Mansoura Nursing Journal (MNJ) Vol. 12. No. 2 – 2025 **Original Article**
Print ISSN: 2735 – 4121 Online ISSN : 2735 – 413X

Cryotherapy Versus Normal Saline Mouth Wash: Its Impact on Chemotherapy-Induced Oral Mucositis among Cancer Patients

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ABSTRACT

Background: Oral mucositis (OM) is a severe consequence of chemotherapy, affecting 20%–40% of cancer pa which can cause interruption or postponement of the treatment. **Aim of the study:** This study aimed to examine the imp cryotherapy versus normal saline mouth wash on chemotherapy-induced oral mucositis (CIOM) among cancer pa **Method:** Randomized controlled trial (RCT) research design was utilized, involving a sample of 96 patients with cance were assigned from the Oncology Center at Mansoura University Hospital over six months. The study sample was di randomly into three equal groups by a ratio of 1:1:1 (32) cancer patients for each. One tool was used in this study that con of two parts: demographic characteristics & a health-relevant data sheet, and the World Health Organization (WHO) muc scale. **Results:** There were highly statistically significant changes in the incidence of OM between the studied samples 14th and 21st days, where the P value was 0.005 and <0.001. **Conclusion and Recommendations:** Oral cryotherapy (OC key approach to reducing the severity and occurrence of OM among cancer patients. So, it's recommended that oncology n use oral cryotherapy (OC) in their daily care.

Keywords: *Cryotherapy, Saline Mouth Wash, Chemotherapy, Ice, Oral Mucositis*

Introduction

Oral mucositis (OM) is one of the most prevalent and serious adverse effects of chemotherapy, which typically manifests within 3–7 days following treatment initiation and peaks around 10 days after treatment (Song et al., 2025). According to the WHO categorization, the intensity of OM ranges between Grades 1 and 4. Grade 1 is characterized by erythema; Grade 2 by painful ulcers; Grade 3 by severe painful ulcers and trouble eating; and Grade 4 by the patient's inability to consume anything orally. (Mogaji et al., 2024).

OM can cause poor food intake, resulting in significant nutritional deficiencies and weight loss, potentially necessitating parenteral nutrition, which might lower the patient's quality of life (QOL). It may also be associated with superinfections, which raises the risk of bacteremia and sepsis. Furthermore, discontinuing anticancer medication in some patients due to OM can impair their overall survival chance (Lavaee et al., 2025).

The incidence of CIOM was around 20%–40% in those who underwent conventional chemotherapy and 80% in patients administered high-dose chemotherapy as a prerequisite for hematopoietic stem cell transplantation (Sun et al., 2025). The MASCC guidelines emphasize the need to sustain CIOM through adequate oral hygiene and a structured preventive program. These recommendations include dietary adjustments to soft foods, the use of treatments including honey, aloe vera, cryotherapy, keratinocyte growth factor, antibiotic pastilles or pastes, and sucralfate, as well as anesthesia and palliative rinses. (Parra-Rojas et al., 2025).

Cryotherapy is a preventive strategy used to prevent and manage CIOM that involves applying cold therapy, such as ice chips or cold water, within the oral cavity. Cold temperatures are intended to minimize the intensity and length of mucositis symptoms (Banat et al., 2024). The primary mechanism of action is to induce vasoconstriction in the oral mucosa, which reduces blood flow to the tissue and limits the delivery of chemotherapeutic drugs to the area. Additionally, the cooling effect may lower the metabolic activity of the basal epithelial layer, rendering these cells less susceptible to damage caused by chemotherapy agents (Alshammari et al., 2024).

Despite the limited data on the use of saline in controlling OM, it has been discovered that utilizing inactive rinses to promote oral clearance may be beneficial for preserving oral hygiene and enhancing patient comfort (Zwicker et al., 2023). Normal saline mouthwash is a non-irritant, neutral

oral cleanser that is useful for maintaining adequate oral hygiene due to its low harmful effects and physiological properties (Dash et al., 2025).

Therefore, it becomes vital to assess the effect of cryotherapy versus normal saline mouth wash on CIOM among cancer patients.

