity of inflammation and the stage of OM and then implement the interventional protocol for seven days . Then, the researcher was doing the second measure after completing seven days from the first measurement. The result of the pilot study was indicated that the questionnaire is clear for patients. The researcher was taken 15-20 minutes to complete the questionnaire for each patient. The questionnaires' items are clear and applied.

Furthermore, each patient of the pilot study samples in clove oil experimental group was provided with 1 box of clove oil 30 ml, 2 box of olive oil 80 ml, 30 single-use small plastic containers, 30 single-use small micropipettes, 1 box of cotton swabs, 1 box of distilled water bottles contain 12 bottles, and a box of single-use cups which contain 100 cups. Also, each patient of the pilot study samples in normal saline solution experimental group was provided with 2 bottles of normal saline solution (NaCl 0.9%), 30 single-use syringes sized 50 ml, and a box of single-use cups which contain 100 cups. Also, a list of clove oil and normal saline solution gargling procedure usage

steps and the instructions that should be followed was printed for all patients in both two experimental groups in the pilot study.

3.13.1. The purpose of pilot study:

1. To test the feasibility and to determine the time required to fill the questionnaire.
2. To assess the clarity and comprehensiveness of the content of the questionnaire by the participants.
3. To find out the reliability of the questionnaire.
4. To detect the total time required for each patient.

3.13.2. Pilot study results:

1. The questionnaire was clear.

2. The time needed to fill out the socio-demographic and clinical data part and the two scales (WHO Oral Toxicity Scale and Oral Mucositis Assessment Tool) was 15-20 minutes.

3.14. Reliability of the questionnaire format items:

One of the major and greatly used tool to collect information is the questionnaire. Obtaining related data in most realistic and righteous manner is the main questionnaire objective. Reliability refers to the extent to which a phenomena measurement offers a balanced and consistent result. Repeatability is also one of the reliability interests. For example, if repeated measurement made by the test under stable conditions will give the same finding, then a scale or test is called reliable. It is very important to test for reliability because it refers to the coordination across the items of a measuring questionnaire (Taherdoost, 2016).

The accepted coefficients reliability of the used study questionnaire regarding internal consistency (Alpha Cronbach) is 0.70 (as shown in table 3-1) by findings calculation in which the instrument was effective, significant,

and valid to the research topic of (effect of using clove oil versus normal saline solution in the management of OM among patients undergoing CT).

Table (3-1): Reliability coefficient of the research instrument concerning internal consistency (Alpha Cronbach):

Reliable coefficient	Alpha (Cronbach - α)	Standard lower value	Assessment
WHO Oral Toxicity Scale	0.82	0.70	Verified
Oral Mucositis Assessment Tool	0.93	0.70	Verified

3.15. Assessment method:

All patients in the three groups were assigned to complete oral cavity assessment to investigate any problems not related to OM. All patients were clinically assessed at two detached time intervals: firstly, before starting the interventional protocol and the second time after seven days from the beginning of an interventional protocol as the following steps:

1. The severity and stage of OM were assessed using the World Health Organization Oral Toxicity Scale (WHO grading system), (1979): grade zero (no symptoms, normal nutrition), grade one (soreness with/without redness or erythema, solid diet possible), grade two (ulcers and oral erythema, soft or liquid diet possible), grade three (ulcerations with/ without exudates, liquids only), and grade four (deep ulcerations and/or necrosis, oral alimentation impossible). The clinical evaluation of each patient was done by the researcher and the supervisor oncologist who supervised the research inside the hospital to identify the stage of OM.
2. The patient's oral cavity and their ability to self-care was assessed and the risks of oral complications was identified using the oral assessment tool. The patients were instructed to answer each question related to their condition from the researcher exactly and truthy and this was repeated two times, in the first day of interview and in the seventh day from the first meet. Also, the

clinical evaluation of each patient was done by the researcher and the supervisor oncologist who supervised the research inside the hospital to determine the severity of the inflammation of the oral cavity resulting from OM.

3.16. Data collection:

The data collection process was carried out through the interview technique. The researcher and the oncologist supervisor measured the oral toxicity and OM level and recorded them in the study instrument. The data were collected for study sample in the period from 13th February 2022 to 19th April 2022. The researcher took 15-20 minutes to collect data and to fill out the questionnaire completely from each patient. The data were collected through two times (as shown in figure 3-2).

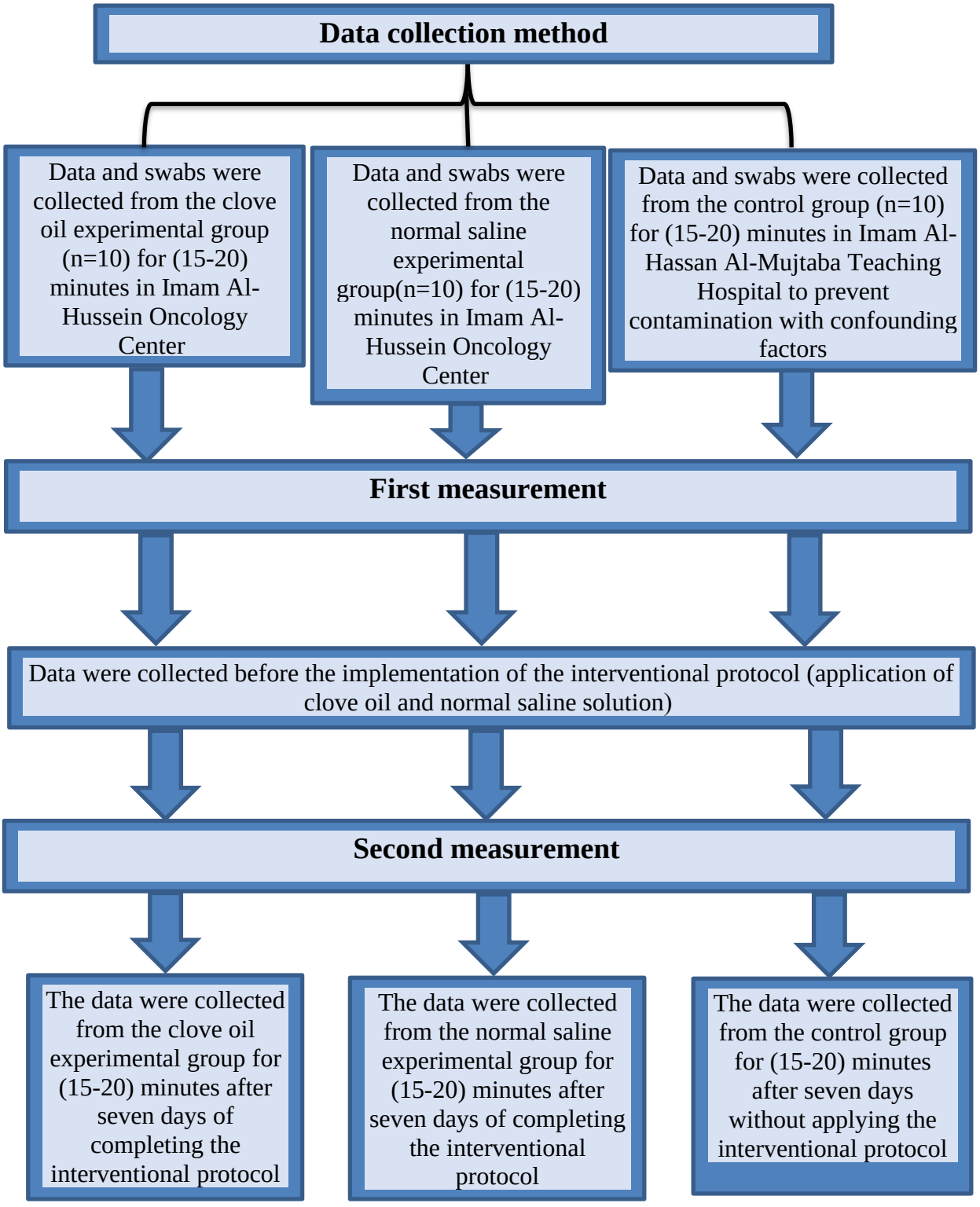


Figure (3-2): (Flowchart of the data collection method)

3.17. Rating and scoring:

The rating and scoring of the items were done according to the following manners:

3.17.1. Rating and scoring for WHO Oral Toxicity Scale:

World Health Organization oral toxicity scale was measured by rating according to the stages of OM as follow:

- No symptoms, (Normal nutrition) = 0
- Soreness ± Erythema, (solid diet possible) = 1
- Erythema, Ulcers, (soft or liquid diet possible) = 2
- Confluent ulcerations with/ without exudates, (liquids only) = 3
- Deep ulcerations and/or necrosis, (oral alimentation impossible) = 4

3.17.2. Rating and scoring for level of oral mucositis:

The oral mucositis severity level was scored according to 13 domains, each of these domains contains three items as a scoring level of severity which was described according to the type of item and the sum of these domains at the end determines the level of OM whether it is mild inflammation, moderate inflammation or severe inflammation and as the following:

- Mild inflammation = 13-20
- Moderate inflammation = 21-26
- Severe inflammation = 27-39

3.18. Statistical data analysis:

The data analysis process was used this study to evaluate the findings of the study by the usage of the Statistical Package of Social Sciences Version 25 Program (SPSS ver.25) that are as follow:

3.18.1. Descriptive statistical analysis:

- **Frequency (f.), mean of score (MS), standard deviation (SD), and percentage (%):** were used in tables in order to get the total results of the sample and to make a comparison between the variables.

$$\% = \frac{Frequencies}{Sample\ Size} \times 100$$

% = Percentage

3.18.2. Inferential statistical analysis:

- Chi square test (X^2) to study the relationship between the socio-demographic characteristics of patients in the three study groups.
- Shapiro-Wilk test to study the normal distribution of the study variables.
- Marginal Homogeneity Test (MH) to study the differences between the level of oral toxicity and OM pre and post applying the procedure in each of the three groups.
- Kendal-Taue test (τ) to study the differences between the study groups pre and post applying the procedure.
- Mann-whitney test (U), to study the differences between the mean levels of oral toxicity and OM between study groups pre and post applying the procedure.
- Independent sample t-test to study the differences between the cumulative total mucositis assessment score pre and post applying the procedure between study groups pre and post applying the procedure.
- The significance threshold differences at (p-value ≤0.05) were considered significant statistically.
- The significance threshold differences at (p-value ≤0.01) were considered significant very important statistically.

3.19. Limitations:

There are a few significant limits to consider:

1. During samples collection, there was shortage in the samples due to the nature of the problem being studied. Therefore, there were restricted patients' number, which confirms the importance of performing a future study on a larger sample size.

2. The researcher was suffered from lack of references because the research is unique and original. So, this articles lack in the field of clove oil effects on OM caused a great difficulty when comparing the findings.
3. Each group of the study was taken long time to confirm the evidence of the presence of infection by taking oral swabs to the laboratory.

Chapter Four

"Results of the Study"

Chapter Four

Results of the Study

This chapter represents a detailed research results as explained through the variables' data analysis and systematically organized in tables in the form that is consistent with the objectives of the research.

First: Sociodemographic and clinical data:

Table (4-1): Distribution of patients in three groups according to their sociodemographic characteristics:

Variable		Clove Oil n=10		Normal saline n=10		Control n=10		X^2 p
		f	%	f	%	f	%	
Age (years)	20-30	2	20	2	20	1	10	6.846 0.339
	31-40	3	30	1	10	5	50	
	41-50	4	40	2	20	2	20	
	>50	1	10	5	50	2	20	
Gender	Male	5	50	7	70	4	40	1.861 0.534
	Female	5	50	3	30	6	60	
Marital status	Single	2	20	2	20	1	10	4.487 0.611
	Married	8	80	8	80	7	70	
	Divorced	0	0	0	0	1	10	
	Widowed	0	0	0	0	1	10	
Educational level	No read or write	0	0	2	20	2	20	8.400 0.590
	Read and write	1	10	3	30	1	10	
	Primary	4	40	4	40	4	40	
	Middle school	1	10	1	10	0	0	
	Secondary	3	30	0	0	2	20	
	University or above	1	10	0	0	1	10	

p: p value, X^2: chi square Test

Table (4-1) show that no statistically significant differences were seen between the three study groups regarding patient demographical characteristics ($P > 0.05$). The highest percentage of patients (40%) are between 41 and 50

years old in the clove oil group, 50% are >50 years old in the normal saline solution group, and 50% are between 41 and 50 years old in the control group. Regarding the gender of patient about half of them are male in clove oil group 50% and 70% in normal saline group, but 60% are female in control group. Most of patients' 80% clove oil group, 80% normal saline group, 70% control group are married. The highest percentage of patients 40% in each group are with a primary education level.

Table (4-2): Distribution of patients in three groups according to their clinical data:

Variable		Clove Oil n=10		Normal saline n=10		Control n=10		X^2 p
		f	%	f	%	f	%	
Smoking	Current smoker	0	0	0	0	1	10	4.200 0.380
	Previous smoker	3	30	6	60	5	50	
	Never smoked	7	70	4	40	4	40	
Chemotherapy duration	< 4 months	4	40	6	60	6	60	7.095 0.192
	4-8 months	5	50	4	40	1	10	
	8-12 months	0	0	0	0	2	20	
	≥12 months	1	10	0	0	1	10	
Chronic disease	Diabetic	1	10	0	0	0	0	0 1
	Hypertension	0	0	1	10	1	10	
	No	9	90	9	90	9	90	
Medications	Insulin Metformin Gloucovance	1	0	0	0	0	0	0 1
	lasix	0	0	0	0	1	10	
	No	9	90	10	100	9	90	

p: p value, X^2: chi square Test

Table (4-2) show that no statistically significant differences are seen between the three study groups regarding patient clinical data (P > 0.05). It

shows that all patients are not smokers and most of them in the clove oil group 70% had never smoked, while in the normal saline solution group by 60% and control group by 50% are previous smoker. The therapy duration for most of them 60% in normal saline solution group and control group is less than 4 months, but it is between 4-8 months for 50% of them in clove oil group.

Second: Comparison of oral toxicity:

Table (4-3): Comparison oral toxicity degree pre and post the application of clove oil:

Oral Toxicity	Clove Oil				MH/p
	pre		post		
	f	%	f	%	
I	0	0	8	80	2.921 0.003**
II	4	40	2	20	
III	4	40	0	0	
IV	2	20	0	0	
V	0	0	0	0	
M±SD	2.8 ± 0.789		1.2 ± 0.422		

MH: Marginal Homogeneity Test, **: p value ≤0.01.

Table (4-3) reveals that the distribution of patients undergoing CT according to the oral toxicity degrees at pre and post self-administered interventional protocol using clove oil, 40% of patients have grade II and III oral toxicity before applying clove oil, but after being given intervention for seven days 80% of patients are at grade (I), and there are significant statistical differences between pre and post applying clove oil (P=0.003). Therefore, the application of clove oil interventional protocol significantly reduces the degree of oral toxicity in patients receiving CT, as symptoms were absent in the majority of patients after applying it.

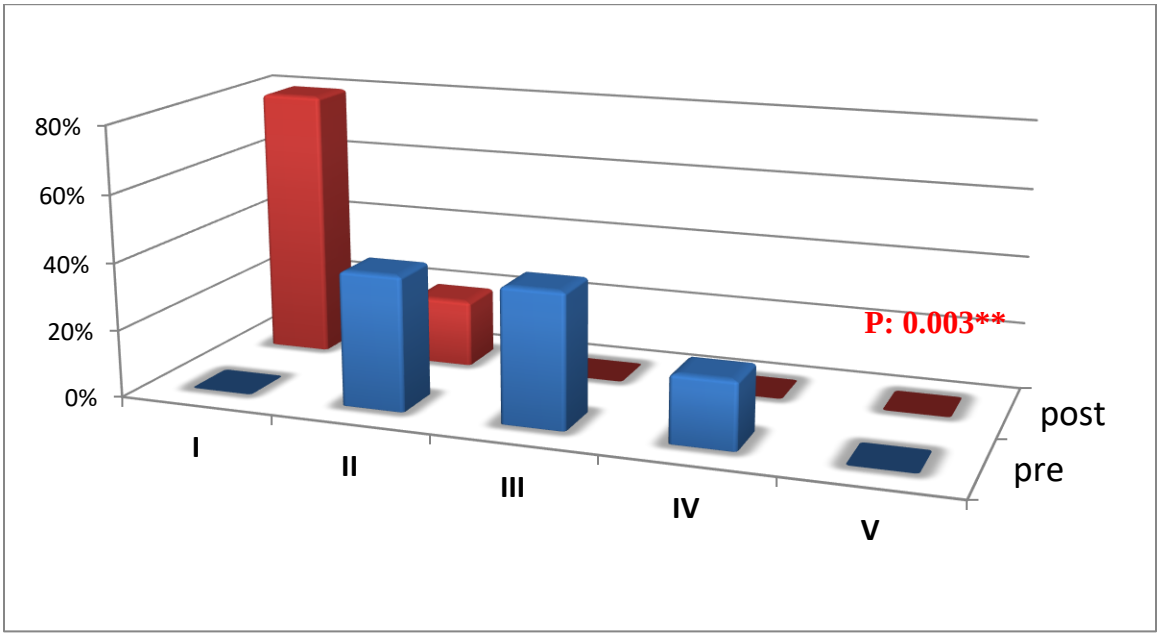


Figure (4-1): (Comparison oral toxicity degree pre and post the application of clove oil)

Table (4-4): Comparison degree of oral toxicity at pre and post the application of normal saline solution:

Oral Toxicity	Normal saline				MH/p
	pre		post		
	f	%	f	%	
I	0	0	2	20	2.714 0.007**
II	4	40	5	50	
III	2	20	3	30	
IV	4	40	0	0	
V	0	0	0	0	
M±SD	3 ± 0.943		2.1 ± 0.738		

MH: Marginal Homogeneity Test, **: p value ≤0.01.

Table (4-4) revealed that the distribution of patients undergoing CT according to the oral toxicity degrees at pre and post self-administered interventional protocol using normal saline solution, 40% of patients have grade II and IV oral toxicity before applying normal saline solution, but after being given treatment for seven days 20% of patients are at grade (I), 50% at grade II, and there were significant statistical differences between pre and post application of normal saline solution (P=0.007). Therefore, the application of normal saline solution significantly reduces the degree of oral toxicity in

patients receiving CT, as symptoms are absent in the 20% of patients, and no patient remained in the IV degree after applying it.

