Effect of Interventional Protocol Using Clove Oil Versus Normal Saline Solution Upon the Degree of Oral Mucositis Among Patients Undergoing Chemotherapy: A Comparative Study

Omnia Abd Ressen[1], and Fatma Makee Mahmood[2]
[1]Academic Nurse, Ministry of Health/ Holly Karbala Health Directorate, Iraq
[2]Associate Professor, Adult Nursing Department/ College of Nursing/ University of Karbala, Iraq.
Email: omnia.a@s.uokerbala.edu.iq

Abstract
Background: Patients undergoing chemotherapy will develop some degree of oral mucositis. It is appeared as erythema and burning sensation, and may develop to significantly painful ulcerative lesions, thus reducing the ability of patients to eat and speak, and negatively affecting patients' quality of life. This study was conducted to investigate the effect of the interventional protocol using clove oil compared with normal saline solution upon the degree of oral mucositis among patients undergoing chemotherapy. Methods: Thirty patients undergoing chemotherapy they were diagnosed with oral mucositis were randomly assigned in this true experimental study. The study was conducted at Imam Al-Hussein Oncology Center and the oncology wards of Imam Al-Hassan Al-Mujtaba Teaching Hospital. The data were collected through the interviewing technique and then analyzed by using the program of SPSS Version 25, both descriptive and inferential statistical procedure were used to analyze the study results. Results: No significant differences at p-value of 0.623, 0.725, and 1.0 are observed before applying the intervention in the oral toxicity degree between clove oil and normal saline solution groups, clove oil and control groups, normal saline solution and the control groups respectively. While a significant statistical differences at p-value of 0.000 are detected after seven days of interventional protocol between clove oil and normal saline solution groups, clove oil and control group, normal saline solution and the control group in favor the clove oil group. Furthermore, a significant statistical difference at p-value of 0.011, 0.042, and 0.000 are reported after seven days of intervention in the levels of oral mucositis between clove oil group and normal saline solution group, clove oil group and control group, and normal saline solution group and control group respectively. Therefore, clove oil cures the oral mucositis much more than normal saline solution. Conclusions: The application of interventional protocol using clove oil is greatly enhances level of oral mucositis and reduces oral mucositis grade. There is a significant statistical difference between both clove oil group and normal saline solution group in favor the clove oil group. Recommendations: It is necessary to conduct further studies on larger sample size for determination of the efficacy of clove oil on the degree of oral mucositis.
Keywords: Clove Oil, Normal Saline Solution, Oral Mucositis, Chemotherapy.

1. Introduction

Cancer's global burden was doubled between 1975 and 2000, and it is double again by 2020 and predicted to triple nearly by 2030. For most tumors, in the early stage of cancer development, surgery is considered the most effective choice of cancer treatment. When occur progression of cancer, the treatments typically include radiation, combination chemotherapy, and other targeted therapies. The treatment options differ significantly with the type of cancer (Kaplan,2013).

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). Traditional chemotherapy destroys normal cells that divide quickly, such as those in the digestive system, 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 chemotherapy are frequently reported: oral mucositis, alopecia, and myelosuppression (Alam et al.,2018).

One of the most frequent adverse effects of cancer therapy is oral mucositis, a painful inflammation and ulceration of the oral mucous membrane. Typically, oral mucositis appears seven days following chemotherapy administration and resolves within 21 days. Pain due to oral mucositis is the most frequent side effect mentioned by patients with chemotherapy. Patients' quality of life is reduced by pain, which also makes it difficult to chew, swallow, and communicate. It also negatively impacts the

doi.org/10.31838/hiv22.02.502 Received: 22.05.22, Revised: 05.07.22, Accepted: 15.08.22

patient's ability to eat properly, which results in nutritional deficiencies and therefore results in weight loss (Avci and Sari, 2019).

Clove essential oil is used topically for a number of health benefits. 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). One may consider clove to be the most effective antioxidant there is. A drop of clove oil has 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. Clove has anti-inflammatory, anesthetic, pain-relieving, antifungal, antiviral, antimicrobial, anti-diabetic, antithrombotic, and antibacterial effects (Nivetha et al., 2014).