Significance of the Study

Cancer is the major cause of mortality before the age of 70 in 112 out of 183 nations (Alvarado-Omenat et al., 2025). The International Agency for Research on Cancer estimates that 9.7 million deaths and about 20 million new cancer cases were reported in 2022. According to demographic predictions, there would be 35 million new cancer cases by 2050 (Bray et al., 2024).

Chemotherapy remains the primary treatment but is often associated with severe side effects such as nausea, vomiting, diarrhea, anorexia, OM, and dysphagia (Song et al., 2025). CIOM impairs nutritional consumption and oral hygiene while increasing the risk of local/systemic infection. OM progression can lead to termination of antineoplastic therapy, which influences patient outcomes and QOL, including physical, functional, and emotional status, as well as oral problems (de Arruda et al., 2024).

So, an oncology nurse has a pivotal role in preventing oral mucositis by applying measures that directly decrease the severity and occurrence of OM in cancer patients undergoing chemotherapy, hence indirectly improving QOL.

1.1. Aim of the Study:

The current study aimed to examine the impact of cryotherapy versus normal saline mouth wash on CIOM among cancer patients.

1.2. Research Hypotheses:

H1: Patients who participated in cryotherapy (cryo-group) would exhibit a lower oral mucositis mean score than those who didn't (control group and normal saline group).

2. Method

2.1. Design**:**

Randomized controlled trial (RCT) research design was employed consistently throughout this study.

2.2. Setting:

This research was conducted at the Oncology Center-Mansoura University (OC-MU) in the chemotherapy installation unit, which is linked with Mansoura University Medical Centers in Egypt, from May 2024 to November 2024.

2.3. Participants

A purposive sample of 96 patients with cancer was assigned randomly from the Oncology Center at Mansoura University Hospital. The sample was randomly divided into three equal groups by a ratio of 1:1:1(32 cancer patients for each).

Inclusion criteria included patients ranging in age from 20 to 60 years old, agreeing to participate in the study, being able to interact vocally, and receiving chemotherapy for the first time. Patients who were critically unwell and had an allergy to ice or regular saline mouthwash, as well as any oral ulcers or mucositis that had occurred before starting chemotherapy, were excluded.

2.4. Data Collection Tool

A structured Interview Questionnaire was utilized to collect data pertinent to this study. It consists of two parts:

Part I :Demographic Characteristics & Health-Relevant Datasheet

This part was created by the researcher after reviewing relevant and recent literature (Correa et al., 2020; Ferreira et al., 2020; Khosroshahi et al., 2023; López-González et al., 2021; Patel et al., 2021; Singh & Singh et al., 2020) to assess cancer patient's socio-demographic characteristics (SDC) and their health-relevant data (HRD). SDC comprised the patient's name, age, gender, marital status, education level, occupation, payment method for treatment, and telephone number. HRD covered diagnosis, cancer type and stage, length of the disease, types of chemotherapy, comorbidity, and oral assessment guide (OAG).

The OAG, developed by Eilers et al. (1988), was used to assess the state of the oral cavity and the severity of stomatitis. It is divided into eight categories: voice, swallow, lips, tongue, saliva, mucous membranes, gingival, and teeth/dentures. Each category is scored on a scale of one, two, and three, with normal findings (1) and severe (3). A sum score is generated from the eight categories, resulting in a range of 8 normal findings to 24 severe alterations.

Part II: The World Health Organization (WHO) Mucositis Scale:

This tool, developed by WHO (1979), measures both subjective and objective signs and symptoms of OM. It consists of 4 grades: Grade zero, absence of OM; Grade I, a presence of erythema in the mucous membrane and soreness; Grade II, is the presence of Painful erythema and

ulcers, with the ability to eat solids. Grade III, painful edema, being able to consume liquid diet, and Grade IV, severe stomatitis, that interferes with eating. Grade III and IV OM are considered severe, unbearable mucositis associated with ulcerations and low QOL.

2.4.1. Validity and Reliability of the Study Tool

The data collection tool was verified and revised for content validity by a panel of seven experts (Jury), five in the field of Medical-Surgical Nursing and two oncologists in Internal Medicine in the field of Medical-Surgical Nursing - Faculty of Nursing in Mansoura University to evaluate tools for comprehension, application, comprehensiveness, clarity, and relevance. The content validity of the tool was assessed in terms of knowledge accuracy, relevance, and comprehensiveness, and no modifications were made. The reliability of the study tool, Parts I and II, was tested using the test-retest method and showed good test-retest reliability (r = 0.70 and 0.83, respectively).