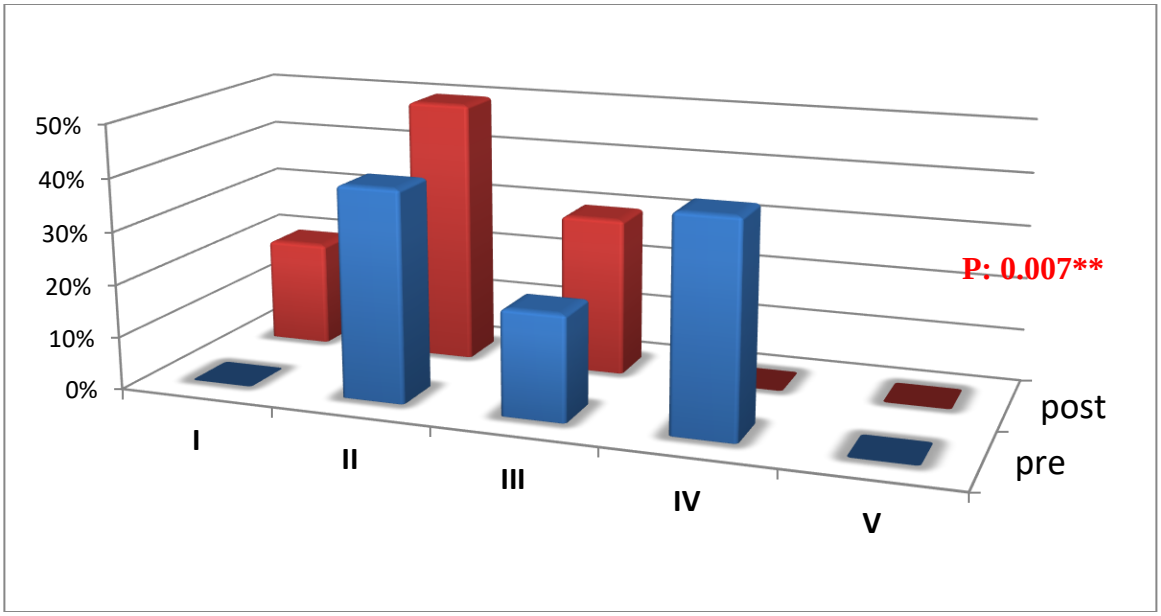


Figure (4-2): (Comparison oral toxicity degree pre and post the application of normal saline solution)

Table (4-5): Comparison degree of oral toxicity at pre and post the first measurement in control group:

Oral Toxicity	Control group				MH/p
	Pre		post		
	f	%	f	%	
I	0	0	0	0	2.236 0.025*
II	3	30	1	10	
III	4	40	3	30	
IV	3	30	6	60	
V	0	0	0	0	
M±SD	3 ± 0.817		3.5 ± 0.707		

MH: Marginal Homogeneity Test, * p value ≤0.05,

Table (4-5) reveals that the distribution of patients undergoing CT according to the oral toxicity degrees in control group, 40% of patients have grade III oral toxicity when starting collecting data, but after seven days 60% of patients at grade (IV), and there are significant statistical differences between pre and post seven days (p=0.025). Therefore, not implementing the

interventional protocols significantly increases the degree of oral toxicity in patients receiving CT.

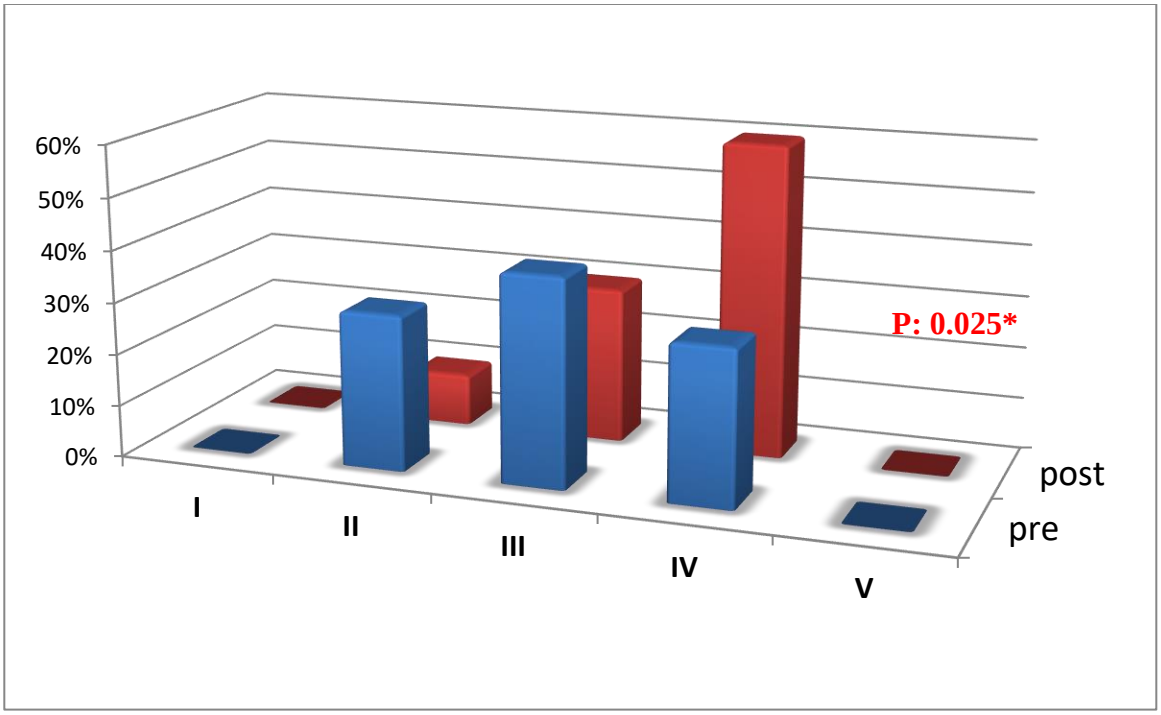


Figure (4-3): (Comparison oral toxicity degree pre and post in the control group)

Table (4-6): Comparison oral toxicity degree between clove oil group and normal saline solution group at pre and post the application of clove oil, and normal saline solution:

Oral Toxicity	pre					post				
	Clove Oil		Normal saline		τ p	Clove Oil		Normal saline		τ p
	f	%	f	%		f	%	f	%	
I	0	0	0	0	0.104 0.623	8	80	2	20	0.600 0.000**
II	4	40	4	40		2	20	5	50	
III	4	40	2	20		0	0	3	30	
IV	2	20	4	40		0	0	0	0	
V	0	0	0	0		0	0	0	0	
M±SD	2.8 ± 0.789		3 ± 0.789		U/p 44/ 0.630	1.2 ± 0.422		2.1 ± 0.738		U/p 17/ 0.006 **

τ: Kendal-Taue test, U; Mann-whitney test, **: p value ≤0.01.

Table (4-6) shows no significant statistical differences (p=0.623, p=0.630) in oral toxicity degree between clove oil and normal saline solution group before interventional protocol, but after seven days of intervention there are significant statistical differences (p=0.000, p=0.006) between both groups in favor the clove oil group. Therefore, clove oil cures oral toxicity much more than normal saline solution.

Table (4-7): Comparison degree of oral toxicity between clove oil group and control group at pre and post the application of clove oil:

Oral Toxicity	pre					post				
	Clove Oil		Control group		τ p	Clove Oil		Control group		τ p
	f	%	f	%		f	%	f	%	
I	0	0	0	0	0.122 0.725	8	80	0	0	0.825 0.000**
II	4	40	3	30		2	20	1	10	
III	4	40	4	40		0	0	3	30	
IV	2	20	3	30		0	0	6	60	
V	0	0	0	0		0	0	0	0	
M±SD	2.8 ± 0.789		3 ± 0.817		U/p 43/ 0.573	1.2 ± 0.422		3.5 ± 0.707		U/p 1/ 0.000**

τ: Kendal-Taue test, U; Mann-whitney test, **: p value ≤0.01.

Table (4-7) reveals no significant statistical differences (P=0.725, P=0.573) in oral toxicity degree between clove oil and control group before interventional protocol, but after seven days there are significant statistical differences (P=0.000, P=0.000) between both groups in favor the clove oil group. Therefore, clove oil cures oral toxicity much more than disapplication of the interventional protocol.

Table (4-8): Comparison degree of oral toxicity between normal saline solution group and control group at pre and post the application of normal saline solution:

Oral Toxicity	pre					post				
	Normal saline		Control group		τ p	Normal saline		Control group		τ p
	f	%	f	%		f	%	f	%	

I	0	0	0	0	0..999	2	20	0	0	0.667 0.000**
II	4	40	3	30		5	50	1	10	
III	2	20	4	40		3	30	3	30	
IV	4	40	3	30		0	0	6	60	
V	0	0	0	0		0	0	0	0	
M±SD	3 ± 0.943		3 ± 0.817		U/p 50/ 0.999	2.1 ± 0.738		3.5 ± 0.707		U/p 10/ 0.002**

τ: Kendal-Taue test, U; Mann-whitney test, **: p value ≤0.01.

Table (4-8) shows no significant statistical differences (P=0.999, P=0.999) in oral toxicity degree between normal saline solution and control group before interventional protocol, but after seven days there are significant statistical differences (P=0.000, P=0.002) between both groups in favor the normal saline solution group. Therefore, normal saline solution cures oral toxicity much more than disapplication of the interventional protocol.

Third: Comparison of oral mucositis levels

Table (4-9): Comparison level and total cumulative score of oral mucositis pre and post the application of clove oil:

Oral Mucositis	Clove Oil				MH	P. Value
	pre		post			
	f	%	f	%		
Mild	1	10	10	100	2.828	0.005**
Moderate	6	60	0	0		
Severe	3	30	0	0		
M±SD	2.2±0.633		1±0.000			
M±SD for Sum	25.1±3.604		14.4±1.350		t/ 12.679	0.000**

MH: Marginal Homogeneity Test, t: Independent sample (t) test , for Sum: the cumulative total mucositis assessment score, **: p value ≤0.01.

Table (4-9) reveals that the distribution of patients undergoing CT according to the OM level pre and post interventional protocol using clove oil, 60% of patients have moderate level of OM pre applying clove oil, after given treatment for seven days is 100% of patients at mild level, and there are significant statistical differences in OM level (p=0.005) and in total cumulative score (p=0.000) of OM between pre and post applying clove oil. Therefore, the

application of clove oil significantly reduces the level of OM in patients receiving CT.

Table (4-10): Comparison level and total cumulative score of oral mucositis pre and post the application of normal saline:

Oral Mucositis	Normal saline				MH	P. Value
	pre		post			
	f	%	f	%		
Mild	0	0	7	70	2.828	0.005**
Moderate	4	40	2	20		
Severe	6	60	1	10		
M±SD	2.6±0.516		1.4±0.699			
M±SD $^{\text{for Sum}}$	28.2±4.022		19.9±4.885		t/ 6.223	0.000**

MH: Marginal Homogeneity Test, t: Independent sample (t) test , $^{\text{for Sum}}$: the cumulative total mucositis assessment score, **: p value ≤0.01.

Table (4-10) reveals that the distribution of patients undergoing CT according to the OM level at pre and post interventional protocol using normal saline solution, 60% of patients had severe level of OM before applying normal saline solution, after given intervention for seven days are 70% of patients at mild level, and there are significant statistical differences in OM level (p=0.005) and in total cumulative score (p=0.000) of OM between pre and post applying normal saline solution. Therefore, the application of normal saline solution significantly reduces the level of OM in patients receiving CT.

Table (4-11): Comparison level and total cumulative score of oral mucositis in control group:

Oral Mucositis	Control group				MH	P. Value
	pre		post			
	f	%	f	%		
Mild	2	20	0	0	2.236	0.025*
Moderate	3	30	2	20		
Severe	5	50	8	80		
M±SD	2.3±0.823		2.8±0.422			
M±SD $^{\text{for Sum}}$	26.5±4.577		29.6±2.875		t/ 12.679	0.000**

MH: Marginal Homogeneity Test, t: Independent sample (t) test , for Sum: the cumulative total mucositis assessment score, * p value ≤0.05, **: p value ≤0.01.

Table (4-11) reveals that the distribution of patients undergoing CT according to the OM level in control group, 50% of patients have severe level of OM when start collecting data, after seven days the number of patients with severe level increased and reached the ratio of 80%, and there are significant statistical differences in OM level (p=0.025) and in total cumulative score (p=0.000) of OM between the first and second measurement. Therefore, not applying the interventional protocol significantly increases the level and total cumulative score of OM in patients receiving CT.

Table (4-12): Comparison level and total cumulative score of oral mucositis between clove oil group and normal saline solution group at pre and post the application of clove oil, and normal saline solution:

Oral Mucositis	pre					post				
	Clove Oil		Normal saline		τ p	Clove Oil		Normal saline		τ p
	f	%	f	%		f	%	f	%	
Mild	1	10	0	0	0.104 0.623	10	100	7	70	0.600 0.011*
Moderate	6	60	4	40		0	0	2	20	
Severe	3	30	6	60		0	0	1	10	
M±SD	2.2±0.633		2.6±0.516		U/p 33 0.147	1±0.000		1.4±0.699		U/p 35 0.068
M±SD for Sum	25.1±3.604		28.2±4.022		t/p: 1.815 0.086	14.4±1.350		19.9±4.885		t/p: 3.431 0.006 **

τ: Kendal-Taue test, U; Mann-whitney test, **t**: Independent sample (t) test , for Sum: the cumulative total mucositis assessment score, * p value ≤0.05, **: p value ≤0.01.

Table (4-12) reveals no significant statistical differences (p=0.623, p=0.086) in level and total cumulative score of OM between clove oil group and normal saline solution group before interventional protocol, but after seven days of intervention there are a significant statistical differences (p=0.011, p=0.006) between both

groups in favor the clove oil group. Therefore, clove oil cures OM much more than normal saline solution.

Table (4-13): Comparison level and total cumulative score of oral mucositis between clove oil group and control group at pre and post the application of clove oil:

Oral Mucositis	pre					post				
	Clove Oil		Control group		τ p	Clove Oil		Control group		τ p
	f	%	f	%		f	%	f	%	
Mild	1	10	2	20	0.099	10	100	0	0	0.928
Moderate	6	60	3	30	0.650	0	0	2	20	0.042*
Severe	3	30	5	50		0	0	8	80	
M±SD	2.2±0.633		2.3±0.823		U/p 44.5 0.651	1±0.000		2.8±0.422		U/p 0 0.000 **
M±SD $^{\text{for Sum}}$	25.1±3.604		26.5±4.577		t/p: 0.760 0.457	14.4±1.350		29.6±2.875		t/p: 15.133 0.000 **

τ: Kendal-Taue test, U; Mann-whitney test, **t**: Independent sample (t) test , $^{\text{for Sum}}$: the cumulative total mucositis assessment score, * p value ≤0.05, **: p value ≤0.01.

Table (4-13) reveals no significant statistical differences (p=0.650, p=0.457) in level and total cumulative score of OM between clove oil group and control group before interventional protocol, but after seven days of intervention there are a significant statistical differences (p=0.042, p=0.000) between both groups in favor the clove oil group. Therefore, clove oil cures OM much more than not applying the interventional protocol.

Table (4-14): Comparison level and total cumulative score oral mucositis between normal saline solution group and control group at pre and post the application of normal saline solution:

Oral Mucositis	pre			post		
	Normal saline	Control group	τ p	Normal saline	Control group	τ p

	f	%	f	%		f	%	f	%	
Mild	0	0	2	20	0.169 0.425	7	70	0	0	0.745 0.000 **
Moderate	4	40	3	30		2	20	2	20	
Severe	6	60	5	50		1	10	8	80	
M±SD	2.6±0.516		2.3±0.823		U/p 41 0.445	1.4±0.699		2.8±0.422		U/p 8 0.001 **
M±SD for Sum	28.2±4.022		26.5±4.577		t/p: 0.882 0.389	19.9±4.885		29.6±2.875		t/p: 5.410 0.000 **

τ: Kendal-Taue test, U; Mann-whitney test, **t**: Independent sample (t) test , for Sum: the cumulative total mucositis assessment score, * p value ≤0.05, **: p value ≤0.01.

Table (4-14) reveals no significant statistical differences (p=0.425, p=0.389) in level and total cumulative score of OM between normal saline solution group and control group before interventional protocol, but after seven days of intervention there are a significant statistical differences (p=0.000, p=0.000) between both groups in favor the normal saline solution group. Therefore, normal saline solution cures OM much more than disapplication of the interventional protocol.

Table (4-15): Differences between oral mucositis level of patients undergoing chemotherapy with their socio-demographic characteristics and clinical data in clove oil group:

Variable		Clove Oil n=10						X^2 p
		Mild		Moderate		Severe		
		f	%	f	%	f	%	
Age (years)	20-30	2	20	0	0	0	0	-
	31-40	3	30	0	0	0	0	
	41-50	4	40	0	0	0	0	
	>50	1	10	0	0	0	0	
Gender	Male	5	50	0	0	0	0	-
	Female	5	50	0	0	0	0	
Marital status	Single	2	20	0	0	0	0	-
	Married	8	80	0	0	0	0	
	Read and write	1	10	0	0	0	0	-

Educational level	Primary	4	40	0	0	0	0	
	Middle school	1	10	0	0	0	0	
	Secondary	3	30	0	0	0	0	
	University or above	1	10	0	0	0	0	
Smoking	Previous smoker	3	30	0	0	0	0	-
	Never smoked	7	70	0	0	0	0	
Chemotherapy duration	< 4m	4	40	0	0	0	0	-
	4 – 8 m	5	50	0	0	0	0	
	>8 – 12 m	0	0	0	0	0	0	
	≥12	1	1	0	0	0	0	

p: p value, X^2: chi square Test

Table (4-15) shows no significant statistical differences in level of OM related to any of socio-demographic and clinical variables in clove oil group.

Table (4-16): Differences between oral mucositis level of patients undergoing chemotherapy with their socio-demographic characteristics and clinical data in normal saline solution group:

Variable		Normal saline n=10						X^2 p
		Mild		Moderate		Severe		
		f	%	f	%	f	%	
Age (years)	20-30	2	20	0	0	0	0	5.362 0.778
	31-40	1	10	0	0	0	0	
	41-50	2	20	0	0	0	0	
	>50	2	20	2	20	1	10	
Gender	Male	4	40	2	20	1	10	1.537 0.650
	Female	3	30	0	0	0	0	
Marital status	Single	2	20	0	0	0	0	1.177 0.999
	Married	5	50	2	10	1	10	
Educational level	No read or write	1	10	1	10	0	0	6.830 0.517
	Read and write	1	10	1	10	1	10	
	Primary	4	40	0	0	0	0	
	Middle school	1	10	0	0	0	0	
Smoking	Previous smoker	3	30	0	0	0	0	2.426 0.467
	Never smoked	4	70	0	0	0	0	
Chemotherapy duration	< 4 Months	4	40	1	10	1	10	0.774 0.679
	4-8 Months	3	30	1	10	0	0	

p: p value, X^2: chi square Test

Table (4-16) shows no significant statistical differences in level of OM related to any of socio-demographic and clinical variables in normal saline solution group.

Table (4-17): Differences between oral mucositis level of patients undergoing chemotherapy with their socio-demographic characteristics and clinical data in control group:

Variable		control group n=10						X^2 p
		Mild		Moderate		Severe		
		f	%	f	%	f	%	
Age (years)	20-30	0	0	1	10	0	0	3.685 0.333
	31-40	0	0	1	10	4	40	
	41-50	0	0	0	0	2	20	
	>50	0	0	0	0	2	20	
Gender	Male	0	0	1	10	3	30	0.104 0.747
	Female	0	0	1	10	5	50	
Marital status	Single	0	0	0	0	1	10	1.071 0.784
	Married	0	0	2	20	5	50	
	Divorced	0	0	0	0	1	10	
	Widowed	0	0	0	0	1	10	
Educational level	No read or write	0	0	0	0	2	20	2.188 0.701
	Read and write	0	0	0	0	1	10	
	Primary	0	0	1	10	3	30	
	Middle school	0	0	1	10	1	10	
	University or above	0	0	0	0	1	10	
Smoking	Current smoker	0	0	0	0	1	10	0.313 0.855
	Previous smoker	0	0	1	10	4	40	
	Never smoked	0	0	1	10	3	30	
Chemotherapy duration	< 4 Months	0	0	1	10	5	50	2.445 0.667
	4-8 Months	0	0	0	0	1	10	
	8-12 Months	0	0	1	10	1	10	
	≥12 Months	0	0	0	0	1	10	

p: p value, X^2: chi square Test

Table (4-17) shows no significant statistical differences in level of OM related to any of socio-demographic and clinical variables in control group.