Using salt mouthwash helps reduce discomfort, keep food debris out of the mouth, and **prevent** infection. 0.9 percent concentration of normal saline is not irritating and is thought to aid in the development of granulation tissue and accelerate healing. Salt mouthwash is affordable, dependable, and safe. When we have oral wounds, saltwater 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). Several studies looked at how normal saline mouthwash affects oral mucositis prevention in a range of treatment groups. Results were contradictory and evidence levels were different. Due to limited and/or inconsistent data, it is not possible to establish guidelines for the use of regular saline mouthwash in the prevention or treatment of oral mucositis in any group. The panel agreed that ordinary normal saline is a risk-free, bland rinse that can be beneficial for maintaining oral hygiene and patient comfort (McGuire et al., 2013).

2. Methodology

A true-experimental design was used to determine the effect of interventional protocol using clove oil versus normal saline solution upon the degree of oral mucositis among patients with cancer undergoing chemotherapy. A probability (systematic random) sample consists of 30 patients selected from patients with cancer undergoing chemotherapy who was confirmed with oral mucositis in Imam Al-Hussein Oncology Center and oncology wards of Imam Al-Hassan Al-Mujtaba teaching hospital in holy Kerbala city. The participants were distributed as follow: 10 patients were enrolled as a control group that are chosen from Imam Al-Hassan Al-Mujtaba teaching hospital to prevent contamination with confounding factors, 10 patients were enrolled as a clove oil experimental group, and 10 patients were enrolled as normal saline solution experimental group and those last two groups were chosen from Imam Al-Hussein Oncology Center. The participants in the two experimental group were exposed to an interventional protocol (applying clove oil for seven days and applying the normal saline solution for the same duration).

In this study, the researchers collected data through face-to-face interview and was used an instrument consisting of three parts, the first part concerned with the patient's socio-demographic characteristics and clinical data, the second part concerned with the Oral Toxicity Scale that was developed by the World Health Organization (WHO), (1979), and the third part concerned with Oral Mucositis Assessment Tool that was developed by Cancer Institute of New South Wales (NSW), (2019).

A detailed medical history and oral cavity history were obtained from each patient in the three groups before starting clove oil and normal saline solution interventional protocol, also oral swab was taken from the patient's oral cavity and then sent to the laboratory for cultivation to confirm that there is bacterial or fungal infection related to oral mucositis. The researchers took 15 to 20 minutes to conduct the interview, collect comprehensive data, and taken an oral swab from each patient. All patients were subjected to thorough oral cavity assessment to identify any problems not related to oral mucositis. All patients were clinically evaluated at two separate time intervals: firstly, before starting the interventional protocol and the second time after seven days from the beginning of interventional protocol. This interventional protocol is designed to include how to facilitate and enhance the healing process of oral mucositis by using clove oil compared with normal saline solution.

The researchers were telephonically followed up the patients three times per day during the period of the clove oil and normal saline solution interventional protocol and reminded them to adhere to the steps of mouth care interventional protocol in each of the two experimental groups using either clove oil or normal saline solution. This was done through phone interaction with the patients by establishing social media communication groups and was named according to the type of intervention used (clove oil experimental group, normal saline experimental group). Also, patients who were not have social media sites were followed up using the SIM-Card telephonic communication.

The gargling procedures of both clove oil and normal saline solution was considered as in-house-adopted protocols and all patients in these two experimental groups were instructed to adhere to the correct method of the steps of the interventional protocols using either clove oil or normal saline, as well as to adhere to the list of instructions attached with the steps (appendix 1), in order to make the interventional protocol successfully. The gargling procedure was prepared according to a standardized method and was administered topically to the mouth and in similar amount, dosage form and duration for all patients in these groups and under the supervision of the

researchers and the practical supervisor medical oncologist.

The interventional protocol using clove oil was including the following steps as supported by Nivetha, et al., (2014) and Basch, et al., (2008):

Putting two to three drops of clove oil into the small single-use container and diluting clove oil by adding one-fourth to one-half small spoon (teaspoonful) of olive oil to the container.

Mixing these oils using disposable spoon, and then saturate a single-use cotton swab in the oil mixture.

After cotton swab saturation, placing it on the painful and inflamed areas of the mouth for 10 seconds, and then gargling with about (20 to 30) ml of distilled water using a disposable cup for 30 seconds and spit out it.

Repeat these steps three times daily after each meal.