2.5. Pilot Study

A pilot study was conducted on 10% of the study participants (9 patients) to assess the feasibility, objectivity, clarity, and applicability of the developed tool, and to estimate the time required to complete the data collection sheets. There were no modifications, and those patients were excepted from the sample and the results of the study.

2.6. Data Collection Process

The Vice Dean of the College of Nursing for Postgraduate Studies and Research, Mansoura University, provided an official letter to the manager of the OC-MU requesting approval to carry out the study. The researcher met the supervisor of nursing staff at the chemotherapy installation unit to introduce herself, provide her with a copy of the approval (Appendix II), and explain the aim of the study and data collection technique. Before the treatment cycle, the researcher conducted interviews with all patients who were included in the study and invited them to participate.

The researcher conducted an initial assessment of patients who accepted to participate in the study to ensure they met the inclusion and exclusion criteria. Then, socio-demographic and health-related data were obtained from their records using Part I of the tool. The needed equipment for the process, including ice, normal saline, syringes, and a single-use cup, was prepared. An oral assessment was performed using a torch and tongue depressor for better visibility of the cavity.

Implementation Phase

The control group received normal hospital care only. For the cryotherapy group, the researcher prepared ice cubes and then stored them in the refrigerator of the installation unit. The patients were instructed to hold & move ice cubes starting five minutes before chemotherapy and continuing until five minutes following it. New ice cubes will be used when the first ones have dissolved. For normal saline group; a suitable amount (about 30 ml) of normal saline solution 0.9% was pulled by the syringe and put into a single-use cup, the patient was instructed to gargle with the solution and ensured that it reached the entire oral cavity then spat the normal saline solution out after gargling was complete. These steps were repeated before, during, and after chemotherapy treatment.

Evaluation Phase

Posttest measurement was taken from the three groups on three occasions using parts II within 7, 14, & 21 days from each chemotherapy cycle. The posttest was applied to the patients over the phone. At the end of the study, four test measurements (onset, at 7, 14, & 21 days) were applied to the three groups.

2.7. Statistical Analysis

SPSS software (Statistical Package for the Social Sciences, version 22) was used to code, organize, tabulate, and statistically analyze the data that had been gathered. The normality assumption was accepted.

2.8. Ethical Considerations

Ethical permission was gained from the Research Scientific Ethics Committee of the Faculty of Nursing – Mansoura University (401). Oral informed consent was gained from each patient enrolled in the study after informing them about the study's aim, procedure, benefits, and risks. The anonymity and confidentiality of the collected data ensured that ethical considerations were met. Patients were advised that their participation was voluntary and confidential. Each participant was able to withdraw from the study at any moment, with no consequence or responsibility.

3. Results

The study sample is described in Table 1. A total of ninety-six patients were assigned to the study, with the mean (SD) age of the patients in the cryotherapy, saline, and control groups being 43.05±10.34, 42.68±10.14, 43.32±9.97 years,

respectively. There were no statistically significant differences observed between the three groups concerning their personal characteristics ($p < 0.05$) as shown.

Similarly, there were no statistically significant changes between the two groups according to cancer type, cancer stage, length of the disease, type of chemotherapy, number of cycles of chemotherapy, interval between cycles, and chronic diseases, as shown in Table 2.

When looking at stomatitis severity according to the oral assessment guide among the studied samples throughout the study period, according to the oral assessment guide. It is observed that there were no significant statistical changes among the groups on the 7th day and the 14th day of assessment. But there were highly statistically significant changes among the three groups on the 21st day with a P value of <0.001 as the highest mean ± SD was found in the control group (18.13±4.05) while the lowest mean ± SD (9.88±3.06) was in the cryotherapy group (9.88±3.06) as shown in figure 1 and table 3.