Table (4-18): Differences between oral mucositis level of patients undergoing chemotherapy pre and post application clove oil with their socio-demographic characteristics and clinical data in clove oil group:

Variable		Clove Oil n=10 /pre/						X^2 p	Clove Oil n=10 /post/					
		Mild		Moderate		Severe			Mild		Moderate		Severe	
		f	%	f	%	f	%		f	%	f	%	f	%
Age (years)	20-30	0	0	1	10	1	10	7.500 0.307	2	20	0	0	0	0
	31-40	1	10	1	10	1	10		3	30	0	0	0	0
	41-50	0	0	4	40	0	0		4	40	0	0	0	0
	>50	0	0	0	0	1	10		1	10	0	0	0	0
Gender	Male	1	10	2	20	2	20	2.000 0.368	5	50	0	0	0	0
	Female	0	0	4	40	1	10		5	50	0	0	0	0
Marital status	Single	0	0	1	10	1	10	0.625 0.732	2	20	0	0	0	0
	Married	1	10	5	50	2	20		8	80	0	0	0	0
Educational level	Read and write	0	0	0	0	1	10	7.222 0.513	1	10	0	0	0	0
	Primary	0	0	2	20	2	20		4	40	0	0	0	0
	Middle school	0	0	1	10	0	0		1	10	0	0	0	0
	Secondary	1	10	2	20	0	0		3	30	0	0	0	0
	University or above	0	0	1	10	0	0		1	10	0	0	0	0
Smoking	Previous smoker	0	0	2	20	1	10	0.476 0.788	3	30	0	0	0	0
	Never smoked	1	10	4	40	2	20		7	70	0	0	0	0
Chemotherapy duration	< 4 Months	0	0	3	30	1	10	2.250 0.690	4	40	0	0	0	0
	4-8 Months	1	10	2	20	2	20		5	50	0	0	0	0
	8-12 Months	0	0	0	0	0	0		0	0	0	0	0	0
	≥12 Months	0	0	1	10	0	0		1	1	0	0	0	0

p: p value, X^2: chi square Test

Table (4-18) shows no significant statistical differences in level of OM related to any of socio-demographic and clinical variables in clove oil group per and post application of interventional protocol.

Table (4-19): Differences between oral mucositis level of patients undergoing chemotherapy per and post application of normal saline solution with their socio-demographic characteristics and clinical data in normal saline solution group:

Variable		Normal saline n=10 /pre/						X^2 p	Normal saline n=10 /post/						X^2 p
		Mild		Moderate		Severe			Mild		Moderate		Severe		
		f	%	f	%	f	%		f	%	f	%	f	%	
Age (years)	20-30	0	0	1	10	1	10	4.583 0.205	2	20	0	0	0	0	5.362 0.778
	31-40	0	0	0	0	1	10		1	10	0	0	0	0	
	41-50	0	0	2	20	0	0		2	20	0	0	0	0	
	>50	0	0	1	10	4	40		2	20	2	20	1	10	
Gender	Male	0	0	4	40	3	30	2.857 0.091	4	40	2	20	1	10	1.837 0.399
	Female	0	0	0	0	3	30		3	30	0	0	0	0	
Marital status	Single	0	0	1	10	1	10	0.104 0.747	2	20	0	0	0	0	1.177 0.585
	Married	0	0	3	30	5	50		5	50	2	10	1	10	
Educational level	No read or write	0	0	0	0	2	20	4.097 0.251	1	10	1	10	0	0	6.830 0.517
	Read and write	0	0	1	10	2	20		1	10	1	10	1	10	
	Primary	0	0	3	30	1	10		4	40	0	0	0	0	
	Middle school	0	0	0	0	1	10		1	10	0	0	0	0	
Smoking	Previous smoker	0	0	3	30	3	30	0.625 0.429	3	30	2	20	1	10	2.426 0.467

	Never smoked	0	0	1	10	3	30		4	70	0	0	0	0	
Chemotherapy duration	< 4 Months	0	0	3	30	3	30	0.774 0.679	4	40	1	10	1	10	0.774 0.679
	4-8 Months	0	0	1	10	3	30		3	30	1	10	0	0	

p: p value, X^2: chi square Test

Table (4-19) shows no significant statistical differences in level of OM related to any of socio-demographic and clinical variables in normal saline solution group per and post application of interventional protocol.

Table (4-20): Differences between oral mucositis level of patients undergoing chemotherapy pre and post first and second measurement with their socio-demographic characteristics and clinical data in the control group:

Variable		control group n=10 /pre/						X^2 p	control group n=10 /post/						X^2 p
		Mild		Moderate		Severe			Mild		Moderate		Severe		
		f	%	f	%	f	%		f	%	f	%	f	%	
Age (years)	20-30	1	10	1	10	1	10	8.692 0.192	0	0	1	10	0	0	3.685 0.333
	31-40	2	20	1	10	5	50		0	0	1	10	4	40	
	41-50	0	0	5	50	1	10		0	0	0	0	2	20	
	>50	0	0	2	20	1	10		0	0	0	0	2	20	
Gender	Male	2	20	3	30	4	40	1.145 0.564	0	0	1	10	3	30	0.104 0.747
	Female	1	10	6	60	4	40		0	0	1	10	5	50	
Marital status	Single	0	0	1	10	2	20	4.222 0.647	0	0	0	0	1	10	1.071 0.784
	Married	3	30	7	70	5	50		0	0	2	20	5	50	
	Divorced	0	0	0	0	1	10		0	0	0	0	1	10	
	Widowed	0	0	1	10	0	0		0	0	0	0	1	10	

Educational level	Read and write	0	0	2	20	0	0	9.972 0.443	0	0	0	0	2	20	2.188 0.701
	Primary	0	0	0	0	2	20		0	0	0	0	1	10	
	Middle school	1	1	3	30	4	40		0	0	1	10	3	30	
	Secondary	0	0	1	10	0	0		0	0	1	10	1	10	
	University or above	2	20	2	20	1	1		0	0	0	0	1	10	
Smoking	Current smoker	0	0	0	0	1	10	2.866 0.580	0	0	0	0	1	10	0.313 0.855
	Previous smoker	1	10	5	50	2	20		0	0	1	10	4	40	
	Never smoked	2	20	4	40	5	50		0	0	1	10	3	30	
Chemotherapy duration	< 4 Months	1	10	4	40	5	50	3.389 0.759	0	0	1	10	5	50	2.445 0.667
	4-8 Months	1	10	3	30	2	20		0	0	0	0	1	10	
	8-12 Months	1	10	1	10	0	0		0	0	1	10	1	10	
	≥12 Months	0	0	1	10	1	10		0	0	0	0	1	10	

p: p value, X^2: chi square Test

Table (4-20) shows no significant statistical differences in level of OM related to any of socio-demographic and clinical variables in control group before and after the first and second measurement.

Chapter Five "Discussion of the Results"

Chapter Five

Discussion of the Results

Oral mucositis is considered from the most common complications of CT as it occurs after the integrity of mucous membrane was broken. Consequently, a wide variety of side effects will occur as a result of CIOM such as discomfort, severe pain, difficulty swallowing, malnutrition, loss of body weight, and dehydration. Different interventional protocols have been developed to treat and prevent OM. Therefore, a safe, potent, and simple protocol is necessary to be established for the treatment and prevention of this problem. It is possible to improve the level of OM through adopting self-administered protocol using clove oil and normal saline solution. A 30 male and female patients who were confirmed to have OM and were treated at Imam Al-Hussein Oncology Center and at Oncology wards of Imam Al-Hassan Al-Mujtaba teaching hospital participated in this study to identify the effect of using clove oil versus normal saline solution in the management of OM among patients with cancer undergoing CT.

This chapter presents an organized discussion which interprets the results that are presented in chapter four in a systematical manner and supported by recent studies.

5.1. Discussion of sociodemographic characteristics of the study sample:

The patients' characteristics in the present study indicate that 40% of patients are between 41-50 years old in the clove oil group, 50% are >50 years old in the normal saline group, and 50% are between 41-50 years old in the control group. Regarding the gender of patient one-half (50%) of them are males in clove oil group and 70% in normal saline group, but 60% are females in control group. The majority (80%) of patients in clove oil group and normal

saline group, and 70% in the control group are married. The highest percentage (40%) of patients in each group are with a primary level of education. No statistically significant differences are seen between the three groups regarding patient socio-demographic characteristics

Kothiwale, et al., (2014) performed a randomized-controlled trial, double-blinded, parallel-group design clinical study, this study was done to evaluate the effectivity of mouthwash consisting the clove oil which are recently formed, for its anti-gingivitis and anti-plaque characteristics and to assess the mouth-rinse impact on the load of plaque microbes. A total of 50 male and female aged between 18 and 60 years were included in the study. The basic and demographic characteristics of this study were the same through both the two study groups. 30.05±11.00 years was the average age of the experimental group, while 37.2±13.63 years was the average age of the control group. There were non-significant statistical differences regarding the age between both two groups.

Jesudasan, et al., (2015) performed a randomized-controlled trial, double-blinded, on 270 patients (160 male and 110 female) with graphical and clinical evidence of affected mandibular third molars. The patients were divided into three equal groups. The findings represent that in the control group, the mean age was 28 (7) years, while in chlorhexidine group, it is 28 (6) years, and also the mean age in clove oil group 29 (8) years. There are no statistically significant differences in the mean ages (at p-value of 0.392). Also, it represents that there were no statistically differences in male to female ratio and it were equally distributed among the three study groups.

Naibaho, et al., (2020) performed a pre-posttest, quasi-experimental design with a control group on forty patients divided into two groups to investigate the effects of mouth-rinsing using normal saline solution and baking soda regarding comfort and pain in patients with OM undergoing CT. The

findings of their study revealed that the sociodemographic characteristics of patients depending on the interventional group age majority were include: arrear elderly patients (56-65 years), whereas for the control group age majority were initial elderly patients (46-55 years). Also, the majority of interventional group depending on the gender was male, so more than half (55%) of the patients' number were male gender, while in the control group more than half (60%) of the patients' number were male gender.

5.2. Discussion of the clinical data of the study sample:

The clinical data table (4-2) showed that all patients were not smokers and most (70%) of them in the clove oil group had never smoked, while 60% in the normal saline and 50% in the control group were previous smoker. The therapy duration for most (60%) of them in normal saline and control group was less than four months, but it was between 4-8 months for 50% of them in the clove oil group. There were no statistically significant differences seen between the three groups regarding patients' clinical data.

Kong, et al., (2016) performed a prospective design on fourteen patients who were randomly enrolled to either an interventional group or a control group to determine the safety and effectivity of herbal mouthwash that based on clove oil in the enhancement of radiation-induced OM in patients with cancer. The findings of this study reported that 42% of patients were current smoker, 57% of patients were previous smoker in the experimental group, whereas 57% of patients were current smoker, 28% of patients were previous smoker, and 14% of patients were never smoked in the control group. Also, this study reported there were no statistically significant differences in the patients' clinical properties between both two study groups.

Naibaho, et al., (2020) stated that the clinical characteristics based on the period of receiving CT treatment in patients with OM, reported that in the

normal saline solution interventional group approximately three quarter (70%) of the patients received CT for less than six months, 20% of patients for six months to one year, and 10% of patients received CT for more than one year.

5.3. Discussion the effect of clove oil and normal saline solution on the degree of oral toxicity:

Regarding the oral toxicity degrees pre and post interventional protocol using clove oil, as shown in table (4-3) it represents that 40% of patients have grade II and III oral toxicity before applying clove oil, after being given interventional protocol for seven days are 80% of patients at grade (I), and there are significant statistical differences between pre and post applying clove oil (at p-value of 0.003). Kong, et al., (2016) a study that conducted at Korean Internal Medicine Department, Cancer Center of Korean Medicine, Kyung Hee University Hospital at Gangdong, in Republic of Korea to assess the safety and effectiveness of herbal mouthwash that based on clove oil in enhancing radiation-induced OM. Reported that herbal mouthwash that based on clove oil was greatly limiting the duration of stage ≥ 2 OM. It also showed that the usage of herbal mouthwash that based on clove oil decreased the duration of stage 3 OM and limited the incidence of stage 3 OM. But however, on the contrary of our study, there were no statistically significant differences in this result (at p-value of 0.069).

Therefore, the application of clove oil significantly reduces the degree of oral toxicity in patients receiving CT, as symptoms were absent in the majority of patients after applying it and the researcher attributes the reason of the current study result to the clove oil effectivity on stopping the growth of different types of bacteria and fungi and relieving oral pain, also it has antioxidant and antiseptic activity toward oral pathogens.

Concerning the use of normal saline solution among patients with OM in the present study, as shown in table (4-4) revealed that the distribution of patients undergoing CT according to the oral toxicity degrees pre and post interventional protocol by normal saline solution, 40% of patients have grade II and IV oral toxicity pre applying normal saline solution, after being given interventional protocol for seven days are 20% of patients at grade (I), 50% at grade II, and there are significant statistical differences between pre and post applying normal saline solution (at p-value of 0.007). Therefore, the application of normal saline solution significantly reduces the degree of oral toxicity in patients receiving CT, as symptoms were absent in 20% of patients, and no patient remained in the grade IV after applying it. Alhamad, (2011) conducted a prospective clinical study on 10 patients with cancer who received combination of treatment to evaluate the effect of caphosol and normal saline solution in reducing the intensity of OM. The findings of this study showed that patients who used normal saline solution developed more stage two, less stage three, and no stage one OM. Similar to the results of the present study, there was no patient in normal saline solution group developed grade 4 OM.

Naibaho, et al., (2020) reported in their study that the characteristics of patients with cancer depending on the stage of OM as a result of the impact of CT revealed that in the normal saline experimental group, 40% was grade four OM. Huang, et al., (2018) conducted a randomized controlled design with two groups consists of 91 patients with OM treated at the cancer center of a medical center in northern Taiwan. The results of this study showed that the patients in the normal saline solution mouthwash group had greatly best quality of life regarding socio-emotional and physical aspects comparing with traditional care group. The general quality of life and the symptoms of OM caused by radiation were not significantly different between the study groups. Also, this study stated

that normal saline solution mouthwash and educational programs improve best socio-emotional and physical quality of life in patients with OM.

Sorensen et al., (2008) conducted a study to assess OM inhibition by using chlorhexidine in comparison with cryotherapy (oral cooling) and with normal saline solution. 206 patients were involved in the study, they were distributed into three different groups: the chloroxidine mouthwash group, cryotherapy group, and normal saline solution group. The findings reported that in the chlorhexidine mouthwash group, OM stage III or IV was significantly less frequent than in the normal saline solution group (at p-value of < 0.01). Furthermore, the duration of OM was significantly longer in the normal saline solution group (at p-value of 0.035). Also, grade 3 and 4 OM were somewhat more frequent than expected, being 32% in patients receiving normal saline solution mouth-rinse in control group. So that unlike the present study, the duration was greatly longer in the normal saline solution group compared with other two study groups.

Whereas in the control group as shown in table (4-5), revealed that the distribution of patients undergoing CT according to the oral toxicity degrees, 40% of patients have grade III oral toxicity when start collecting data, after seven days are 60% of patients at grade IV, and there are a significant statistical differences between pre and post seven days (at p-value of 0.025). Kartin, et al., (2014) performed a randomized-controlled, true-experimental design which includes 20 patients received oral care protocol in an experimental group and the control group which consists of 30 patients, to investigate the impact of an OM inhibition protocol on the quality of life and nutrition status for patients with cancer. They stated in their study that 14 patients in the control group got stage one OM in the second week but just two experimental group patients got stage one OM (at p-value of < 0.05). In addition, one intervention group patient

while six control group patients were got stage 4 OM (at p-value of < 0.001) by the seventh week.

Yavuz and Yılmaz, (2015) performed a longitudinal study on 16 children in the clinics of child oncology and hematology for the aim of investigating the effectiveness of the development of oral care education programs to the pediatric patients having tumors on the stage of OM. The researchers assigned the samples to a control group at the first step and the findings showed that there was significant statistical difference between the stage of OM in the control group and after application of educational program (at p-value of < .05). Finally, it was revealed that both the OM degree and the levels of pain reduced when the a properly planned educational program regarding mouth hygiene being given to the patients and when the patients were strongly and regularly committed to the oral hygiene.

Therefore, the researcher attributes this result to not implementing the interventional protocols which significantly increases the stage of oral toxicity in patients receiving CT.

5.4. Discussion the comparison of the effect on oral toxicity degree between the three study groups:

As shown in table (4-6), there are no statistically significant differences (at p-value of 0.623, at p-value of 0.630) in oral toxicity degree between clove oil and normal saline group before interventional protocol, but after seven days of intervention there are a significant statistical differences (at p-value of 0.000, at p-value of 0.006) between both group in favor the clove oil group.

Kong, et al., (2016) showed in their study conducted to assess the safety and effectiveness of herbal mouthwash that based on clove oil in minimizing and enhancing OM caused by RT in patients with cancer that this mouthwash can provide a useful impact on decreasing or inhibiting radiation-induced OM

in patients with cancer of the head and neck. As seem in this result, clove oil cures oral toxicity much more than normal saline solution. Therefore, the researcher attributes this result to the biological activities of clove oil such as antifungal, antibacterial, and antioxidant properties, as well as its antiseptic activity in oral infection which comes in the same line with a study conducted by Nuñez, et al., (2012) stated that clove oil consider potential antimicrobial product for topical usage because it is not remarkably not activated by mitigation or submit to the influence of organic materials.

Regarding comparison degree of oral toxicity between clove oil group and control group, table (4-7) show that there are no statistically significant differences at p-value of 0.725, at p-value of 0.573 in oral toxicity degree between clove oil and control group before the application of interventional protocol, but after seven days of interventional protocol there are significant statistical differences at p-value of 0.000, at p-value of 0.000 between both groups in favor the clove oil group. Therefore, clove oil cures oral toxicity much more than not applying the interventional protocol. Cupta and Prakash, (2021) stated in their study that clove oil was active against both groups of bacteria (oral pathogens) and fungi, thus clove oil was proved to be more effective. Also, they stated that clove oil was proved to be a much better antagonistic agent, exhibiting wide range of antimicrobial activity against the microbes causing oral or dental problems, and that it had antifungal effect.

Also, concerning comparison degree of oral toxicity between normal saline solution group and control group, as shown in the table (4-8), there are no statistically significant differences at p-value of (0.999) and (0.999) in oral toxicity degree between normal saline and control group before applying the interventional protocol, but after seven days of interventional protocol there are a significant statistical differences at p-value of (0.000), and (0.002) between both groups in favor the normal saline solution group. Therefore, normal saline

solution cures oral toxicity much more than disapplication of the interventional protocol. This result was agreed with Alhamad, (2011) study which revealed that normal saline solution mouth wash was considered safe and potent in decreasing the intensity of OM in high risk patients with cancer who get combination of CT. Thus, this finding encourages the result of the current study toward the effectivity of normal saline solution on OM. Also, the result was in the same line with a study performed by Naibaho, et al., (2020) which reported that the intensity of OM in respondents before being given normal saline mouthwash was severe pain (60%) in the intervention group, but it was mild pain (60%) post given intervention for five days. But, in the control group who having OM previously was severe (55%), and after five days was moderate (85%).