The interventional protocol using normal saline solution was including the following steps:

Using the syringe, pull 30 ml of normal saline solution 0.9%.

Empty the normal saline solution into a single-use cup.

Gargle 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.

Spit out the normal saline solution after the time allotted for gargling is complete.

Repeat these steps three times daily after each meal.

The steps of both interventional protocols were firstly applied by researchers 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 occur in the steps when the patients start interventional protocol using the clove oil or normal saline solution.

Each patient in the clove oil experimental group was provided with 1 box of clove oil 30 ml, 2 boxes 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 vials, and a box of single-use cups contain 100 cups. Whereas each patient 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.

For the control group, all patients were subjected to thorough oral cavity assessment to identify any problems not related to oral mucositis and were clinically evaluated at two separate time intervals: firstly, when interviewing the patients and the second time after seven days from the first evaluation.

The interviewing technique by the researchers was used in order to collect the relevant data, and then analyzed by using IBM Statistical Package of Social Sciences (SPSS) Version 25 program, and the statistical procedures that used were included: Independent sample t-test to study the differences between the cumulative total mucositis assessment score at the pre-test and post-test period of applying the procedure, Mann-Whitney test (U), to study the differences between the mean levels of oral toxicity and mucositis between both study groups at pre-test and post-test period of applying the interventional protocol, and Kendal-Taue test (τ) to study the differences between the study groups at pre-test and post-test period of applying the interventional protocol.

3. Results

Table (1): Distribution of patients according to their socio-demographic characteristics and duration of chemotherapy:

Variables		Experimental (clove oil) group		Experimental (normal saline) group		Control group		X2 p-value
		f.	%	f.	%	f.	%	
Age (years)	20-30	2	20.0	2	20.0	1	10.0	6.846 0.339
	31-40	3	30.0	1	10.0	5	50.0	
	41-50	4	40.0	2	20.0	2	20.0	
	>50	1	10.0	5	50.0	2	20.0	
Gender	Male	5	50.0	7	70.0	4	40.0	1.861 0.534
	Female	5	50.0	3	30.0	6	60.0	
Marital status	Single	2	20.0	2	20.0	1	10.0	4.487 0.611
	Married	8	80.0	8	80.0	7	70.0	
	Divorced	0	0.0	0	0.0	1	10.0	
	Widowed	0	0.0	0	0.0	1	10.0	
Educational levels	Read and write	1	10.0	2	20.0	2	20.0	8.400 0.590
	Primary	4	40.0	3	30.0	1	10.0	
	Middle school	1	10.0	4	40.0	4	40.0	
	Secondary	3	30.0	1	10.0	2	20.0	
	University or above	1	10.0	0	0.0	1	10.0	
Smoking	Current smoker	0	0.0	0	0.0	1	10.0	4.200 0.380
	Previous smoker	3	30.0	6	60.0	5	50.0	
	Never smoked	7	70.0	4	40.0	4	40.0	
Duration of chemotherapy	< 4 months	4	40.0	6	60.0	6	60.0	7.095 0.192
	4 – 8 months	5	50.0	4	40.0	1	10.0	
	8 – 12 months	0	0.0	0	0.0	2	20.0	
	≥12 months	1	1.0	0	0.0	1	10.0	

The result in table (1) shows that no significant statistical differences were observed between the three groups regarding patient demographical characteristics. 40% of patients were between 41-50 years old in the clove oil group, 50% were >50 years old in the normal saline solution group, and 50% were between 31-40 years old in the control group. Regarding the patients' gender, 50% and 70% of patients in the clove oil group and normal saline group were males, but 60% of patients in the

control group were females. The highest (40%) percentage of patients in the clove oil group were with a primary education level, while the same percentage of the normal saline and control groups were had a middle school level.

Table (2): Comparison the degree of oral toxicity between clove oil group and normal saline solution group at the pre-test and post-test periods:

Degree of Oral Toxicity	Pre-test					Post-test				
	Clove Oil		Normal saline		T p-value	Clove Oil		Normal saline		T p-value
	f.	%	f.	%		f.	%	f.	%	
I	0	0.0	0	0.0	0.104 0.623	8	80.0	2	20.0	0.600 0.000**
II	4	0.0	4	0.0		2	20.0	5	50.0	
III	4	40.0	2	20.0		0	0.0	3	30.0	
IV	2	20.0	4	40.0		0	0.0	0	0.0	
V	0	0.0	0	0.0		0	0.0	0	0.0	
MS±SD	2.8 ± 0.789		0.0		U/p-value 44/ 0.630	0.0		2.1 ± 0.738		U/p-value 17/ 0.006**

τ: Kendal-Taue test, U; Mann-Whitney test, **=highly significant (p-value ≤0.01), MS=Mean of score, SD=Standard deviation.