Table 4 illustrates that there were highly significant statistical changes in OM incidence and severity between the studied samples on the 14th and 21st days, where the P value was 0.005 and <0.001. Consistent with the WHO mucositis scale, all study samples were free from OM at the beginning of the study. On the 7th day, the highest proportion of patients (68.8%, 65.6%, 53.1%) in the cryotherapy, saline, and control groups had normal oral membranes, respectively. While mild oral mucositis was discovered in the three groups (31.3%, 34.4%, and 46.9%), respectively.

On the 14th day, (56.2%, 40.6%, and 25.1%) of the cryotherapy, saline, and control groups were free from OM, respectively. While mild OM was observed in the (43.8%, 53.1%, 53.1%) cryotherapy, saline, and control groups, respectively. And moderate OM was detected in (6.3%, 21.9%) of saline and the control group, respectively. However, severe OM wasn't detected in all studied groups.

On the 21st day, (56.2%, 37.5%) of the cryotherapy and saline groups were free of OM, whereas nobody in the control group was free of it. Mild OM was identified in (34.4%, 40.6%, 34.3%) in cryotherapy, saline, and control groups, respectively. Moderate OM was found (9.4%, 15.6%, 46.9%) in the three groups, respectively. Severe OM was discovered (6.3%, 18.7%) in the saline and control groups, respectively. And it wasn't detected in the cryotherapy group.

Table 1. *Distribution of the Study Participants According to Their Personal Characteristics* **(***n=96)*

Variable	Cryotherapy group		Saline group		Control group		Significance test (P)
	N=32	%	N=32	%	N=32	%	
Age (Years)							
20 to less than 30	4	12.5	2	6.3	3	9.4	Mc= 1.605 (0.952)
30 to less than 40	4	12.5	7	21.9	6	18.8	
40 to less than 50	11	34.4	11	34.4	10	31.3	
50 to less than 60	13	40.6	12	37.5	13	40.6	
Mean ± SD	43.05±10.34		42.68±10.14		43.32±9.97		F=0.144 (0.866)
Sex							
Male	12	37.5	14	43.8	13	40.6	X2=0.259 (0.878)
Female	20	62.5	18	56.2	19	59.4	
Marital status							
Single	5	15.6	7	21.9	4	12.5	Mc=2.389 (0.665)
Married	25	78.1	22	68.8	27	84.4	
Divorced	2	6.3	3	9.4	1	3.1	
Educational level							
Illiterate	5	15.6	3	9.4	6	18.8	X2=2.222 (0.898)
Read and write	7	21.9	5	15.6	5	15.6	
Secondary education	14	43.8	15	46.9	13	40.6	
Higher education	6	18.8	9	28.1	8	25.0	
Occupation							
Governate work	7	21.9	6	18.8	8	25.0	Mc= 2.030 (0.980)
Private work	8	25.0	9	28.1	8	25.0	
Student	3	9.4	2	6.3	2	6.3	
House wife	11	34.4	14	43.8	12	37.5	
Hand work	3	9.4	1	3.1	2	6.3	
Payment method for treatment							
Government's expense	13	40.6	14	43.8	15	46.9	X2= 1.575 (0.813)
Own expense	9	28.1	8	25.0	5	15.6	
Health insurance	10	31.3	10	31.3	12	37.5	

X^2: Pearson Chi-Square, Mc: Monte Carlo test, F: One Way ANOVA. *Data are expressed by number (n) and percentage (%),*

Table 2. *Distribution of the Study Participants According to their Health Relevant Data (n=96)*