5.5. Discussion the effect of clove oil and normal saline solution on oral mucositis level:

The distribution of patients undergoing CT according to the OM level pre and post clove oil interventional protocol as shown in table (4-9) are 60% of patients had moderate level of OM before applying clove oil, but after being given interventional protocol for seven days are 100% of patients at mild level, and there were significant statistical differences in OM level at p-value of (0.005) and in total cumulative score at p-value of (0.000) of OM between pre and post applying clove oil. Therefore, the application of clove oil significantly reduces the degree and enhances OM level in patients undergoing CT. Vagliano, et al., (2011) conducted a descriptive study design which is nurse-led and was performed in 19 centers member of the Italian national transplant group to evaluate the occurrence and intensity of OM in patients receiving hematopoietic stem-cell transplantation. The findings of this study revealed that 142 (54.2%) of the 262 patients aged 0-18 years developed mild or moderate OM, while 67

of 262 patients (25.6%) got severe OM. Furthermore, the occurrence of severe OM in adult patients was identified in 300 patients (24.4%), but severe OM was observed in 32 patients (9.2%) in the elderly patient group.

Concerning the effect of normal saline solution on the level of OM, the distribution of patients receiving CT pre and post normal saline solution interventional protocol showed that 60% of patients had severe level of OM before applying normal saline solution, but after being given interventional protocol for seven days was 70% of patients at mild level, and there were significant statistical differences in OM level at p-value of (0.005) and in total cumulative score at p-value of (0.000) of OM between pre and post applying normal saline solution as shown in table (4-10). Brown and Gupta, (2020) stated in their study that normal saline solution can provide relief of mild or moderate oral mucositis pain, they also revealed that such salt mouthwash is inexpensive, safe, and effective in treating OM. Furthermore, patients can make a formulation of this solution at home, and can use it as frequently as every four hours. Huang, et al., (2000) performed a study on 17 patients with cancer of the head and neck to investigate the effectiveness of oral glutamine on OM caused by RT in patients with head and neck cancer who receiving RT. The results of their study showed that many patients had a readiness to get much intense OM in the normal saline solution group, also significant statistically differences were observed only in objective OM analysis at p-value of (0.0060) rather than subjective OM at p-value of (0.1073).

The researcher attributes the causes that make the application of normal saline solution significantly reduces the level of OM in patients receiving CT to the disinfectant properties of normal saline solution and its basic role in dry out and disinfect wounds, therefore rinsing the mouth with a normal saline solution promote healthy oral cavity and encourage recovery from mouth ulcers caused by OM.

Whereas in the control group, the distribution of patients undergoing CT according to the OM level as shown in table (4-11) reveals that 50% of patients have severe level of OM when start collecting data, but after seven days the number of patients with severe level increased and reached the ratio of 80%, and there are significant statistical differences in OM level at p-value of (0.025) and in total cumulative score at p-value of (0.000) of OM between the first and second measurement. Therefore, the disapplication of interventional protocol increases the level and total cumulative score of OM in patients receiving CT. Shieh, et al., (1997) conducted a randomized trial for the comparison of the effectiveness of three mouth care protocols in delay the appearance of OM and decreasing oral cavity wounds on 30 patients with cancer undergoing RT, they reported in their study that 60 percent of the control group patients got OM in the primary two weeks comparing with 40 percent in the first experimental group and 20 percent in the second experimental group. Also, the result of this study revealed that all control group patients got OM in the primary four weeks comparing with 75 percent in the first experimental group and 45% in the second experimental group.

Kartin, et al., (2014), according to their true-experimental study design, randomized-controlled trail, which includes 20 patients received oral care protocol in an intervention group and 30 control group patients, OM degree in the control group was progressed more rapidly as cancer treatment weeks progressed compared to the intervention group that received oral care protocol. Pai, et al., (2019) conducted an outcome-evaluator, randomized-blinded study design on nine patients who admitted at particular units of a hospital of tertiary care and radiation oncology in India. This study revealed that there was a great needed to have an ideal protocol regarding oral care of patients with cancer. Also, the findings of this study reported that OM, infection, and difficulty swallowing were delayed when applying interventional protocol comparing

with the control group. Therefore, from the researcher opinion of the current study and the results of the previous studies which indicate that it is useful for monitoring the current information and practice regarding oral care among staff of the nursing profession and improving the patient result by performing and assessing the protocol of oral care for the inhibition or minimization of oral cavity problems of patients who stay in the hospitals and receiving CT or RT.

5.6. Discussion the comparison of the effect on oral mucositis level between the three study groups:

Concerning comparison effect of clove oil and normal saline solution on oral mucositis level, there were no significant statistical differences at p-value of (0.623 and (0.086) in level and total cumulative score of OM between clove oil group and normal saline solution group before the interventional protocol as shown in table (4-12), but after seven days of interventional protocol there are a significant statistical differences at p-value of (0.011) and (0.006) between both groups in favor the clove oil group. Al-Barrak and Mahmoud, (2011) performed a study to evaluate the antibacterial activity of clove oil, they were reported in their study that clove oil was known for its antibacterial activity which is due to several components and may be tested as an alternative to traditional antibiotics therapy. Cloves were strongly effective due to their high content of eugenol, which was known to inhibit the growth of gram negative and positive and acid-fast bacterium as well as fungi. Also, clove oil was shown to have both antibacterial and anti-adhesion capabilities. These anti-adhesion activities beside of their previously known antibacterial activity were in favor of using this oil in oral treatment.

Thus, the researcher attributes this result to the significant role of clove oil in antibacterial, antifungal, and antioxidant activity, furthermore its activity

to promote healing process and pain relieve. Therefore, clove oil cures OM much more than normal saline solution.

Whereas the effect on level and total cumulative score of OM between clove oil group and control group shows no significant statistical differences at p-value of (0.650), at p-value of (0.457) before the application of an interventional protocol as table (4-13) revealed, but after seven days of intervention there are a significant statistical differences (at p-value of 0.042, at p-value of 0.000) between both groups in favor the clove oil group. Thus, clove oil cures OM much more than disapplication of the interventional protocol. Kartin, et al., (2014) reported that OM intensity or severity was low in both two experimental groups that taking the protocol of oral care comparing with the control group, also the result of their study clarifies that OM rate may be decreased with the application of the protocol of oral care. Probable OM symptoms and pain may be eliminated and occur nutritional improvement with oral care protocol that should be applied by nurses.

Baker, et al., (2018) stated in their study that clove oil was effective against yeasts and fungi, as well as against a wide range of acid-fast, gram-positive and negative bacteria. Also, various fungi were susceptible to clove oil. Agrawal et al., (2014) reported in their study that clove oil shows an antimicrobial activity and this suggests its usage as an adjuvant to oral cavity therapy. It acts as an antioxidant and anti-inflammatory agent at low concentration. Clove oil is an important herbal medication which have a variety of different uses like antifungal, antioxidant, antiviral, anti-inflammatory, antibacterial, antipyretic, analgesic, antimycotic, antiulcerogenic, and a wide variety of uses.

Therefore, from the researcher's opinion the reason for significant OM healing when using clove oil compared to the control group is due to many of

the chemical properties in the composition of clove oil that accelerate the healing process and facilitate wound healing.

Also, regarding comparison the effect on OM level between normal saline solution and control group as noted in table (5-14), there are no statistically significant differences at p-value of (0.425) and (0.389) in level and total cumulative score of OM between both groups prior to the interventional protocol application, but after seven days of applying normal saline solution interventional protocol appeared significant statistical differences at p-value of (0.000) and (0.000) between both groups in favor the normal saline solution group. So that, normal saline solution cures OM much more than not applying the interventional protocol. Naibaho, et al., (2020) performed a pre-posttest study, quasi-experimental design with a control group on 40 patients divided into two groups to determine the effectivity of mouth-rinsing using normal saline solution and baking soda regarding the comfort and pain in patients with OM receiving CT. The findings of their study stated that the distribution of respondents' comfort before being given normal saline mouthwash in the experimental group, 55% of patients was a few not-good comfort (score 2), but post given oral care mouthwash for five days 65% of patients was a highly good comfort (score 4). While in the obtaining control group who got OM before, 70% of patients was a few not-good comfort (score 2), but after five days 65% of patients was a little good comfort (score 3).

5.7. Discussion the differences between oral mucositis level with patient's socio-demographic and clinical data in clove oil group, normal saline solution group, and control group:

There are no statistically significant differences in level of OM related to any of socio-demographic and clinical variables in all three groups: (clove oil group, normal saline solution group, and control group) as shown in tables

(4-15),(4-16), and (4-17). Shieh, et al., (1997) in their randomized trial using protocol of mouth care for retarding the onset of OM and decreasing oral cavity wound on patients with cancer revealed that, none of the sociodemographic characteristics and clinical data were having significantly statistical differences across the three groups of the study at p-value of (0.295).

Kartin, et al., (2014) conducted a randomized-controlled experimental study which consists of two groups: 20 patients who received oral care protocol and 30 control group patients, and showed that social and demographic properties of both groups of the study were similar and there is no statistically significant. Therefore, as shown in the result of these three tables, there was good outcomes regarding OM level but not differently between sociodemographic characteristics and clinical data between these three study groups, and the researcher think that the cause of these results is due to the effect of interventional protocol which did not apply to one characteristic without another, but rather positively affected all sociodemographic characteristics and clinical data especially in clove oil experimental group. For example, the effect of clove oil was positive in all age groups.

Whereas concerning the differences between level of OM among patients undergoing CT with their sociodemographic characteristics and clinical data before and after application of interventional protocol in clove oil group, normal saline solution group, and control group respectively, as shown in tables (4-18), (4-19), and (4-20) exposed that there are no significant statistical differences in level of OM related to any of socio-demographic and clinical variables in the three groups before and after the application of interventional protocol. The researcher shows that there are no clear differences between the three OM levels (mild, moderate, and severe) and the sample's aggregative in one level, which is the mild level. This means that the effect of clove oil was not different between sociodemographic characteristics and clinical data as it

was positively effective on all clove oil group's category evenly including age, gender, marital status, educational level, smoking, and CT duration , so there were no significantly statistical differences appeared.

Finally, as a result of the findings of the current study the researcher proved that both clove oil and normal saline solution interventional protocols were positively effect on decreasing the level of oral mucositis and oral toxicity grades but in varied degrees of more effectivity in favor to the clove oil as it more potent and effective.

Chapter Six "Conclusions & Recommendations"

Chapter Six

Conclusions & Recommendations

6.1. Conclusions:

The study concluded that:

1. Most of patients enrolled in clove oil experimental group are between 41-50 years of age, males, have primary level of education, and the majority of them are married.
2. Mouth care using clove oil gargling procedure is potent in decreasing OM grade and enhancing the comfort of patients undergoing CT, clove oil was considered effective in minimizing the severity of OM and the degree of oral toxicity in patients with cancer undergoing CT.
3. Normal saline solution was considered effective in minimizing the severity of OM and the degree of oral toxicity in patients with cancer undergoing CT, but in less effectivity than clove oil gargling procedure.
4. The effect of clove oil on level of OM was not different between sociodemographic characteristics and clinical data as it was positively effective on all clove oil group's category evenly.

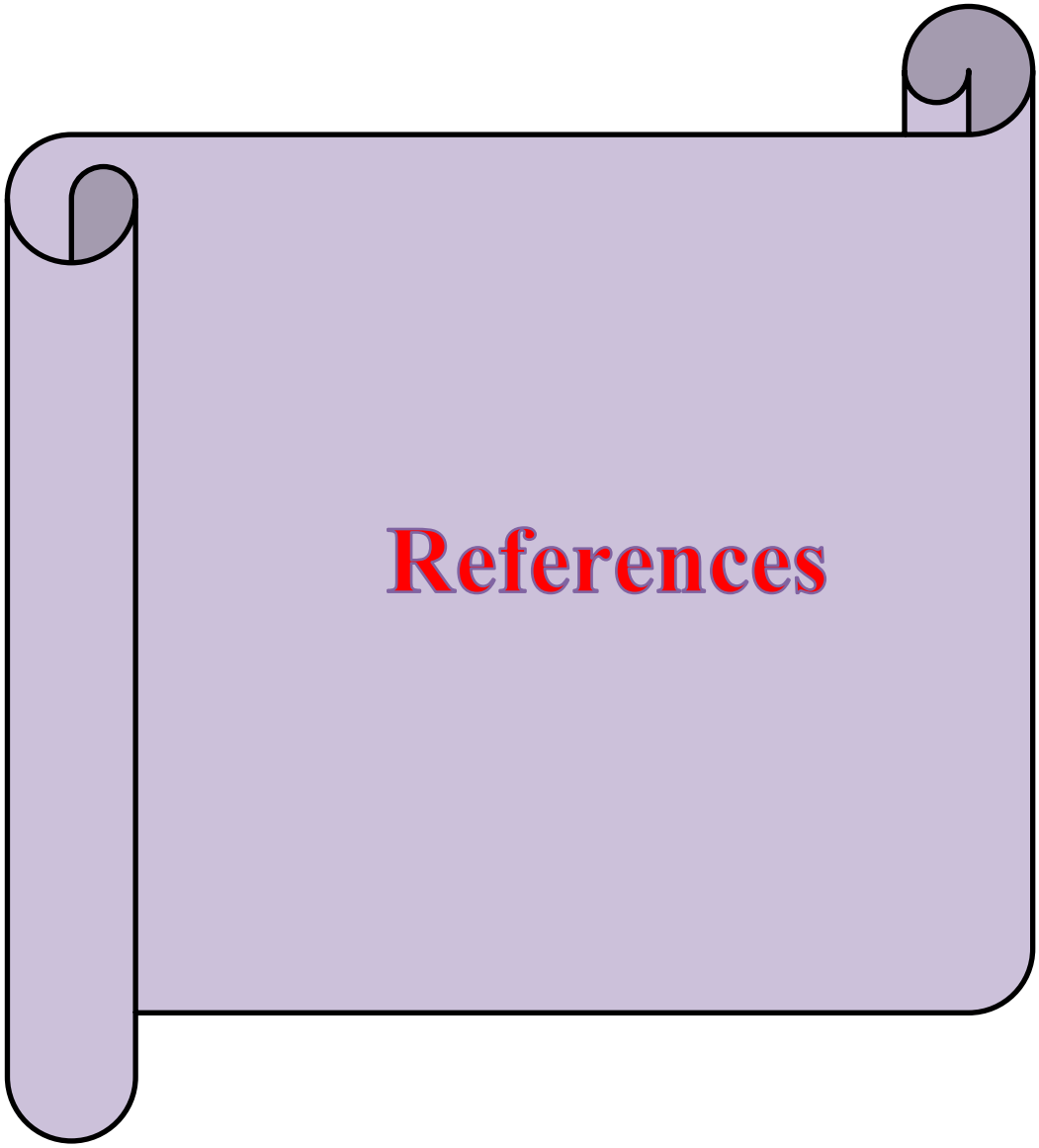
6.2. Recommendations:

The researcher recommends the following issues:

1. Clove oil is preferred to be adopted for daily use like toothpastes and to be used three times per day because this can help to decrease the overall burden of OM complications and treatment budget on both patients and hospital.
2. It's necessary to provide regular and continuous instructions and information for patients undergoing CT to improve their oral care using clove oil or normal saline solution, to explain the importance of oral care protocol by the nurses to those before starting treatment, and also to

assess a patient's mouth daily with a standardized form to early discover any problems in the oral cavity before they got worsen.

3. Nursing staff must give additional focus on the prevention of OM, early diagnosis, managing it when it occurs, decreasing and preventing oral infection related to OM, and patient education regarding oral care.
4. An instructional teaching program should be provided for nurses working at oncology wards regarding care of OM in patients undergoing CT, and also providing patients with a booklet on how to care for their mouth and identifying oral problems at an early time.
5. Further and future research efforts on larger sample size are needed for the evaluation of efficacy of clove oil gargling procedure for its regular use in the OM care products to determine its effect on the level and grade of oral mucositis especially regarding the healing process.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Appendices

Appendix A-I

Official permission from Nursing College Council/ University of Kerbala

Republic of Iraq
Ministry of higher education & scientific research
University of Karbala
College of Nursing
Graduate studies Division

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جـــامعة كربلاء
كـلية التـمريـض
شعبة الدراسات العليا

العدد : د ع / 138

التاريخ : 30 / 12 /2021

الى / مركز التدريب و تنمية الموارد

م/ تسهيل مهمة

تحية طيبة...

يرجى التفضل بالموافقة على تسهيل مهمة السيدة (امنية عبد رسن) لغرض الحصول على احصائيات تتضمن الاعداد والنسب المئوية للمرضى المصابين بالاورام وبشكل تفصيلي واعداد المرضى الخاضعين منهم للعلاج الكيمياوي للسنوات من 2015 ولغاية 2021 في مركز الامام الحسين (ع) للاورام وامراض الدم وذلك بهدف الاستفادة منها في رسالة الماجستير الموسومة (اثر استخدام زيت القرنفل بالضد من المحلول الملحي المتعادل في علاج التهاب الغشاء المخاطي للفم بين المرضى الخاضعين للعلاج الكيمياوي)و هي احدى طلبة الدراسات العليا / الماجستير في كليتنا / للعام الدراسي (2020-2021) و مستمرة في الدوام في الوقت الحاضر.

... مع التقدير ...

أ.د علي كريم خضير
العميد وكالة
30 / 12 / 2021

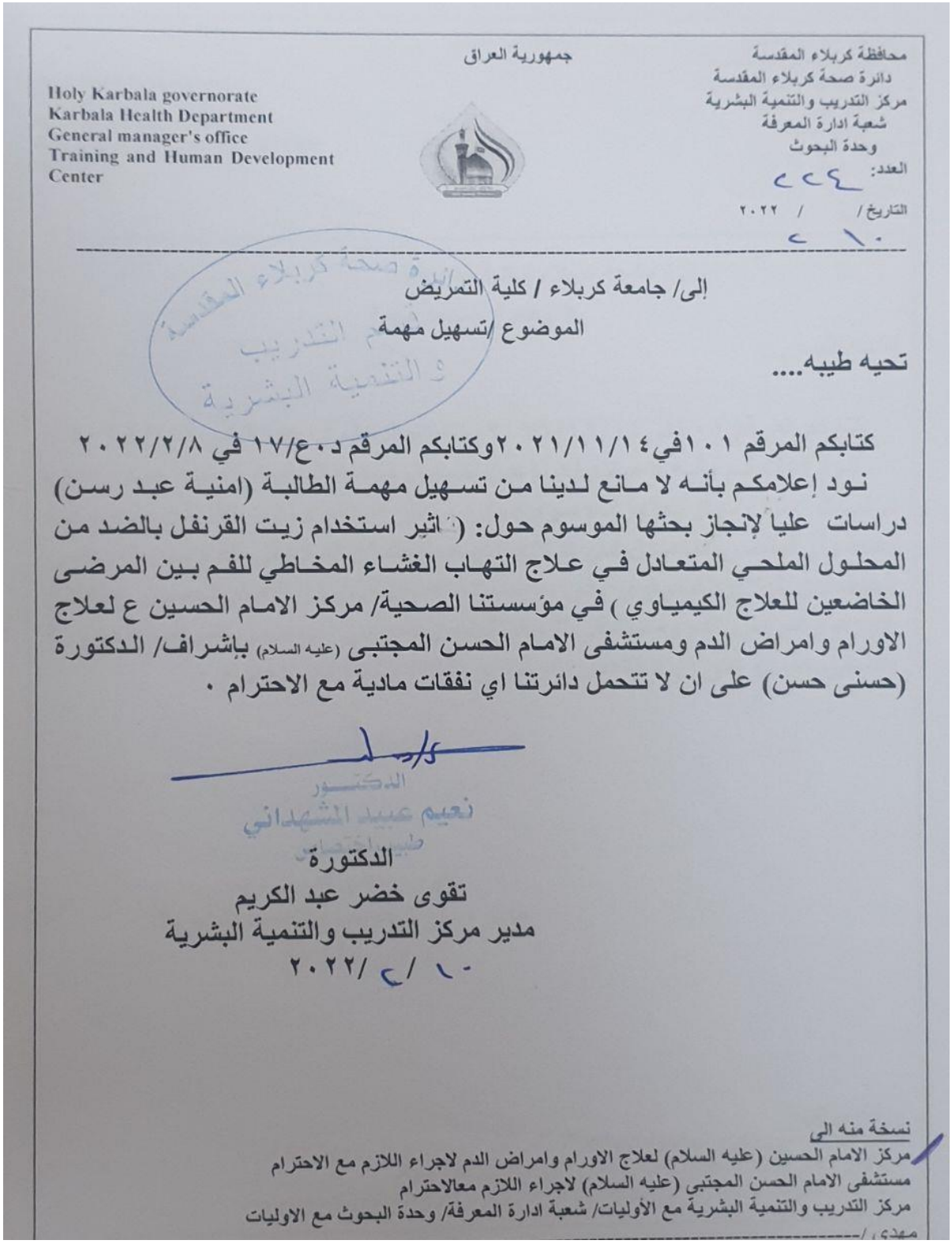
جامعة كربلاء - كلية التمريض
شعبة الدراسات العليا

نسخة منه الى :-
- مكتب السيد المعاون العلمي المحترم.
- شعبة الدراسات العليا.