Table (2) shows no significant statistical differences at p-value of 0.623 in oral toxicity degree between clove oil and normal saline solution groups before applying the intervention protocol, but after seven days of interventional protocol there are a significant statistical difference at p-value of 0.000 between both groups in favor the clove oil group. Therefore, clove oil cures the oral toxicity much more than normal saline solution.

Table (3): Comparison the degree of oral toxicity between clove oil group and control group at the pre-test and post-test periods:

Degree of Oral Toxicity	Pre-test					Post-test				
	Clove Oil		Control group		T p-value	Clove Oil		Control group		T p-value
	f.	%	f.	%		f.	%	f.	%	
I	0	0.0	0	0.0	0.122 0.725	8	80.0	0	0.0	0.825 0.000**
II	4	40.0	3	30.0		2	20.0	1	10.0	
III	4	40.0	4	40.0		0	0.0	3	30.0	
IV	2	20.0	3	30.0		0	0.0	6	60.0	
V	0	0.0	0	0.0		0	0.0	0	0.0	
MS±SD	2.8 ± 0.789		3 ± 0.817		U/p-value 43/ 0.573	1.2 ± 0.422		3.5 ± 0.707		U/p-value 1/ 0.000**

τ: Kendal-Taue test, U; Mann-Whitney test, **=highly significant (p-value ≤0.01), MS=Mean of score, SD=Standard deviation.

Table (3) shows no significant statistical differences at p-value of 0.725 in oral toxicity degree between clove oil and control group before the intervention, but after seven days of interventional protocol there are a highly significant statistical differences at p-value of 0.000 was found between both groups in favor the clove oil group. Therefore, clove oil cures the oral toxicity much more than the disapplication of the interventional protocol.

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

Degree of Oral Toxicity	Pre-test					Post-test				
	Normal saline		Control group		T p-value	Normal saline		Control group		T p-value
	f.	%	f.	%		f.	%	f.	%	
I	0	0.0	0	0.0	0 1.0	2	20.0	0	0.0	0.667 0.000**
II	4	40.0	3	30.0		5	50.0	1	10.0	
III	2	20.0	4	40.0		3	30.0	3	30.0	
IV	4	40.0	3	30.0		0	0.0	6	60.0	
V	0	0.0	0	0.0		0	0.0	0	0.0	
MS±SD	3 ± 0.943		3 ± 0.817		U/p-value 50/ 1	2.1 ± 0.738		3.5 ± 0.707		U/p-value 10/0.002**

τ: Kendal-Taue test, U; Mann-Whitney test, **=highly significant (p-value ≤0.01), MS=Mean of score, SD=Standard deviation.

Table (4) shows no significant statistical differences at p-value (1.0) in oral toxicity degree between normal saline solution and the control group before the intervention, while after seven days a highly significant statistical differences are found at p-value of 0.000 between both groups in favor the normal saline group. Therefore, normal saline solution cures the oral toxicity much more than disapplication of the interventional protocol.

Table (5): Comparison the levels of oral mucositis between clove oil group and normal saline solution group at the pre-test and post-test periods:										
Oral Mucositis levels	Pre-test					Post-test				
	Clove Oil		Normal saline		T p-value	Clove Oil		Normal saline		T p-value
	f.	%	f.	%		f.	%	f.	%	
Mild	1	10.0	0	0.0	0.104 0.623	10	100.0	7	70.0	0.600 0.011*
Moderate	6	60.0	4	40.0		0	0.0	2	20.0	
Severe	3	30.0	6	60.0		0	0.0	1	10.0	
MS±SD	2.2±0.633		2.6±0.516		U/p-value 33/0.14	1±0.000		1.4±0.69		U/p-value 35/0.068
MS±SD for Sum	25.1±3.604		28.2±4.022		t/ p-value 1.815 0.08	14.4±1.350		19.9±4.88		t/ p-value 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, **=highly significant (p-value ≤0.01), MS=Mean of score, SD=Standard deviation.										