Variable	Cryotherapy group		Saline group		Control group		Significance test
	N=32	%	N=32	%	N=32	%	(P)
Cancer type							
Breast cancer	13	40.6	12	37.5	9	28.1	
Colorectal cancer	7	21.9	5	15.6	6	18.8	
Pancreatic cancer	5	15.6	4	12.5	6	18.8	X2= 5.365
Lung cancer	4	12.5	6	18.8	5	15.6	(0.866)
Uterine cancer	3	9.4	2	6.3	4	12.5	
Cervical cancer	0	0.0	3	9.4	2	6.3	
Cancer stage							
Stage I	17	53.1	13	40.6	15	46.9	
Stage II	9	28.1	11	34.4	10	31.3	X2= 1.019
Stage III	6	18.8	8	25.0	7	21.9	(0.907)
Length of the disease							
Since 3 months	16	50.0	21	65.6	19	59.4	
3 to 9 months	12	37.5	4	12.5	7	21.9	Mc= 5.763
> 9 months	4	12.5	7	21.9	6	18.8	(0.218)
Type of chemotherapy							
Taxotel	11	34.4	9	28.1	8	25.0	
Folfox	5	15.6	6	18.8	8	25.0	
Taxol	6	18.8	7	21.9	5	15.6	Mc 7.147
Xelon	5	15.6	1	3.1	6	18.8	(0.711)
Plantinol	3	9.4	6	18.8	4	12.5	
Gemezar	2	6.3	3	9.4	1	3.1	
Numbers of chemotherapy cycles							
2-3	13	40.6	14	43.8	16	50.0	
4-5	11	34.4	12	37.5	13	40.6	Mc = 2.728
>5	8	25.0	6	18.8	3	9.4	P=0.604
Interval between cycles							
2 weeks	6	18.8	8	25.0	9	28.1	X2=0 .800
3 weeks	26	81.2	24	75.0	23	71.9	(0.670)
Chronic diseases							
No	21	65.6	18	56.3	20	62.5	
Diabetes Mellitus	7	21.9	10	31.3	5	15.6	Mc 5.646
Hypertension	4	12.5	3	9.4	4	12.5	(0.464)
Cardiac disease	0	0.0	1	3.1	3	9.4	

[#] More than one answer, X^2: Pearson Chi-Square, Mc: Monte Carlo test. *Data are expressed by number (n) and percentage (%),*

Table 3. *Mean Score of Stomatitis Severity According to the Oral Assessment Guide Among the Studied samples Throughout the Study Period (n=96)*

Oral assessment guide (OAG).	Cryotherapy group	Saline group	Control group	Significance test (P)
	Mean ± SD	Mean ± SD	Mean ± SD	
Stomatitis severity				
On the 7th day	8.78±1.36	9.03±2.02	9.69±2.46	F=1.756 (0.178)
On the 14th day	9.44±2.05	10.53±3.05	12.72±4.00	F= 9.086 (0 .001) **
On the 21th day	9.88±3.06	12.91±4.73	18.13±4.05	F= 34.789 (<0.001) **

F: One Way ANOVA, * Statistically significant at p<0.05

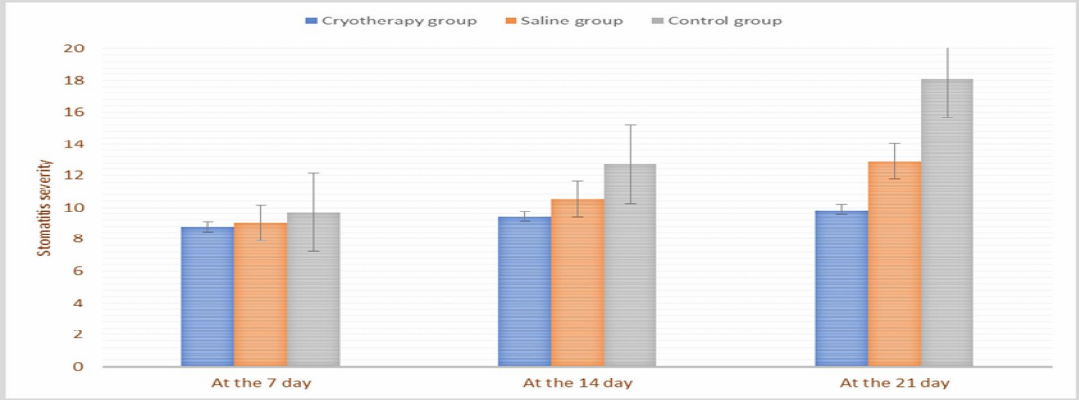

Figure 1. Stomatitis severity according to the oral assessment guide among the studied samples throughout the study period (n=96)

Table 4. *Oral Mucositis Severity According to the WHO Mucositis Scale During the Study Phase on the 7th ,14th and 2st days (n=96)*