العنوان : العراق - محافظة كربلاء المقدسة - حي الموظفين - جامعة كربلاء
Mail: nursing@uokerbala.edu.iq websitnursing.uokerbala.edu.iq

Appendix A-II

Official permission from Iraqi Ministry of Health/ Training and Human Development Center/ Kerbala Health Department



جمهورية العراق

محافظة كربلاء المقدسة
دائرة صحة كربلاء المقدسة
مركز التدريب والتنمية البشرية
شعبة ادارة المعرفة
وحدة البحوث
العدد: ٢٢٤
التاريخ / / ٢٠٢٢
١٠ / ٢

Holy Karbala governorate
Karbala Health Department
General manager's office
Training and Human Development Center

إلى/ جامعة كربلاء / كلية التمريض
الموضوع /تسهيل مهمة

تحيه طيبه....

كتابكم المرقم ١٠١في٢٠٢١/١١/١٤وكتابكم المرقم د٠ع/١٧ في ٢٠٢٢/٢/٨
نود إعلامكم بأنه لا مانع لدينا من تسهيل مهمة الطالبة (امنية عبد رسن) دراسات عليا لإنجاز بحثها الموسوم حول: (اثير استخدام زيت القرنفل بالضد من المحلول الملحي المتعادل في علاج التهاب الغشاء المخاطي للفم بين المرضى الخاضعين للعلاج الكيمياوي) في مؤسستنا الصحية/ مركز الامام الحسين ع لعلاج الاورام وامراض الدم ومستشفى الامام الحسن المجتبى (عليه السلام) بإشراف/ الدكتورة (حسنى حسن) على ان لا تتحمل دائرتنا اي نفقات مادية مع الاحترام ٠

الدكتور
نعيم عبيد الشهداني

الدكتورة
تقوى خضر عبد الكريم
مدير مركز التدريب والتنمية البشرية
٢٠٢٢/ ٦ / ١٠

نسخة منه الى
مركز الامام الحسين (عليه السلام) لعلاج الاورام وامراض الدم لاجراء اللازم مع الاحترام
مستشفى الامام الحسن المجتبى (عليه السلام) لاجراء اللازم معالاحترام
مركز التدريب والتنمية البشرية مع الأوليات/ شعبة ادارة المعرفة/ وحدة البحوث مع الاوليات
مهدي /

Appendix A-III

Official permission from Iraqi Ministry of Health/ Kerbala Health Department/ Imam Al-Hussein Oncology Center

Karbala Health Directorate

Karbala Center for Oncological and hematological disease

محافظة كربلاء المقدسة

دائرة صحة كربلاء

مكتب المدير العام

مركز الامام الحسين (ع)

لعلاج الاورام وامراض الدم

العدد:

التاريخ:

الى / دائرة صحة كربلاء المقدسة/مركز التدريب والتنمية البشرية

م/ بيان راي

السلام عليكم.....

كتابكم ذو العدد 3837 في 2021/11/21

لا مانع لدينا من تسهيل مهمة الطالبة (امنية عبد رسن) لانجاز بحثها الموسوم(أثر استخدام زيت القرنفل بالضد من المحلول الملحي المتعادل في علاج التهاب الغشاء المخاطي للفم بين المرضى الخاضعين للعلاج الكيمياوي) في مركزنا ويكون المشرف العملي للبحث الدكتورة (حسنى حسن) على ان لا تتحمل دائرتنا اي نفقات مادية مع الاحترام.

الطبيب

د. كرار كاظم الموسوي

مدير مركز الامام الحسين لعلاج الاورام

وامراض الدم

2021/ /

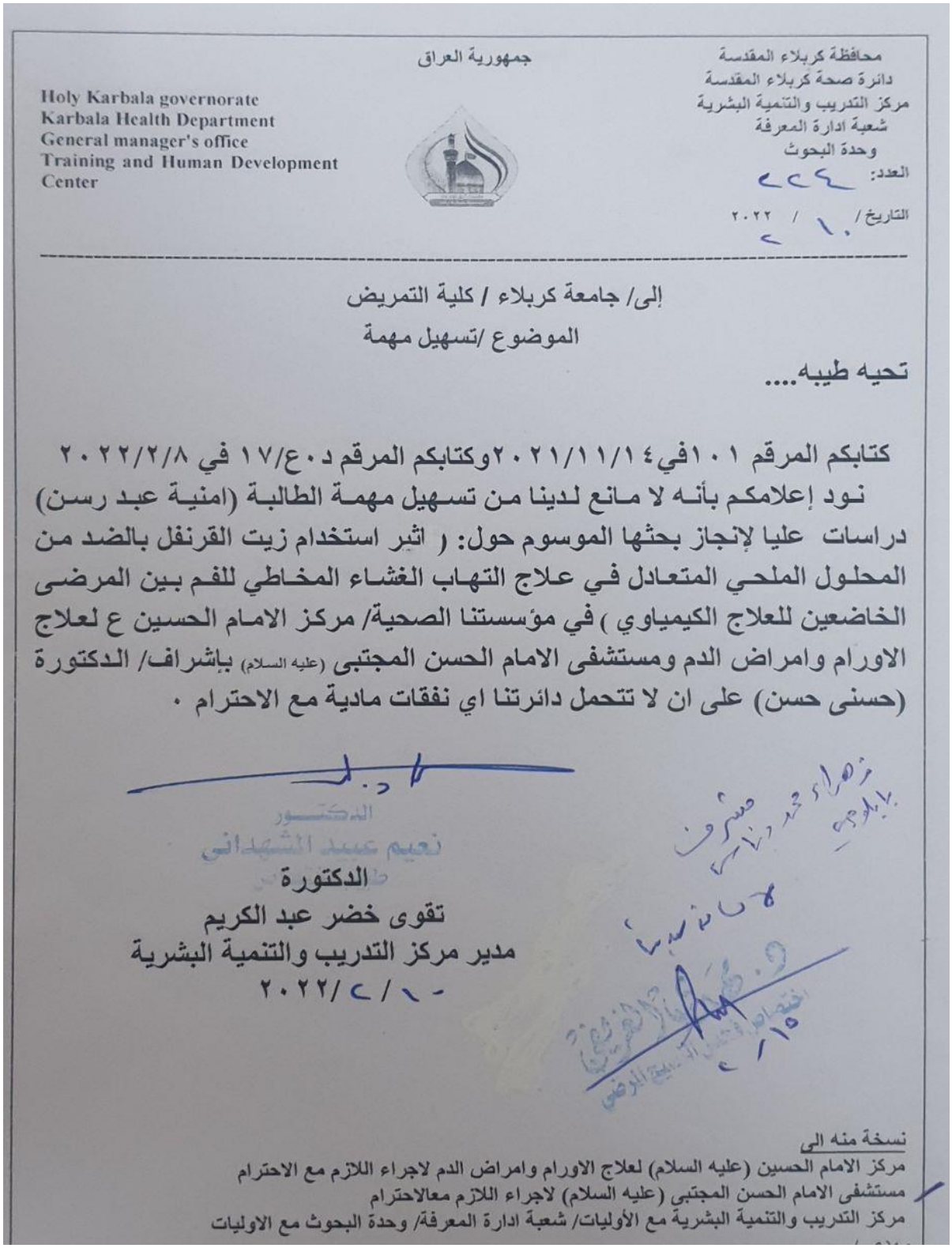
نسخه منه الى :

- الموارد البشرية
- التدريب والتطوير

11/21

Appendix A-III

Official permission from Iraqi Ministry of Health/ Kerbala Health Department/ Imam Al-Hassan AL-Mujtaba teaching hospital



جمهورية العراق

محافظة كربلاء المقدسة
دائرة صحة كربلاء المقدسة
مركز التدريب والتنمية البشرية
شعبة ادارة المعرفة
وحدة البحوث
العدد: ٤٤٤
التاريخ / ١٠ / ٢٠٢٢

Holy Karbala governorate
Karbala Health Department
General manager's office
Training and Human Development Center

إلى/ جامعة كربلاء / كلية التمريض
الموضوع /تسهيل مهمة

تحيه طيبه....

كتابكم المرقم ١٠١في٢٠٢١/١١/١٤وكتابكم المرقم د٠ع/١٧ في ٢٠٢٢/٢/٨
نود إعلامكم بأنه لا مانع لدينا من تسهيل مهمة الطالبة (امنية عبد رسن) دراسات عليا لإنجاز بحثها الموسوم حول: (اثير استخدام زيت القرنفل بالضد من المحلول الملحي المتعادل في علاج التهاب الغشاء المخاطي للفم بين المرضى الخاضعين للعلاج الكيمياوي) في مؤسستنا الصحية/ مركز الامام الحسين ع لعلاج الاورام وامراض الدم ومستشفى الامام الحسن المجتبى (عليه السلام) بإشراف/ الدكتورة (حسنى حسن) على ان لا تتحمل دائرتنا اي نفقات مادية مع الاحترام ٠

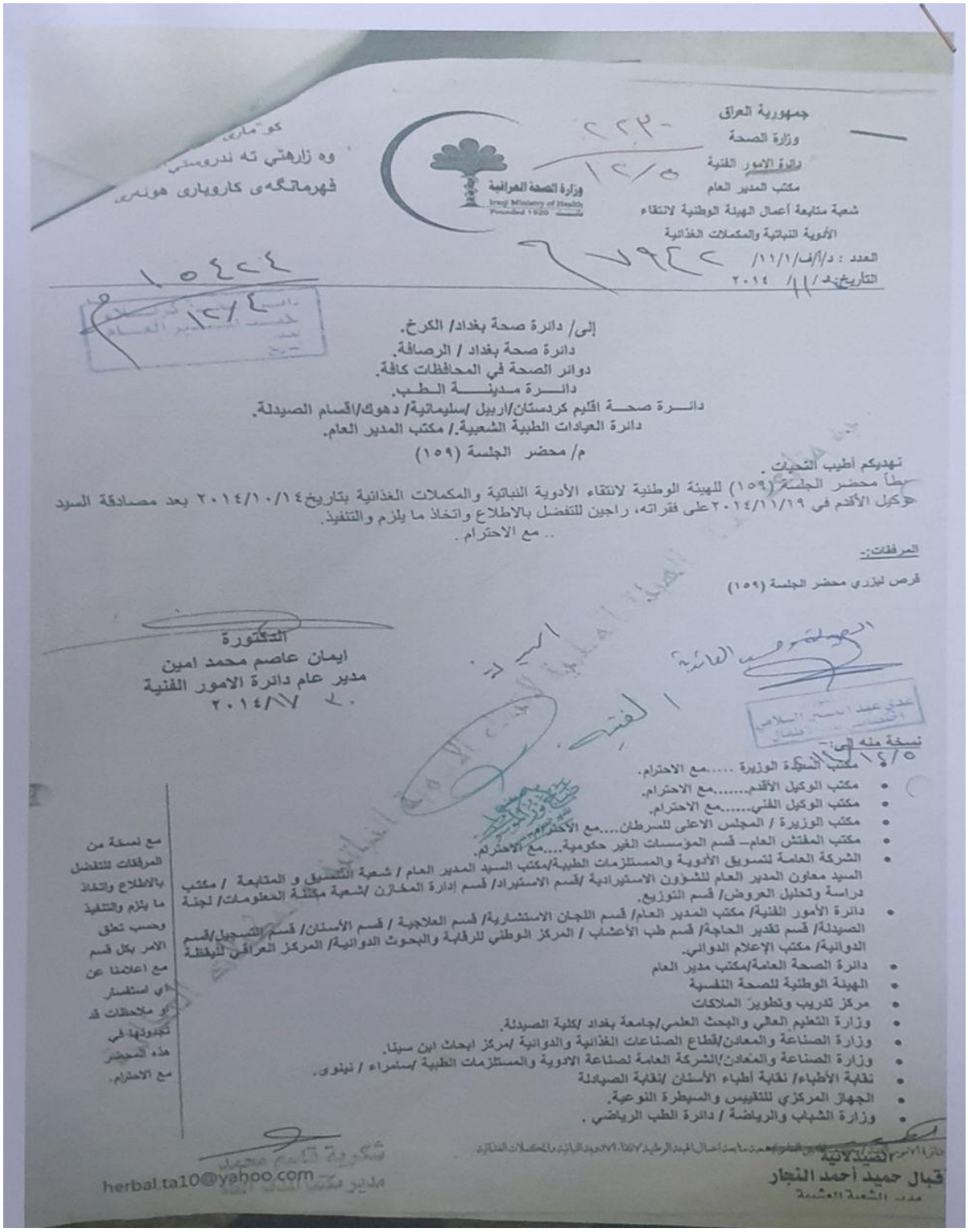
الدكتور
نعيم عبيد الشهداني

الدكتورة
تقوى خضر عبد الكريم
مدير مركز التدريب والتنمية البشرية
٢٠٢٢/ ٤ / ١٠

نسخة منه الى
مركز الامام الحسين (عليه السلام) لعلاج الاورام وامراض الدم لاجراء اللازم مع الاحترام
مستشفى الامام الحسن المجتبى (عليه السلام) لاجراء اللازم معالاحترام
مركز التدريب والتنمية البشرية مع الأوليات/ شعبة ادارة المعرفة/ وحدة البحوث مع الاوليات

Appendix A-IV

Official permission for safety usage of clove oil liquid on human being from Iraqi Ministry of Health/ Registered Health Products



جمهورية العراق
وزارة الصحة
دائرة الامور الفنية
مكتب المدير العام
شعبة متابعة أعمال الهيئة الوطنية لانتقاء
الأدوية النباتية والمكملات الغذائية
العدد : د/أ/ف/١/١١/ ٧٩٢٢
التاريخ: ١٤/ ١١/ ٢٠١٤

وزارة الصحة العراقية
Iraqi Ministry of Health
Founded 1920

إلى/ دائرة صحة بغداد/ الكرخ.
دائرة صحة بغداد / الرصافة.
دوائر الصحة في المحافظات كافة.
دائـــرة مـدينـــة الـطـب.
دائـــرة صحـــة اقليم كردستان/اربيل /سليمانية/ دهوك/اقسام الصيدلة.
دائرة العيادات الطبية الشعبية./ مكتب المدير العام.
م/ محضر الجلسة (١٥٩)

تهديكم أطيب التحيات .
طياً محضر الجلسة (١٥٩) للهيئة الوطنية لانتقاء الأدوية النباتية والمكملات الغذائية بتاريخ٢٠١٤/١٠/١٤ بعد مصادقة السيد وكيل الأقدم في ٢٠١٤/١١/١٩على فقراته، راجين للتفضل بالاطلاع واتخاذ ما يلزم والتنفيذ.
.. مع الاحترام .

المرفقات:-
قرص ليزري محضر الجلسة (١٥٩)

الدكتورة
ايمان عاصم محمد امين
مدير عام دائرة الامور الفنية
٢٠١٤/١١/ ٢٠

نسخة منه إلى:-
- مكتب السيدة الوزيرة .....مع الاحترام.
- مكتب الوكيل الأقدم.....مع الاحترام.
- مكتب الوكيل الفني.....مع الاحترام.
- مكتب الوزيرة / المجلس الاعلى للسرطان....مع الاحترام.
- مكتب المفتش العام– قسم المؤسسات الغير حكومية....مع الاحترام.
- الشركة العامة لتسويق الأدوية والمستلزمات الطبية/مكتب السيد المدير العام / شعبة التنسيق و المتابعة / مكتب السيد معاون المدير العام للشؤون الاستيرادية /قسم الاستيراد/ قسم إدارة المخازن /شعبة مكننة المعلومات/ لجنة دراسة وتحليل العروض/ قسم التوزيع.
- دائرة الأمور الفنية/ مكتب المدير العام/ قسم اللجان الاستشارية/ قسم العلاجية / قسم الأسنان/ قسم التسجيل/قسم الصيدلة/ قسم تقدير الحاجة/ قسم طب الأعشاب / المركز الوطني للرقابة والبحوث الدوائية/ المركز العراقي لليقظة الدوائية/ مكتب الإعلام الدوائي.
- دائرة الصحة العامة/مكتب مدير العام
- الهيئة الوطنية للصحة النفسية
- مركز تدريب وتطوير الملاكات
- وزارة التعليم العالي والبحث العلمي/جامعة بغداد /كلية الصيدلة.
- وزارة الصناعة والمعادن/قطاع الصناعات الغذائية والدوائية /مركز ابحاث ابن سينا.
- وزارة الصناعة والمعادن/الشركة العامة لصناعة الادوية والمستلزمات الطبية /سامراء / نينوى.
- نقابة الأطباء/ نقابة أطباء الأسنان /نقابة الصيادلة
- الجهاز المركزي للتقييس والسيطرة النوعية.
- وزارة الشباب والرياضة / دائرة الطب الرياضي .

مع نسخة من المرفقات للتفضل بالاطلاع واتخاذ ما يلزم والتنفيذ وحسب نطاق الامر بكل قسم مع اعلامنا عن اي استفسار او ملاحظات قد تجدونها في هذا المحضر مع الاحترام.