Table (5) shows no significant statistical differences at p-value of 0.623 in the levels and total cumulative score of oral mucositis between clove oil group and normal saline solution group before the application of intervention, while after seven days of interventional protocol a highly significant statistical differences are found at p-value of 0.011 between both groups in favor the clove oil group. Therefore, clove oil cures oral mucositis much more than normal saline solution.

Table (6): Comparison the levels of oral mucositis between clove oil group and control group at the pre-test and post-test periods										
Oral Mucositis Levels	pre					post				
	Clove Oil		Control group		T p-value	Clove Oil		Control group		T p-value
	f.	%	f.	%		f.	%	f.	%	
Mild	1	10.0	2	20.0	0.099 0.650	10	100.0	0	0.0	0.928 0.042*
Moderate	6	60.0	3	30.0		0	0.0	2	20.0	
Severe	3	30.0	5	50.0		0	0.0	8	80.0	
MS±SD	2.2±0.633		2.3±0.823		U/p-value 44.5 0.651	1±0.000		2.8±0.42		U/p-value 0 0.000**
MS±SD for Sum	25.1±3.604		26.5±4.57		t/p-value 0.760 0.457	14.4±1.350		29.6±2.87		t/p-value 15.133 0.000**
τ: Kendal-Taue test, U; Mann-Whitney test, t: Independent sample t-test, for Sum: the cumulative total mucositis assessment score, **=highly significant (p-value ≤0.01), *= significant (p-value ≤0.05), MS=Mean of score, SD=Standard deviation.										

Table (6) shows no significant statistical differences at p-value of 0.650 was found in levels of oral mucositis between clove oil group and control group before the application of interventional protocol, while after seven days of intervention significant statistical differences are found at p-value of p-value of 0.042 between both groups in favor the clove oil group. Therefore, clove oil cures the oral mucositis much more than not applying the interventional protocol.

Table (7): Comparison the levels and total cumulative score of oral mucositis between normal saline solution group and control group pre and post the application of normal saline solution										
Oral Mucositis levels	Pre-test					Post-test				
	Normal saline		Control group		T p-value	Normal saline		Control group		T p-value
	f.	%	f.	%		f.	%	f.	%	
Mild	0	0.0	2	20.0	0.169 0.425	7	70.0	0	0.0	0.745 0.000**
Moderate	4	40.0	3	30.0		2	20.0	2	20.0	
Severe	6	60.0	5	50.0		1	10.0	8	80.0	
MS±SD	2.6±0.516		2.3±0.82		U/p-value 41 0.445	1.4±0.699		2.8±0.42		U/p-value 8 0.001**
MS±SD for Sum	28.2±4.02		26.5±4.57		t/p-value 0.882 0.389	19.9±4.88		29.6±2.87		t/p-value 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, **=highly significant (p-value ≤0.01), *= significant (p-value ≤0.05), MS=Mean of score, SD=Standard deviation.										

Table (7) shows no significant statistical differences at p-value of 0.425, and 0.389 in the levels and total cumulative score of oral mucositis between normal saline solution group and control group before the application of interventional protocol, while after seven days of intervention a highly significant statistical differences are found at p-value of 0.000 between both groups in favor the normal saline solution group. Therefore, normal saline solution cures oral mucositis much more than disapplication of the interventional protocol.

4. Discussion

Oral mucositis is considered a potentially very common severe side effect caused by cancer treatments including chemotherapy and

radiotherapy, it is lead to limitation and even interruption of the treatment regimen with minimizing its effectiveness. 30 patients who were confirmed to have oral mucositis and were undergoing chemotherapy at Imam Al-Hussein Oncology Center and at Oncology wards of Imam Al-Hassan Al-Mujtaba Teaching Hospital participated in this study. This study considered the first comparative study to identify the effect of an interventional protocol using clove oil versus normal saline solution upon the degree of oral mucositis in patients with cancer undergoing chemotherapy. No adverse effects were reported from participants of both groups.