WHO Mucositis grade	Cryotherapy group		Saline group		Control group		Significance test (P)
	N=32	%	N=32	%	N=32	%	
At the 7 day							
Normal	22	68.8	21	65.6	17	53.1	X^2=3.105 (0.212)
Mild	10	31.3	11	34.4	15	46.9	
Moderate	0	0.0	0	0.0	0	0.0	
Severe	0	0.0	0	0.0	0	0.0	
At the 14 day							
Normal	18	56.2	13	40.6	8	25.0	X^2=7.726 (0.005) **
Mild	14	43.8	17	53.1	17	53.1	
Moderate	0	0.0	2	6.3	7	21.9	
Severe	0	0.0	0	0.0	0	0.0	
At the 21 day							
Normal	18	56.2	12	37.5	0	0.0	Mc=34.811 (<0.001) **
Mild	11	34.4	13	40.6	11	34.4	
Moderate	3	9.4	5	15.6	15	46.9	
Severe	0	0.0	2	6.3	6	18.7	

X^2: Pearson Chi-Square, Mc: Monte Carlo test, * Statistically significant at p<0.05. *Data are expressed by number (n) and percentage (%),*

4. Discussion

This current study aimed to assess the impact of cryotherapy versus normal saline mouthwash on CIOM among cancer patients. The study's results reveal that there was a similar distribution among patients in the studied samples, with no statistically significant differences observed between them regarding demographic characteristics & health-relevant data before the intervention.

According to the current study, after completing the interventions, there were highly significant statistical changes between the cryotherapy, saline group, and the control in terms of OM incidence and severity on the 7th, 14th, and 21st days.

Consistent with the WHO mucositis scale, the results revealed that the percentage of normal oral mucosa at the end of the 21st day of assessment was more than the half in the cryotherapy, more than one third in saline group and no one in control group had normal oral membrane in which all study samples were free from oral mucositis (OM) at the beginning of the study. Consequently, there is clear evidence that cryotherapy improves mucositis grade more than normal saline or control.

The result displayed by Dash et al. (2025) confirmed the benefits of using cryotherapy over the normal saline group, as there was a great improvement in mucositis grade with a highly significant difference and p value on day 21.

Furthermore, the results of this study were confirmed by KURT et al. (2025), who compared cryotherapy (OC) to gargling with cold water (GCW) in managing and treating OM for the first 21 days. And found that OC was efficacious and safe for treating OM, with grade 0 considerably higher in the OC group after 21 days compared to the GCW and control groups.

Similarly, a study entitled "Effect of Ice Chips on Severity of Chemotherapy Induced Oral Mucositis" supported our results, which reported that applying ice chips (oral cryotherapy) is a common, affordable, easy-to-use technique that helps prevent OM without any side effects. At the end of the 1st, 2nd & 3rd weeks of intervention, there was a marked decline in the OM symptoms mean scores in the study group compared to the control group (Tharwat et al., 2024).

Another study, performed by Ebrahim et al. (2024), confirmed our findings by reporting that there were significant variances in the mean total scores, and those who used oral ice cubes showed slight clinical manifestations of OM. It demonstrates that using oral ice cubes to reduce clinical manifestations of OM was beneficial for cancer patients following chemotherapy.

The present study agrees with the findings of Soliman (2019), who stated that the highest percentage of patients in the cryotherapy group didn't have OM on the 7th, 14th, or 21st days of assessment. In addition, grades 1 and 2 OM were considerably lower in the cryotherapy group versus the control group.

4.1. Limitations of the Study

- Small sample size.
- Limited research on the effectiveness of saline mouthwash in preventing OM in oncology.

5. Conclusion and Recommendations:

This study demonstrated that using cryotherapy is more beneficial than normal saline mouthwash in decreasing CIOM among cancer patients according to the WHO mucositis grade, particularly on the 7th and 14th, and 21st days.

The recent study recommends that oncology nurses use oral cryotherapy (OC) in their daily care. In addition to an educational program for patients about how to apply OC correctly. To ensure generalizability, the study should be conducted using a large, randomly selected sample to ensure generalizability.

6. Acknowledgements

I want to extend special thanks to the participating patients and staff who participated and helped in this study.

7. Declaration of Conflicting Interests

The authors declared they have no conflicting interests.

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