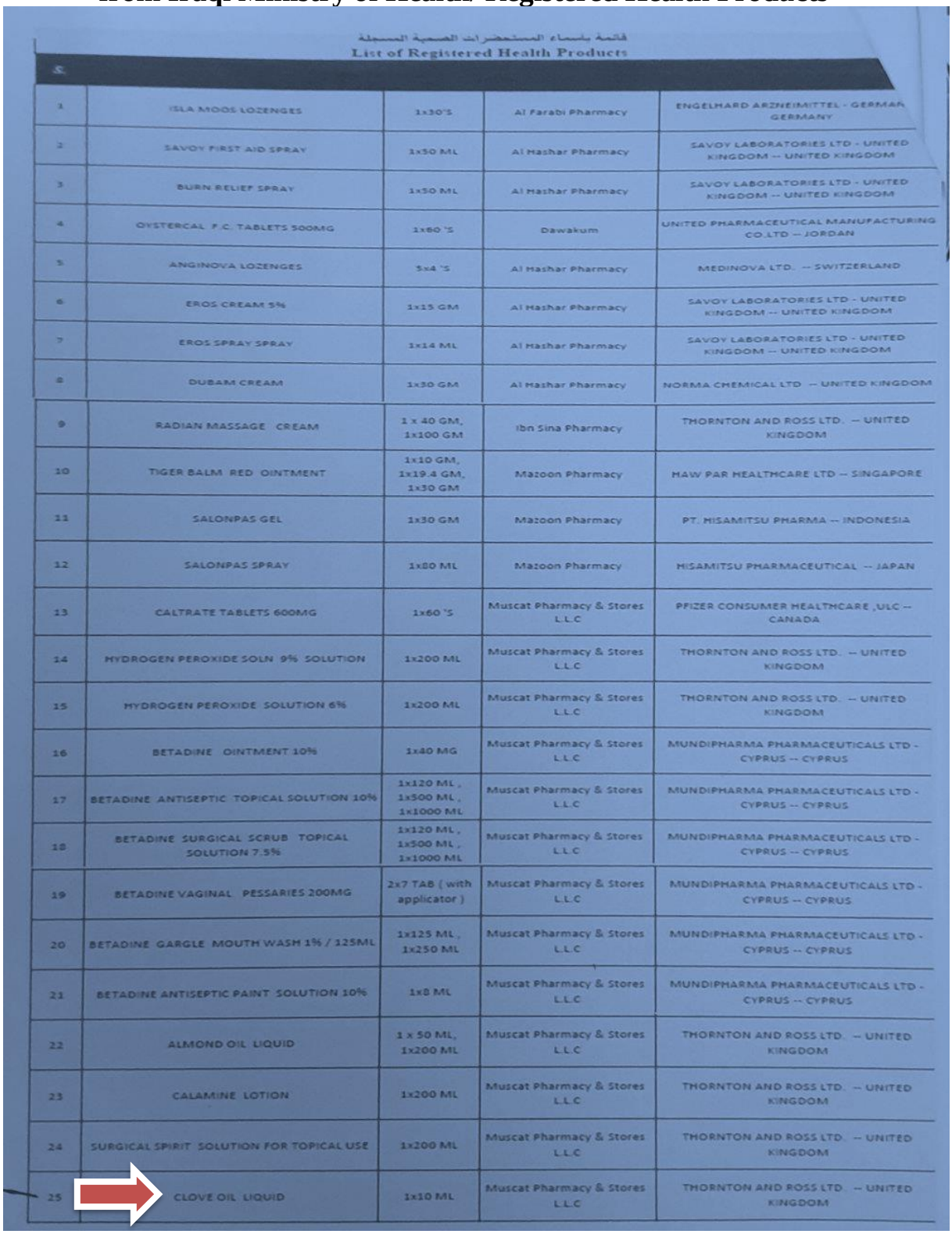
شكوة تاتم محمد
مدير مكتب

herbal.ta10@yahoo.com

قبال حميد أحمد النجار
مدير الشعبة العشبية

Appendix A-IV

Official permission for safety usage of clove oil liquid on human being from Iraqi Ministry of Health/ Registered Health Products



قائمة بأسماء المستحضرات الصيدلية المسجلة
List of Registered Health Products

S.				
1	ISLA MOOS LOZENGES	1x30'S	Al Farabi Pharmacy	ENGELHARD ARZNEIMITTEL - GERMAN GERMANY
2	SAVOY FIRST AID SPRAY	1x50 ML	Al Hashar Pharmacy	SAVOY LABORATORIES LTD - UNITED KINGDOM -- UNITED KINGDOM
3	BURN RELIEF SPRAY	1x50 ML	Al Hashar Pharmacy	SAVOY LABORATORIES LTD - UNITED KINGDOM -- UNITED KINGDOM
4	OYSTERCAL F.C. TABLETS 500MG	1x60 'S	Dawakum	UNITED PHARMACEUTICAL MANUFACTURING CO.LTD -- JORDAN
5	ANGINOVA LOZENGES	5x4 'S	Al Hashar Pharmacy	MEDINOVA LTD. -- SWITZERLAND
6	EROS CREAM 5%	1x15 GM	Al Hashar Pharmacy	SAVOY LABORATORIES LTD - UNITED KINGDOM -- UNITED KINGDOM
7	EROS SPRAY SPRAY	1x14 ML	Al Hashar Pharmacy	SAVOY LABORATORIES LTD - UNITED KINGDOM -- UNITED KINGDOM
8	DUBAM CREAM	1x30 GM	Al Hashar Pharmacy	NORMA CHEMICAL LTD -- UNITED KINGDOM
9	RADIAN MASSAGE CREAM	1 x 40 GM, 1x100 GM	Ibn Sina Pharmacy	THORNTON AND ROSS LTD. -- UNITED KINGDOM
10	TIGER BALM RED OINTMENT	1x10 GM, 1x19.4 GM, 1x30 GM	Mazoon Pharmacy	HAW PAR HEALTHCARE LTD -- SINGAPORE
11	SALONPAS GEL	1x30 GM	Mazoon Pharmacy	PT. HISAMITSU PHARMA -- INDONESIA
12	SALONPAS SPRAY	1x80 ML	Mazoon Pharmacy	HISAMITSU PHARMACEUTICAL -- JAPAN
13	CALTRATE TABLETS 600MG	1x60 'S	Muscat Pharmacy & Stores L.L.C	PFIZER CONSUMER HEALTHCARE ,ULC -- CANADA
14	HYDROGEN PEROXIDE SOLN 9% SOLUTION	1x200 ML	Muscat Pharmacy & Stores L.L.C	THORNTON AND ROSS LTD. -- UNITED KINGDOM
15	HYDROGEN PEROXIDE SOLUTION 6%	1x200 ML	Muscat Pharmacy & Stores L.L.C	THORNTON AND ROSS LTD. -- UNITED KINGDOM
16	BETADINE OINTMENT 10%	1x40 MG	Muscat Pharmacy & Stores L.L.C	MUNDIPHARMA PHARMACEUTICALS LTD - CYPRUS -- CYPRUS
17	BETADINE ANTISEPTIC TOPICAL SOLUTION 10%	1x120 ML , 1x500 ML , 1x1000 ML	Muscat Pharmacy & Stores L.L.C	MUNDIPHARMA PHARMACEUTICALS LTD - CYPRUS -- CYPRUS
18	BETADINE SURGICAL SCRUB TOPICAL SOLUTION 7.5%	1x120 ML , 1x500 ML , 1x1000 ML	Muscat Pharmacy & Stores L.L.C	MUNDIPHARMA PHARMACEUTICALS LTD - CYPRUS -- CYPRUS
19	BETADINE VAGINAL PESSARIES 200MG	2x7 TAB (with applicator)	Muscat Pharmacy & Stores L.L.C	MUNDIPHARMA PHARMACEUTICALS LTD - CYPRUS -- CYPRUS
20	BETADINE GARGLE MOUTH WASH 1% / 125ML	1x125 ML , 1x250 ML	Muscat Pharmacy & Stores L.L.C	MUNDIPHARMA PHARMACEUTICALS LTD - CYPRUS -- CYPRUS
21	BETADINE ANTISEPTIC PAINT SOLUTION 10%	1x8 ML	Muscat Pharmacy & Stores L.L.C	MUNDIPHARMA PHARMACEUTICALS LTD - CYPRUS -- CYPRUS
22	ALMOND OIL LIQUID	1 x 50 ML, 1x200 ML	Muscat Pharmacy & Stores L.L.C	THORNTON AND ROSS LTD. -- UNITED KINGDOM
23	CALAMINE LOTION	1x200 ML	Muscat Pharmacy & Stores L.L.C	THORNTON AND ROSS LTD. -- UNITED KINGDOM
24	SURGICAL SPIRIT SOLUTION FOR TOPICAL USE	1x200 ML	Muscat Pharmacy & Stores L.L.C	THORNTON AND ROSS LTD. -- UNITED KINGDOM
25	CLOVE OIL LIQUID	1x10 ML	Muscat Pharmacy & Stores L.L.C	THORNTON AND ROSS LTD. -- UNITED KINGDOM

Ethical Considerations

Appendix B-I

Ministry of Higher Education and Scientific Research
University of Karbala / College of Nursing
Scientific Research Ethics Committee

وزارة التعليم العالي والبحث العلمي
جامعة كربلاء / كلية التمريض
لجنة اخلاقيات البحث العلمي

استمارة اخلاقيات البحث العلمي

عنوان مشروع البحث	
English	باللغة العربية
Effect of Using Clove Oil Versus Normal Saline Solution in the Management of Oral Mucositis among Patients Undergoing chemotherapy	أثر استخدام زيت القرنفل بالضد من المحلول الملحي المتعادل في علاج التهاب الغشاء المخاطي للفم بين المرضى الخاضعين للعلاج الكيمياوي

بيانات عن الباحث الرئيسي			
الاسم الثلاثي	اللقب العلمي او العنوان الوظيفي	رقم الهاتف/ الموبايل	الايميل
أمنية عبد رسن	ممرض جامعي	٠٧٧٣٥٣٧٢٢٨٢	omnia.a@s.uokerbala.edu.iq

بيانات الباحث او الباحثين المشتركين			
الاسم الثلاثي	اللقب العلمي او العنوان الوظيفي	رقم الهاتف/ الموبايل	الايميل
د. فاطمة مكي محمود	أستاذ مساعد	٠٧٧٠٢٩٣٤٠٣١	ftm_satar@yahoo.com

(Importance of the research and its objectives) اهمية موضوع البحث واهدافه

Importance of the research:
Oral Mucositis develops in (20%–40%) of patients receiving chemotherapy (CT), and almost all patients receiving head and neck radiotherapy (RT) (Avci and Sari, 2019). Thus, it is necessary to alleviate the suffering of these patients and enhance their health status.

Objectives:
1. Determine the effect of using clove oil versus normal saline solution in the management of oral mucositis among patients undergoing chemotherapy.
2. Find out the differences between levels of oral mucositis of patients undergoing chemotherapy with their sociodemographic characteristics and clinical data.

Time and Setting of the Research_ وقت ومكان اجراء البحث (الاماكن المقترحة لأجراء البحث فيها)

الوقت: (من ١ ديسمبر ٢٠٢١ الى ٢٠ اغسطس ٢٠٢٢)
مكان اجراء البحث: (مركز الأمام الحسين "ع" لعلاج الأورام وأمراض الدم ومستشفى الامام الحسن المجتبى "ع" التعليمي)

(Methodology) منهجية البحث

Study Design: Randomize Control Trial Study
The Sampling Method: Systematic Random Sampling
The Expected Number of Sample : 30 Patients
Statistical Analysis: SPSS (Statistical Package for Social Sciences).

Sample of the study عينة الدراسة

Patients with cancer undergoing chemotherapy and confirmed with oral mucositis.

(Ethical consideration during research) الاعتبارات الاخلاقية خلال اجراء البحث

التعهد

- إني الموقع ادناه (أمنية عبد رسن طالب) اتعهد بان اقوم باجراء البحث وفقا لما ذكر في البروتوكول اعلاه وان التزم باتباع القوانين والتعليمات فيما يخص اجراء البحوث والالتزام بأخلاقياتها، كما واتعهد باخذ الموافقة من افراد العينة للمشاركة في الدراسة واخذ موافقة من ولي أمر المشارك الشرعي في حال كون عمر الشخص المشارك اقل من ١٨ سنة، او كونه غير قادر على الفهم، وان أقدم الايضاحات والمعلومات الخاصة بالدراسة لافراد العينة للمشاركين في حال طلبها. وان اتعامل بسرية تامة مع بيانات افراد العينة.

اسم وتوقيع الباحث أمنية عبد رسن

توصية لجنة اخلاقيات البحوث في الكلية

نحن اعضاء اللجنة الاخلاقية نوصي بان موضوع الباحث: ذو قيمة علمية ومهم للمجتمع والمريض

رئيس اللجنة — عضو — عضو — عضو — عضو

Appendix B-II

Consent Form

صفحة موافقة المبحوث

أخي العزيز/ أختي العزيزة..

بين يديك استبانة لدراسة..

(أثر استخدام زيت القرنفل بالضد من المحلول الملحي المُتعادل في علاج التهاب الغشاء المُخاطي للفم بين المرضى الخاضعين للعلاج الكيمياوي)

(Effect of Using Clove Oil Versus Normal Saline Solution in the Management of Oral Mucositis among Patients Undergoing Chemotherapy)

لذا يرجى التفضل بملئ المعلومات المتعلقة بالبحث اعلاه وأود اعلامك بأن المعلومات التي ستدلي بها ستكون في غاية السرية فقط لغرض البحث العلمي خدمة لدراسة الماجستير..

هل توافق بالمشاركة ...؟

نعم ☐

لا ☐

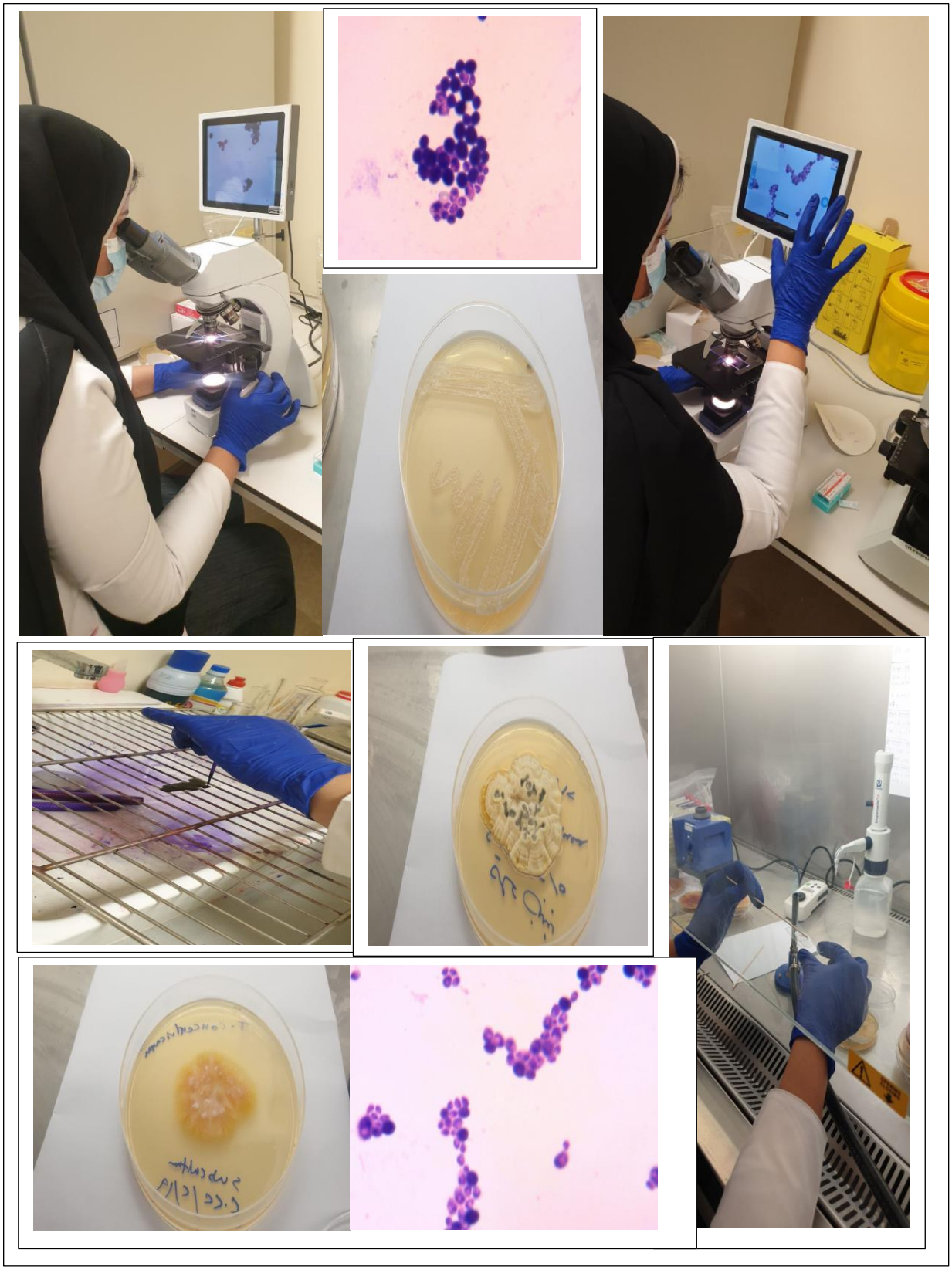
اسم الباحثة:

أمنية عبد رسن طالب

طالبة ماجستير / تمريض البالغين

Appendix C-I

Preparation of Swabs and Cultivation Procedure



Appendix C-II

Certification of Microbiologist Supervisor

Ministry of Higher Education and Scientific Research
University of Babylon
Department of Research and Development

وزارة التعليم العالي والبحث العلمي
جامعة بابل
قسم البحث و التطوير

العدد : ٩٦٣١
التاريخ: ١٧/٤/١٢

Ref. No.:
Date: / /

رئاسة جامعة بابل
الصادرة
العدد:
التاريخ: / /

أمر جامعي

استناداً إلى الصلاحيات المخولة لنا وإشارة الى كتاب أمانة مجلس الجامعة المرقم ج س /١٠١٦ في ٢٠١٧/٣/٢٢ وبناءا على ما أقره مجلس كلية العلوم للبنات بجلسته الثامنة المنعقدة بتاريخ ٢٠١٧/٢/٢٨ تقرر :

- تمنح **زهراء محمد وناس درجة الماجستير في علوم الحياة / احياء مجهرية بمعدل ٨١،٧٥ بتقدير جيد جداً** مع تمنعها بكافة الحقوق والامتيازات التي تخولها هذه الشهادة .