Concerning the comparison of oral toxicity degree between clove oil group and normal saline solution group as shown in table (2), the result exposed that there were no significant statistical differences in oral toxicity degree between clove oil and normal saline group before the application of an interventional protocol, while after seven days of intervention a highly significant statistical differences at p-value of 0.000 was found between both group in favor the clove oil group. This finding was compatible with the result of the study that was done by Kong, et al., (2016) reported that a clove-based herbal mouthwash can have a beneficial effect on minimizing or preventing oral mucositis in patients with cancer. Therefore, clove oil cures oral toxicity much more than normal saline solution (as shown in figure 1). The researchers attribute 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, and this opinion is in the same line with the study conducted by Nuñez, et al., (2012) which stated that clove essential oil can be considered as a possible antimicrobial agent for external use because it is not markedly inactivated by dilution or affected by organic substance.

Figure (1)

Before implementing interventional protocol using clove oil ***After implementing interventional protocol using clove oil***

The results in table (3) shows that are no significant statistical differences in oral toxicity degree between clove oil and the control group before the application of interventional protocol, but after seven days of interventional protocol a highly significant statistical differences at p-value of 0.000 are found between both groups in favor the clove oil group. This result agreed with the study performed by Gupta and Prakash, (2021) revealed 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 a wide range of antimicrobial activity against the microbes causing oral problems and that it had an antifungal effect. Therefore, clove oil cures oral toxicity much more than not applying the interventional protocol.

The result in table (4) revealed that are no significant statistical differences in oral toxicity degree between the normal saline solution group and control group before applying the interventional protocol, while after seven days of interventional protocol a highly significant statistical differences at p-value of 0.000 are found between both groups in favor the normal saline solution group. This result regarding the effectivity of normal saline solution on oral mucositis was supported and agreed by the result of the study conducted by Alhamad, (2011) revealed that normal saline solution mouth wash was considered safe and effective in reducing the severity of oral mucositis in patients with cancer who received chemotherapy. Naibaho, et al., (2020) reported that the intensity of oral mucositis in respondents before being given normal saline mouthwash was severe pain (60%) in the intervention group, but after being given intervention for 5 days was mild pain (60%). Whereas, in the control group who experienced oral mucositis before was severe (55%), and after 5 days was moderate (85%). Therefore, a normal saline solution cures oral toxicity much more than the disapplication of the interventional protocol.

Concerning the comparison level and total cumulative score of oral mucositis between the clove oil group and the normal saline solution group as illustrated in table (5), the result shows that are no significant statistical differences between the clove oil group and normal saline solution group before the application of an interventional protocol, while after seven days of interventional protocol a highly significant statistical differences at p-value of 0.011 are found between both groups in favor the clove oil group, this result was in the same line with a study done by Al- Barrak and Mahmoud, (2011) stated 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. These anti-adhesion activities besides of their previously known antibacterial activity were in favor of using this oil in oral treatment. Thus, the researchers attribute this result to the significant role of clove oil in antibacterial, antifungal, and antioxidant properties, furthermore its activity to promote the healing process. Therefore, clove oil cures oral mucositis much more than a normal saline solution.

The study results in table (6) revealed that are no

significant statistical differences in level and a total cumulative score of oral mucositis between the clove oil group and the control group before the application of the interventional protocol, but after seven days of intervention, a significant statistical difference at p-value of p-value of 0.042 was seen between both groups in favor the clove oil group. This finding was compatible with Kartin, et al., (2014) study, reported that oral mucositis severity was lower in the experimental groups that received oral care protocol compared to the control group, also the result of their study demonstrates that oral mucositis rate may be reduced with the application of oral care protocol. Probable oral mucositis symptoms and pain may be eliminated and occur nutritional improvement with oral care protocol that should be applied by nurses. Thus, clove oil cures oral mucositis much more than the disapplication of the interventional protocol. In researchers' opinion, the reason for significant oral mucositis healing when using clove oil compared to the control group is due to many of the chemical properties in the composition of cloves that accelerate the healing process and facilitate wound healing, and this opinion is supported by Agrawal et al., (2014) stated that clove oil shows 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 concentrations. Clove oil is an important herbal medication that has a variety of different uses like antifungal, antioxidant, antiviral, anti-inflammatory, antibacterial, antipyretic, analgesic, antimycotic, antiulcerogenic, and wide variety of uses.