أ.د. عادل هادي البغدادي
رئيس الجامعة وكالة
٢٠١٧/ ٤ /

نسخة منه إلى:
- وزارة التعليم العالي و البحث العلمي/ دائرة البحث و التطوير.. مع الاحترام
- وزارة التعليم العالي و البحث العلمي/ دائرة الدراسات و التخطيط و المتابعة .. مع الاحترام
- كلية العلوم للبنات / الدراسات العليا كتابكم ذو العدد ١٢٦٤ في ٢٠١٧/٣/٢٠ .. مع الاحترام
- قسم البحث والتطوير .. مع الأوليات
- قسم الدراسات و التخطيط والمتابعة / الإحصاء .. مع الاحترام
- شعبة التأهيل والتوظيف والمتابعة .. مع الاحترام
- المعلوماتية الإدارية .. مع الاحترام
- أمانة مجلس الجامعة .. مع الاحترام
- الطالبة **زهراء محمد وناس** .. مع تمنياتنا بالتوفيق
- الصادرة

سامره ه تاثر

Babylon_research@yahoo.com
babylon_research@uobabylon.edu.iq
Researchdep@gmail.com
Researchdep@uobabylon.edu.iq
www.uobabylon.edu.iq

Appendix C-III

The Results of Patients' Swabs

Patient's Number		Swab's Result
Pilot Study Patients	Patient number (1)	Positive
	Patient number (2)	Positive
	Patient number (3)	Positive
	Patient number (4)	Positive
	Patient number (5)	Positive
	Patient number (6)	Positive
Patients of (Clove oil group, normal saline solution group, and control group)	Patient number (7)	Positive
	Patient number (8)	Positive
	Patient number (9)	Positive
	Patient number (10)	Positive
	Patient number (11)	Negative
	Patient number (12)	Positive
	Patient number (13)	Positive
	Patient number (14)	Positive
	Patient number (15)	Positive
	Patient number (16)	Positive
	Patient number (17)	Positive
	Patient number (18)	Negative
	Patient number (19)	Positive
	Patient number (20)	Positive
	Patient number (21)	Positive
	Patient number (22)	Positive
	Patient number (23)	Positive
	Patient number (24)	Positive
	Patient number (25)	Positive
	Patient number (26)	Positive
	Patient number (27)	Positive
	Patient number (28)	Positive
	Patient number (29)	Positive
	Patient number (30)	Positive
	Patient number (31)	Positive
	Patient number (32)	Positive
	Patient number (33)	Positive
	Patient number (34)	Negative
	Patient number (35)	Positive
	Patient number (36)	Positive
	Patient number (37)	Positive
	Patient number (38)	Positive
	Patient number (39)	Positive
	Patient number (40)	Positive
	Patient number (41)	Positive
	Patient number (42)	Positive

Appendix D-I

The study Instrument Sociodemographic and Clinical Data

استبانة رقم (1)
البيانات الديموغرافية ـ الاجتماعية والصحية:

رقم الاستبانة

☐

1. العمر:

☐ سنة

2. الجنس:

ذكر ☐ انثى ☐

3. الحالة الاجتماعية:

a. أعزب ☐

b. متزوج ☐

c. منفصل أو مطلق ☐

d. أرمل ☐

4. مستوى التعليم (التحصيل الأكاديمي):

a. لا يقرأ ولا يكتب ☐

b. يقرأ ويكتب ☐

c. ابتدائية ☐

d. متوسطة ☐

e. اعدادية ☐

f. خريج جامعة فأكثر ☐

5. التدخين:

a. مدخن حالي ☐

b. مدخن سابق ☐

c. لم يدخن أبدًا ☐

6. الأمراض المزمنة:

☐

7. الأدوية المستخدمة للأمراض المزمنة:

☐

8. مدة المعالجة بالعلاج الكيمياوي:

☐

Appendix D-II

The World Health Organization (WHO) Oral Toxicity Scale

استبانة رقم (2)

* مقياس السمية الفموية

درجة التهاب الغشاء المخاطي للفم	الأعراض المرضية	الغذاء	القياس الأول	القياس الثاني
الدرجة صفر	لا توجد أعراض	تغذية طبيعية		
الدرجة الأولى	ألم ± التهاب احمراري	يمكن للمريض ابتلاع الغذاء الصلب		
الدرجة الثانية	• التهاب احمراري • وجود تقرحات • مؤلمة	يمكن للمريض ابتلاع الأطعمة الهشة والناعمة		
الدرجة الثالثة	• تقرحات متقاربة مع / بدون إفرازات • مؤلمة جدا	قادر على ابتلاع السوائل ولكن ليس الطعام الصلب		
الدرجة الرابعة	• تقرحات عميقة و / أو تنخر • مؤلمة بشكل شديد	تناول الغذاء لم يعد ممكنا		

*تم تصميمه من قبل منظمة الصحة العالمية

Appendix D-III

Oral Mucositis Assessment Tool

استبانة رقم (3):

* أداة تقييم التهاب الغشاء المخاطي الفموي

الحالة	التاريخ	
	القياس الأول	القياس الثاني
❖ **الصوت:** 1. عادي 2. غليظ أو خشن 3. صعوبة الكلام		
❖ **البلع:** 1. عادي 2. ألم عند البلع 3. غير قادر على البلع		
❖ **الغشاء المخاطي:** 1. وردي ورطب 2. أحمر أو / سليم 3. متقرح +/- نزيف		
❖ **اللعاب:** 1. مائي 2. سميك أو لزج (افرازات مختلطة قيحية ومخاطية) 3. لا يوجد لعاب		
❖ **اللسان:** 1. وردي ورطب 2. عليه غشاء أو لامع +/- نزيف 3. تقرحات +/- نزيف		
❖ **الشفاه:** 1. ناعمة، وردية ورطبة 2. جافة / متشققة 3. نزيف / متقرحة		

❖ **اللثة:** 1. وردية وثابتة 2. متوذمة أو متورمة +/- احمرار 3. نزيف تلقائي		
❖ **الأسنان / أطقم الأسنان:** 1. نظيفة، لا توجد بقايا متقشرة 2. لويحات صلبة متلونة بشكل موضعي، بقايا متقشرة 3. لويحات صلبة متلونة وبقايا متقشرة بشكل تام		
❖ **قدرة الحفاظ على التغذية:** 1. طعام عادي 2. طعام خفيف 3. سوائل فقط أو لا شيء عن طريق الفم		
❖ **الحاجة الى مهدئات الألم:** 1. لا شيء 2. تسكين موضعي 3. تسكين عام		
❖ **دليل على العدوى:** 1. لا يوجد دليل 2. بعض الأدلة المرئية 3.عدوى (فيروسية / فطرية)		
❖ **التذوق:** 1. طبيعي 2. ضعف / تغيير 3. لا يوجد مذاق		
❖ **تقييم العناية الذاتية:** 1.يجري العناية بالفم بنفسه 2. يحتاج إلى التشجيع والتعليم 3. غير راغب / غير قادر على أداء العناية بالفم		
مجموع نقاط التقييم		
التهاب خفيف = (13-20) التهاب متوسط = (21-26) التهاب شديد= (27-39)		
*** تم تصميمها من قبل (Cancer Institute of New South Wales)**		

Appendix-E

Researcher's instructions toward interventional protocol usage steps

Appendix-F

List of Clove Oil Gargling Procedure Usage Steps and Instructions

"الصِّحَّة تاج على رُءُوس الأصِحَّاء"

طريقة استخدام زيت القرنفل:

أخي العزيز/ أختي العزيزة اليكم طريقة استخدام زيت القرنفل لعلاج التهاب الغشاء المخاطي للفم، لذلك نرجو منكم الالتزام بالإجراء الصحيح وحسب الخطوات التالية:

١. ضع قطرتين إلى ثلاث قطرات من زيت القرنفل في وعاء صغير يستخدم لمرة واحدة.
٢. أضف ربع إلى نصف ملعقة صغيرة (ملعقة شاي) من زيت الزيتون في الوعاء.
٣. امزج هذه الزيوت باستخدام ملعقة ذات استخدام واحد.
٤. ضع مسحة القطن أحادية الاستخدام في خليط الزيت حتى تتشبع.
٥. ضع مسحة القطن المشبعة بالزيت على المناطق المؤلمة والملتهبة من الفم لمدة ١٠ ثوانٍ، وتأكد من عدم ابتلاع هذا الزيت.
٦. بعد أن تقوم بوضع الزيت على جميع مناطق الفم الملتهبة والمؤلمة، قم بالغرغرة بحوالي ٢٠ إلى ٣٠ مل من الماء المقطر باستخدام كوب احادي الاستخدام لمدة ٣٠ ثانية ثم ابصقه.
٧. كرر هذه الخطوات ثلاث مرات يوميًا بعد كل وجبة.

التعليمات الواجب الالتزام بها:

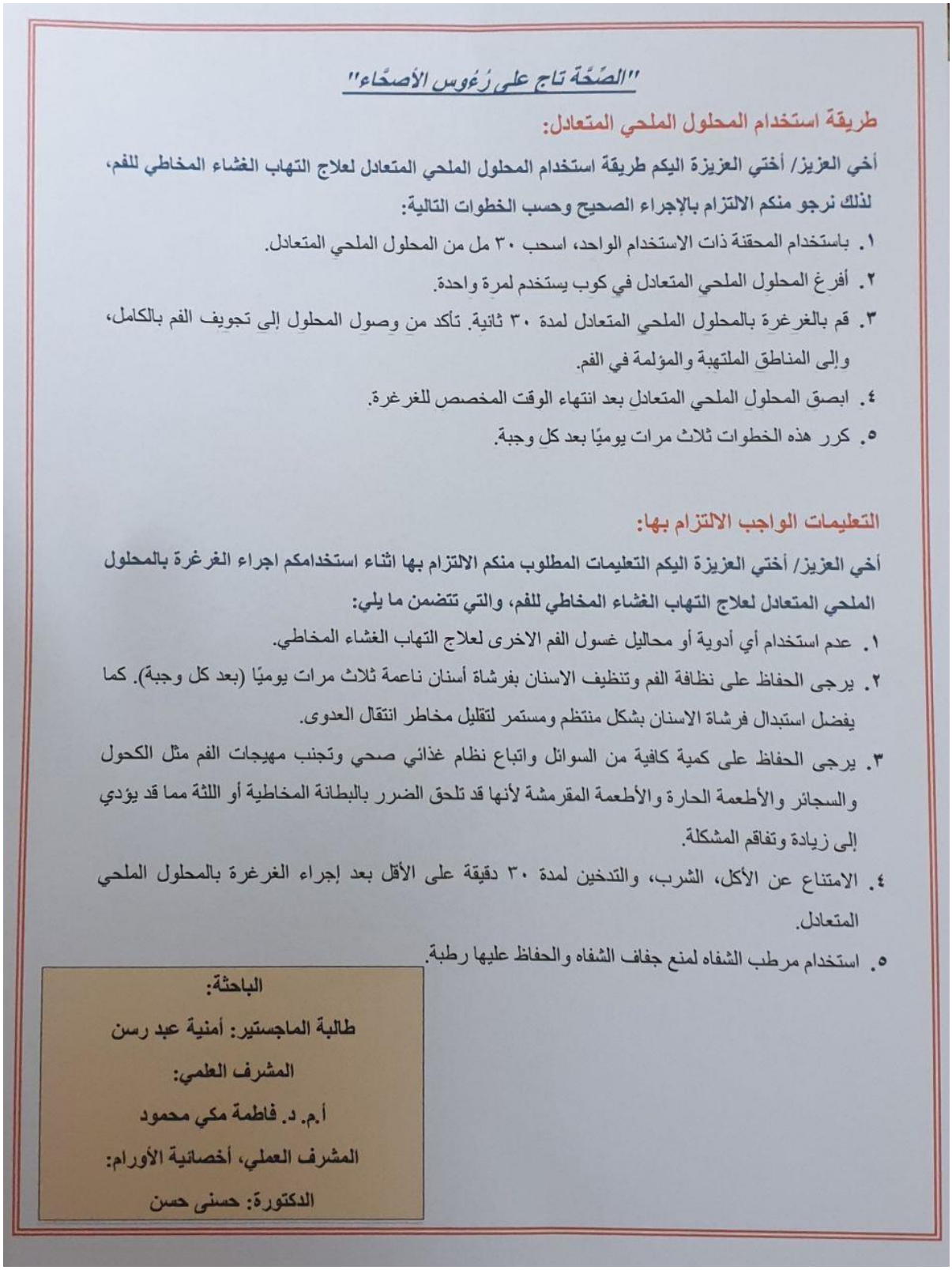
أخي العزيز/ أختي العزيزة اليكم التعليمات المطلوب منكم الالتزام بها اثناء استخدامكم اجراء الغرغرة بزيت القرنفل لعلاج التهاب الغشاء المخاطي للفم، والتي تتضمن ما يلي:

١. عدم استخدام أي أدوية أو محاليل غسول الفم الاخرى لعلاج التهاب الغشاء المخاطي.
٢. يرجى الحفاظ على نظافة الفم وتنظيف الاسنان بفرشاة أسنان ناعمة ثلاث مرات يوميًا (بعد كل وجبة). كما يفضل استبدال فرشاة الاسنان بشكل منتظم ومستمر لتقليل مخاطر انتقال العدوى.
٣. يرجى الحفاظ على كمية كافية من السوائل واتباع نظام غذائي صحي وتجنب مهيجات الفم مثل الكحول والسجائر والأطعمة الحارة والأطعمة المقرمشة لأنها قد تلحق الضرر بالبطانة المخاطية أو اللثة مما قد يؤدي إلى زيادة وتفاقم المشكلة.
٤. الامتناع عن الأكل، الشرب، والتدخين لمدة ٣٠ دقيقة على الأقل بعد إجراء الغرغرة بزيت القرنفل.
٥. استخدام مرطب الشفاه لمنع جفاف الشفاه والحفاظ عليها رطبة.

الباحثة:
طالبة الماجستير: أمنية عبد رسن
المشرف العلمي:
أ.م. د. فاطمة مكي محمود
المشرف العملي، أخصائية الأورام:
الدكتورة: حسنى حسن

Appendix-G

List of Normal Saline Solution Gargling Procedure Usage Steps and Instructions



"الصِّحَّة تاج على رُءوس الأصِحَّاء"

طريقة استخدام المحلول الملحي المتعادل:

أخي العزيز/ أختي العزيزة اليكم طريقة استخدام المحلول الملحي المتعادل لعلاج التهاب الغشاء المخاطي للفم، لذلك نرجو منكم الالتزام بالإجراء الصحيح وحسب الخطوات التالية:

١. باستخدام المحقنة ذات الاستخدام الواحد، اسحب ٣٠ مل من المحلول الملحي المتعادل.
٢. أفرغ المحلول الملحي المتعادل في كوب يستخدم لمرة واحدة.
٣. قم بالغرغرة بالمحلول الملحي المتعادل لمدة ٣٠ ثانية. تأكد من وصول المحلول إلى تجويف الفم بالكامل، وإلى المناطق الملتهبة والمؤلمة في الفم.
٤. ابصق المحلول الملحي المتعادل بعد انتهاء الوقت المخصص للغرغرة.
٥. كرر هذه الخطوات ثلاث مرات يوميًا بعد كل وجبة.

التعليمات الواجب الالتزام بها:

أخي العزيز/ أختي العزيزة اليكم التعليمات المطلوب منكم الالتزام بها اثناء استخدامكم اجراء الغرغرة بالمحلول الملحي المتعادل لعلاج التهاب الغشاء المخاطي للفم، والتي تتضمن ما يلي:

١. عدم استخدام أي أدوية أو محاليل غسول الفم الاخرى لعلاج التهاب الغشاء المخاطي.
٢. يرجى الحفاظ على نظافة الفم وتنظيف الاسنان بفرشاة أسنان ناعمة ثلاث مرات يوميًا (بعد كل وجبة). كما يفضل استبدال فرشاة الاسنان بشكل منتظم ومستمر لتقليل مخاطر انتقال العدوى.
٣. يرجى الحفاظ على كمية كافية من السوائل واتباع نظام غذائي صحي وتجنب مهيجات الفم مثل الكحول والسجائر والأطعمة الحارة والأطعمة المقرمشة لأنها قد تلحق الضرر بالبطانة المخاطية أو اللثة مما قد يؤدي إلى زيادة وتفاقم المشكلة.
٤. الامتناع عن الأكل، الشرب، والتدخين لمدة ٣٠ دقيقة على الأقل بعد إجراء الغرغرة بالمحلول الملحي المتعادل.
٥. استخدام مرطب الشفاه لمنع جفاف الشفاه والحفاظ عليها رطبة.

الباحثة:

طالبة الماجستير: أمنية عبد رسن

المشرف العلمي:

أ.م. د. فاطمة مكي محمود

المشرف العملي، أخصائية الأورام:

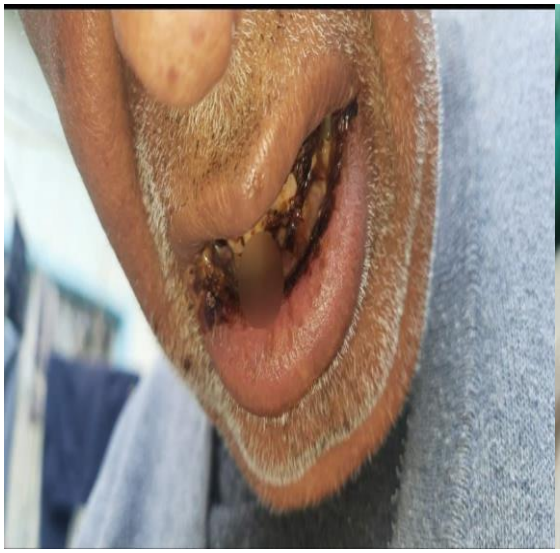
الدكتورة: حسنى حسن

Appendix-H

Patients' Follow-up Method

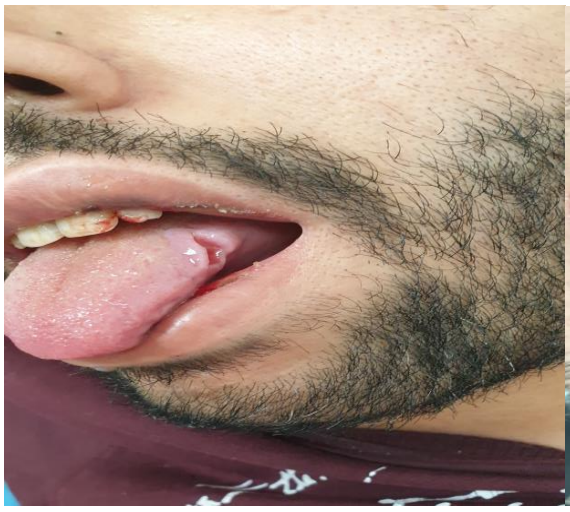
Appendix-I

Pictures of Patients Before and After Applications of Interventional Protocols

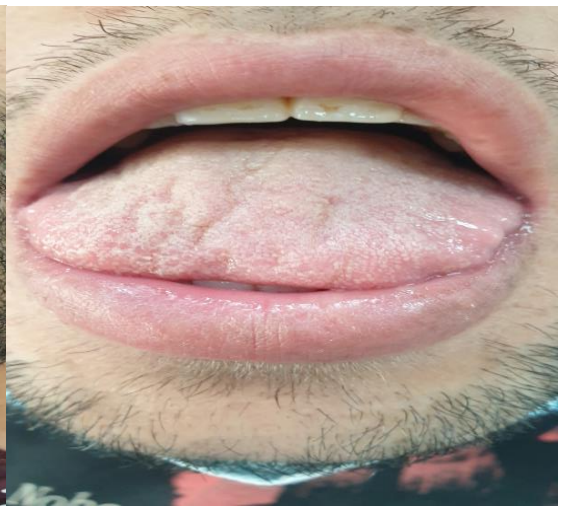


Before application of clove oil interventional protocol

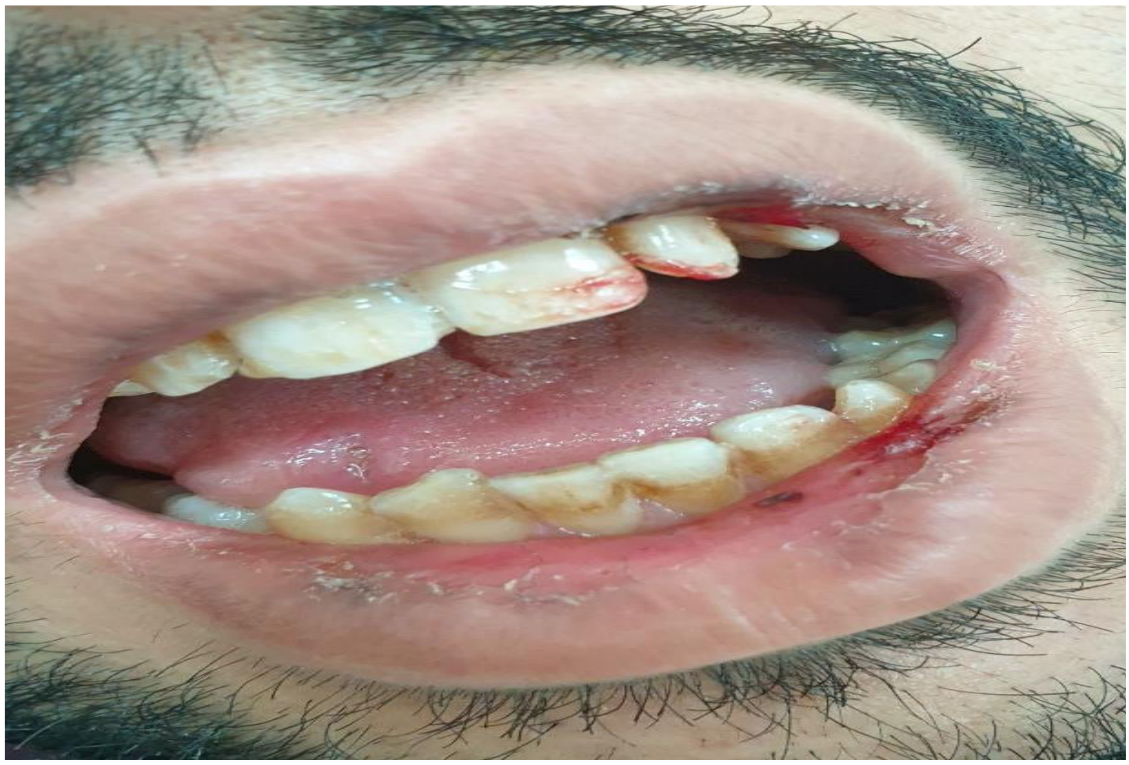
After application of clove oil interventional protocol