Concerning comparison level and a total cumulative score of oral mucositis between the normal saline solution group and the control group as shown in table (7), the result shows no significant statistical differences before interventional protocol, while after seven days of applying normal saline solution interventional protocol appeared a highly significant statistical differences at p-value of 0.000 was reported between both groups in favor the normal saline solution group. This study result was in the same line with Naibaho, et al., (2020) study, revealed that the distribution of respondents' comfort before being given normal saline mouthwash in the intervention group was a little bad comfort (score 2) (55%), but after being given oral care mouthwash for 5 days was very good comfort (score 4) (65%). Whereas the control group obtained who experienced oral mucositis before was a little bad comfort (score 2) (70%), but after 5 days was slightly good comfort (score 3) (65%). So, normal saline solution cures oral mucositis much more than not applying the interventional protocol and the researchers attributed the causes that make the application of normal saline solution significantly reduces the level of oral mucositis among patients with chemotherapy 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 oral mucositis.

5. Conclusions

The application of interventional protocol using clove oil is greatly promoting and enhances the level of oral mucositis and reduces oral mucositis grade.

There were significant statistical differences between both clove oil group and normal saline solution group in favor the clove oil group.

Both normal saline solution and clove oil gargling procedures are considered effective and safe interventional protocols in minimizing the severity of oral mucositis in patients with cancer undergoing chemotherapy, but clove oil was preferred and considered more potent.

6. Recommendations

It is necessary to conduct further studies on a larger sample size for the determination of the efficacy of clove oil herbal product on the degree of oral mucositis. Also, an interventional protocol toward oral mucositis management should be adopted by the nurses and they should update their knowledge regarding oral mucositis care especially in oncology units.

7. Acknowledgments

Great thanks to the Research Ethics Committee in College of Nursing/ University of Kerbala for research advice and guidance, also the deepest thankfulness to the Kerbala Health Directorate/ Imam Al-Hussein Oncology Center and Imam Al-Hassan Al-Mujtaba teaching hospital staff especially those in oncology wards for their cooperation and assistance in supporting this study. Furthermore, special thanks to all the patients who participated in this study whether volunteers in the experimental groups or participants in the control group.

Financial disclosure: No financial support

Conflict of interest

No adverse effects were reported from patients of both groups, and no one was harmed during the conduction of the study.

Ethical clearance

This study was done after obtaining the approval from the Ethical Committee of College of Nursing/ University of Karbala.

References

Abbas, Z., & Rehman, S. (2018). An overview of cancer treatment modalities. Neoplasm, 1, 139-157. Retrieved from: http://dx.doi.org/10.5772/intechopen.76558

Agrawal, M., Agrawal, S., Rastogi, R., Singh, P., Adyanthaya, B., & Gupta, H. (2014). A review on

uses of clove in oral and general health. Indian Journal of Research in Pharmacy and Biotechnology, 2(4), 1321. Retrieved from https://www.ijrpb.com/issues/Volume%202_Issue%204/ijrpb%202(4)%2016%20Mayank%20Agarwal%201321-1324.pdf.

Alam, A., Farooq, U., Singh, R., Dubey, V., Kumar, S., Kumari, R.,. & Dhar, K. (2018). Chemotherapy treatment and strategy schemes: A review. Open Access J Toxicol, 2(5), 555600. Retrieved from: http://DOI: 10.19080/OAJT.2018.02.555600.

Al-Barrak, A., & Mohammed, Z. (2011). Effect of clove oil on adhesion of Staphylococcus aureus to buccal cavity epithelial cells in vitro. Iraqi J. Comm. Med, 24(4), 295-301. https://www.iasj.net/iasj/download/e4ebfc99e1b005c5

Alhamad, H. Q. (2008). Evaluating the effect of normal saline and caphosol® (calcium phosphate) mouth washes in the prevention and treatment of oral mucositis in patients who receive combination chemotherapy for haematological malignancies and are at high risk of developing oral mucositis.