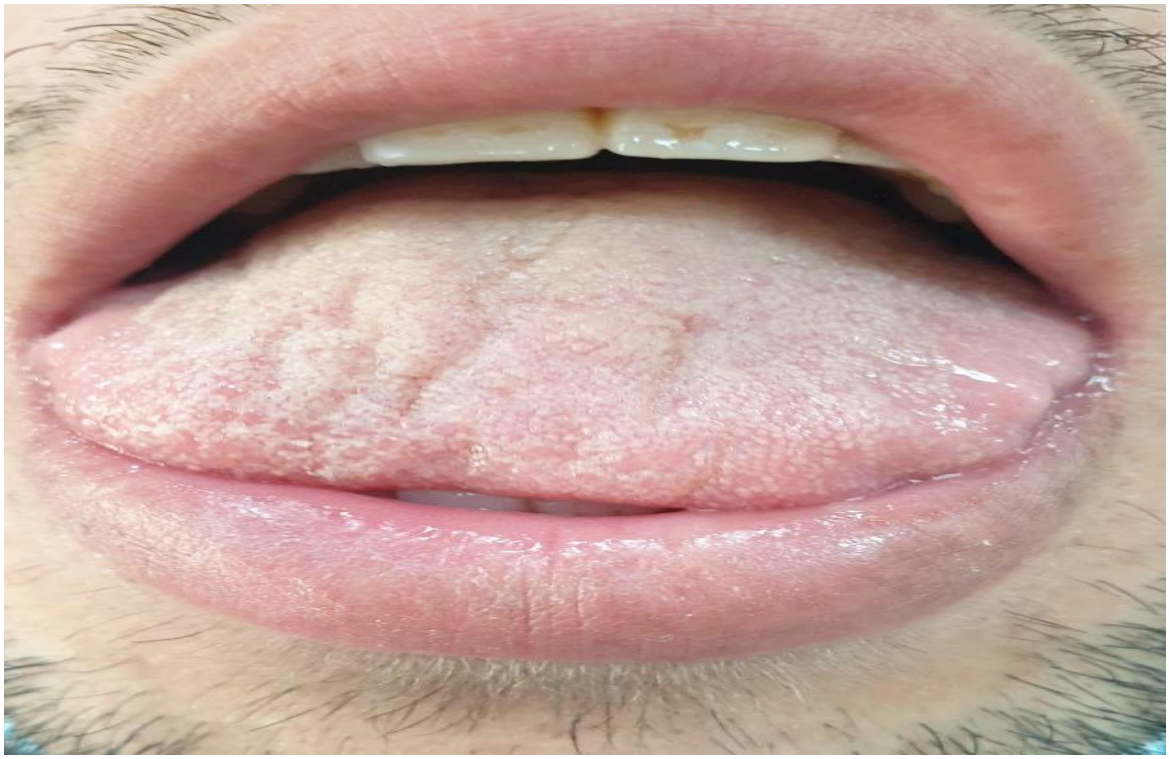
Before implementing interventional protocol using clove oil



After implementing interventional protocol using clove oil



Before application of normal saline solution interventional protocol



Before application of normal saline solution interventional protocol

Appendix J-I (Experts' List)

ت	اسم الخبير	اللقب العلمي	التخصص	سنوات الخبرة	مكان العمل	الغرض
.1	د. راجحة عبد الحسن حمزة	استاذ	تمريض البالغين	37 سنة	كلية التمريض/ جامعة الكوفة	Content Validity
.2	د. هدى باقر حسن	استاذ	تمريض البالغين	34 سنة	كلية التمريض/ جامعة بغداد	
.3	د. حسن عبد الله عذبي	أستاذ مساعد	تمريض البالغين	19 سنة	كلية التمريض/ جامعة كربلاء	
.4	د. جهاد جواد كاظم	أستاذ مساعد	تمريض البالغين	13 سنة	كلية التمريض/ جامعة الكوفة	
.5	د. رهف عقل رجوب	مدرس	تمريض البالغين	10 سنة	تمريض/ كلية الصفوة الجامعة	
.6	د. علي كريم خضير	استاذ	تمريض الصحة النفسية والعقلية	30 سنة	كلية التمريض/ جامعة كربلاء	Face Validity (Response Process Validity)
.7	د. سلمان حسين فارس	أستاذ مساعد	تمريض صحة المجتمع	30 سنة	كلية التمريض/ جامعة كربلاء	
.8	د. ضياء كريم عبد علي	أستاذ مساعد	تمريض البالغين	15 سنة	كلية التمريض/ جامعة العميد	
.9	د. وفاء عبد علي حطاب	أستاذ مساعد	تمريض البالغين	14 سنة	كلية التمريض/ جامعة بغداد	
.10	د. نسيم سمير صقر	أستاذ مساعد	تمريض البالغين	13 سنة	كلية التمريض/ جامعة وارث الأنبياء	
.11	د. سيروآن جعفر باقي	أستاذ مساعد	تمريض البالغين	13 سنة	كلية التمريض/ جامعة بغداد	
.12	د. صادق عبد الحسين حسن	أستاذ مساعد	تمريض البالغين	12 سنة	كلية التمريض/ جامعة بغداد	
.13	د. محمد شنين علي	دكتوراه بورد	أمراض الدم	23 سنة	كلية طب الأسنان/ جامعة الزهراوي	
.14	د. حسنى حسن عباس	دكتوراه بورد	طبيبة اختصاص أورام وأمراض الدم	16 سنة	مركز الأمام الحسين (ع) لعلاج الأورام وأمراض الدم	
.15	د. كرار مسلم سلمان	دبلوم عالي	طبيب اختصاص أورام وأمراض الدم	14 سنة	مركز الأمام الحسين (ع) لعلاج الأورام وأمراض الدم	

Appendix J-II

Content Validity of Oral Mucositis Assessment

Item \ Expert	1	2	3	4	5	ne	N	I-CVI	UA
Q1	1	1	1	1	1	5	5	1	1
Q 2	1	1	1	1	1	5	5	1	1
Q 3	1	1	1	1	1	5	5	1	1
Q 4	1	1	1	1	1	5	5	1	1
Q 5	1	1	1	1	1	5	5	1	1
Q 6	1	1	1	1	1	5	5	1	1
Q 7	1	1	1	1	1	5	5	1	1
Q 8	1	1	1	1	1	5	5	1	1
Q 9	1	1	1	1	1	5	5	1	1
Q 10	1	1	1	1	1	5	5	1	1
Q 11	1	1	1	1	1	5	5	1	1
Q12	1	1	1	1	1	5	5	1	1
Q13	1	1	1	1	1	5	5	1	1
Proportion relevance	1	1	1	1	1				
S-CVI/UA									**1**
S-CVI/Ave									**1**
Average proportion of items Judged as relevance across the fifth experts									**1**

I-CVI = CVR=(ne – N/2) / (N/2), S- CVI/Ave= (∑CVR/ N) , UA = Universal Agreement, Content Validity Ratio CVR= I- CVI (Item Level Content Validity Index), S-CVI\Ave =Scale-Level Content Validity Index, ne= Number of Experts in Agreement , ne = The Number of Experts Who Rated an Item as "Essential" , N = The Total Number of Experts.

Appendix J-III

Face Validity of Oral Mucositis Assessment

Item \ Expert	1	2	3	4	5	6	7	8	9	10	RA	UA	N	I-FVI
Q1	1	1	1	1	1	1	1	0	1	0	8	0	10	0.8
Q 2	1	1	1	1	1	1	1	1	1	1	10	1	10	1
Q 3	1	1	1	1	1	1	1	1	1	1	10	1	10	1
Q 4	1	1	1	1	1	1	1	1	1	1	10	1	10	1
Q 5	1	1	1	1	1	1	1	1	1	1	10	1	10	1
Q 6	1	1	1	1	1	1	1	1	1	1	10	1	10	1
Q 7	1	1	1	1	1	1	1	1	1	1	10	1	10	1
Q 8	1	1	1	1	1	0	1	1	0	1	8	0	10	0.8
Q 9	1	1	1	1	1	1	1	1	1	1	10	1	10	1
Q 10	1	1	0	1	1	1	1	1	1	1	9	0	10	0.9
Q 11	1	1	1	0	1	1	0	1	1	1	8	0	10	0.8
Q 12	1	1	1	1	1	1	1	1	1	1	10	1	10	1
Q 13	1	1	1	1	1	1	1	1	1	1	10	1	10	1
Proportion clarity and comprehension	1	1	0.9	0.9	1	0.9	0.9	0.9	0.9	0.9				

S-FVI/UA	**0.9**
S- FVI/Ave	**0.94**
Average Proportion of Items Judged as Relevance Across the Ten Experts	**0.93**

I-FVI (Agreed Item)/(Number of Rater), S- FVI/Ave= (Sum of I-FVI Scores)/ (Number of Item) , S-FVI/UA= (Sum of UA Scores)/ (Number of Item), UA = Universal agreement= Rates in Agreement, I-FVI = Item Face Validity, S-FVI= Scale Face Validity

Appendix-K

The Statistician's Opinion

Republic of Iraq
Ministry of higher education & scientific research
University of Kerbala
College of Nursing

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة كربلاء
كلية التمريض
الدراسات العليا

اقرار الخبير الاحصائي

اشهد بان الرسالة الموسومة :

(اثر استخدام زيت القرنفل بالضد من المحلول الملحي المتداول في علاج التهاب الغشاء المخاطي للفم بين المرضى الى خضعوا للعلاج الكيماوي)

قد تم الاطلاع على الاسلوب الاحصائي المتبع في تحليل البيانات واظهار النتائج الاحصائية وفق مضمون الدراسة ولأجله وقعت.

توقيع الخبير الاحصائي:
الاسم واللقب العلمي: م.د. بيداء عصام حسين
الاختصاص الدقيق: احصاء حيوي
مكان العمل: جامعة كربلاء / كلية الادارة والاقتصاد / قسم الاحصاء
التاريخ: ٢١ / ٨ / 2022

College of Nursing
2012
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University of Kerbala
جامعة كربلاء
كلية التمريض

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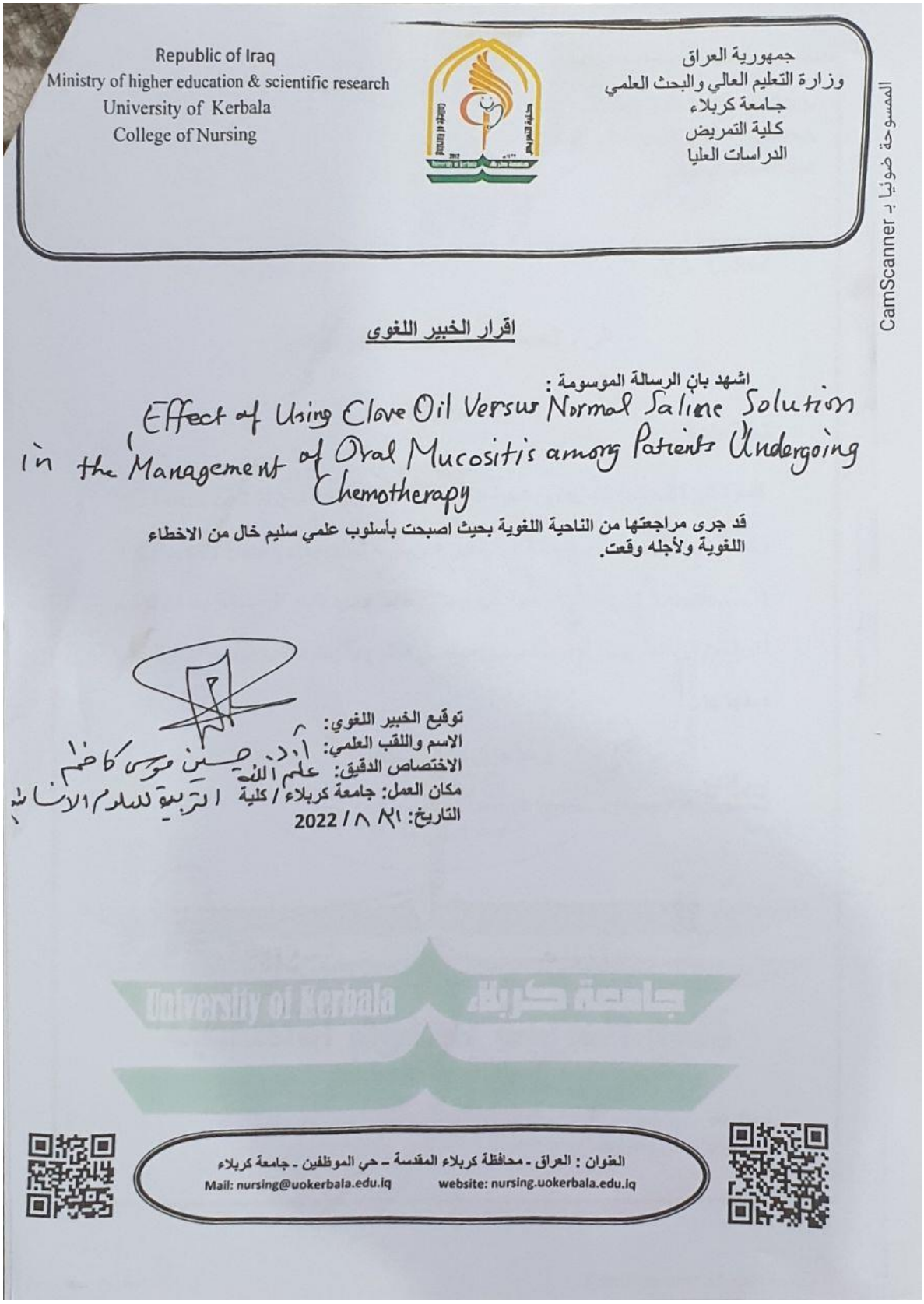
Appendix L

Linguist's Opinion



Republic of Iraq
Ministry of higher education & scientific research
University of Kerbala
College of Nursing

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة كربلاء
كلية التمريض
الدراسات العليا

الممسوحة ضوئيا بـ CamScanner

اقرار الخبير اللغوي

اشهد بان الرسالة الموسومة :
Effect of Using Clove Oil Versus Normal Saline Solution in the Management of Oral Mucositis among Patients Undergoing Chemotherapy

قد جرى مراجعتها من الناحية اللغوية بحيث اصبحت بأسلوب علمي سليم خال من الاخطاء اللغوية ولأجله وقعت.

توقيع الخبير اللغوي:
الاسم واللقب العلمي: أ.د. حسين موسى كاظم
الاختصاص الدقيق: علم اللغة
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الخلاصة

الخلفية العلمية: يعد العلاج الكيمياوي أحد الخيارات الرئيسية لعلاج المرضى المصابين بالأورام. يعاني المرضى الذين يتلقون جرعات عالية من العلاج الكيمياوي من التهاب الغشاء المخاطي للفم.

الأهداف: تهدف الدراسة الحالية إلى تحديد أثر استخدام زيت القرنفل بالضد من المحلول الملحي المتعادل في علاج التهاب الغشاء المخاطي للفم بين المرضى الخاضعين للعلاج الكيمياوي.

المنهجية: تم اجراء دراسة تجريبية في مركز الإمام الحسين للأورام وردهات الأورام بمستشفى الإمام الحسن المجتبى التعليمي. تم اختيار عينة عشوائية منتظمة مكونة من 30 مريضا من الخاضعين للعلاج الكيمياوي ولديهم التهاب الغشاء المخاطي للفم. تم جمع البيانات من خلال أسلوب المقابلة وباستخدام مقياس السمية الفموية لمنضمة الصحة العالمية واداة تقييم التهاب الغشاء المخاطي للفم ثم بعد ذلك تحليلها باستخدام برنامج الحزمة الإحصائية للعلوم الاجتماعية اصدار (25). تم استخدام كل من التحليل الاحصائي الوصفي والاستدلالي لتحليل نتائج الدراسة.

النتائج: أظهرت نتائج الدراسة ان 40٪ من المرضى كانوا مصابين بالتهاب الغشاء المخاطي للفم من الدرجة الثانية والثالثة في فترة ما قبل الاختبار، وبعد سبعة أيام من استخدام زيت القرنفل، أظهرت النتائج أن 80٪ من المرضى كانوا يعانون من التهاب الغشاء المخاطي للفم من الدرجة الأولى. تم توثيق فروق ذات دلالة إحصائية في مستويات التهاب الغشاء المخاطي للفم عند قيمة احتمالية تبلغ 0.011, 0.042, و0.000 بعد سبعة أيام من التداخل بين المجموعات (زيت القرنفل والمحلول الملحي المتعادل، زيت القرنفل والضابطة، والمحلول الملحي المتعادل والضابطة) على التوالي.

الاستنتاجات: إن العناية بالفم باستخدام الغرغرة بزيت القرنفل فعال في تقليل درجة التهاب الغشاء المخاطي للفم وتحسين راحة المرضى الخاضعين للعلاج الكيمياوي وهو أكثر فعالية من إجراء الغرغرة بالمحلول الملحي المتعادل في تقليل شدة التهاب الغشاء المخاطي للفم.

التوصيات: أوصت الدراسة بضرورة استخدام زيت القرنفل ثلاث مرات يوميًا بشكل غرغرة للفم لأن هذا يمكن أن يساعد في تقليل العبء الإجمالي لمضاعفات التهاب الغشاء المخاطي للفم وكلفة العلاج على كل من المرضى والمستشفى.

جامعة كربلاء
كلية التمريض

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رسالة مقدمة الى مجلس كلية التمريض / جامعة كربلاء وهي جزء من متطلبات نيل درجة الماجستير في علوم التمريض

الطالبة:

أمنية عبد رسن

بإشراف:

أ.م. د. فاطمة مكي محمود

محرم – 1444هـ **أغسطس – 2022 م**