Avci, S., & Sari, H. (2019). Effect of an evidence-based nursing intervention on the diagnosis of oral mucositis in the pediatric stem cell transplant unit. Asia-Pacific Journal of Oncology Nursing, 6(3), 292-299. Retrieved from: https://doi.org/10.4103/apjon.apjon_5_19

Basch, E., Gasparyan, A., Giese, N., Hashmi, S., Miranda, M., Sollars, D., & Weissner, W. (2008). Clove (Eugenia aromatica) and clove oil (eugenol). Natural standard monograph (www. naturalstandard. com) copyright© 2008. Journal of Dietary Supplements, 5(2), 117-146. DOI: 10.1080/19390210802335391

Cancer Institute NSW, 2019. Version 5. https://www.eviq.org.au/clinical-resources/assessment-tools/10-oral-mucositis-assessment-tool.

Gupta, C., & Prakash, D. (2021). Comparative Study of the Antimicrobial Activity of Clove Oil and Clove Extract on Oral Pathogens. Retrieved from: doi: 10.17140/DOJ-6-144

Han, X., & Parker, T. (2017). Anti-inflammatory activity of clove (Eugenia caryophyllid) essential oil in human dermal fibroblasts. Pharmaceutical biology, 55(1), 1619-1622. Retrieved from: https://doi.org/10.1080/13880209.2017.1314513

Kaplan, W. (2013). Background paper 6.5 cancer and cancer therapeutics. World Health Organization (ed) Priority medicines for Europe and the world: update, 6-5.

Kartin, P., TAŞCI, S., Soyuer, S., & Elmali, F. (2014). Effect of an oral mucositis protocol on quality of life of patients with head and neck cancer treated with radiation therapy. Clinical Journal of Oncology Nursing, 18(6). Retrieved from: http://doi.org/10.1188/14.cjon.e118-e125

Kong, M., Hwang, D., Yoon, S., & Kim, J. (2016). The effect of clove-based herbal mouthwash on radiation-induced oral mucositis in patients with head and neck cancer: a single-blind randomized preliminary study. OncoTargets and therapy, 9, 4533. Retrieved from: https://doi.org/10.2147%2FOTT.S108769

McGuire, D., Fulton, J., Park, J., Brown, C., Correa, M., Eilers, J.,. & Lalla, R. (2013). Systematic review of basic oral care for the management of oral mucositis in cancer patients. Supportive Care in Cancer, 21(11), 3165-3177. Retrieved from: https://link.springer.com/article/10.1007/s00520-013-1942-0

Naibaho, E., Dharmajaya, R., & Harahap, I. (2020). Effectiveness of Oral Care Using Normal Saline and Baking Soda Towards Pain and Comfort in Mucositis Patients Undergoing Chemotherapy. EXECUTIVE EDITOR, 11(10), 215. Retrieved from: file:///C:/Users/AGK/Downloads/ojsadmin,+37%20(1).pdf

Nivetha, R., Murthykumar, K., Ashwin, K., Kumar, N., & Priyadarshini, R. (2014). Effects of natural products on oral health: A review. Asian J Pharm Clin Res, 7(5), 279-282. Retrieved from: https://doi.org/10.1111/scd.12358

Normando, A., de Menêses, A., de Toledo, I., Borges, G., de Lima, C., Dos Reis, P., & Guerra, E. (2019). Effects of turmeric and curcumin on oral mucositis: A systematic review. Phytotherapy Research, 33(5), 1318-1329. Retrieved from: https://doi.org/10.1002/ptr.6326

Nuñez, L., & D'Aquino, M. (2012). Microbicide activity of clove essential oil (Eugenia caryophyllata). Brazilian journal of microbiology, 43, 1255-1260. Retrieved from: https://doi.org/10.1590/S1517-83822012000400003

Saldanha, S., & Almeida, V. (2014). A comparative study to assess the effectiveness of turmeric mouth wash versus saline mouth wash on treatment induced oral mucositis (Tiom) in a selected hospital at Mangalore. Journal of Clinical Research & Bioethics, 5(6), 1. Retrieved from: DOI: 10.4172/2155-9627.1000200

World Health Organization. (1979). WHO handbook for reporting results of cancer treatment. World Health Organization. Retrieved from: https://apps.who.int/iris/bitstream/handle/10665/37200/WHO_OFFSET_48.pdf?sequenc.

Appendix (1)

The instructions that must be followed by the patients

1. Any medications or mouthwash solutions for oral mucositis were not allowed in all study groups.
2. All patients were also instructed to maintain good oral hygiene and clean their teeth with a soft toothbrush three times a day (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 rough or crunchy foods because they may damage the mucosal lining 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.