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The Effect of Oral Cryotherapy and Gargling with Cold Water in the Prevention and Symptom Management of Oral Mucositis the Patients with Breast Cancer Undergoing Chemotherapy: An Assessor-Blinded, Parallel-Group, Three-Arm, Randomized Controlled Study

Kemoterapi Tedavisi Gören Meme Kanserli Hastalarda Oral Mukozitin Önlenmesinde ve Semptom Yönetiminde Oral Kriyoterapi ve Soğuk Suyla Gargara Yapmanın Etkisi: Değerlendirici-Kör, Paralel Gruplu, Üç-Kollu, Randomize Kontrollü Çalışma

Berna KURT[a], Zeynep SİPAHİ KARSLI[b], Nurdan ALTINÖZ[b], Berna Ömür ÇAKMAK ÖKSÜZOĞLU[c]

[a]Hacettepe University Faculty of Nursing, Department of Internal Medicine Nursing, Ankara, Türkiye
[b]University of Health Sciences Dr. Abdurrahman Yurtaslan Ankara Oncology Health Application and Research Center, Ankara, Türkiye
[c]University of Health Sciences Dr. Abdurrahman Yurtaslan Ankara Oncology Health Application and Research Center, Department of Internal Medicine, Department of Medical Oncology, Ankara, Türkiye

ABSTRACT Objective: To determine the effects of oral cryotherapy (OC) and gargling with cold water (GCW) in the prevention and symptom management of oral mucositis (OM) in patients with breast cancer undergoing chemotherapy. **Material and Methods:** This parallel-grouped, three-arm, randomized, and assessor-blinded trial used the OC and GCW. 105 eligible patients with breast cancer were assigned to 3 groups. OC (n=35) and GCW (n=35) for intervention groups were performed in three stages: I) instructions on by the investigator at the hospital; II) the implementation accompanied by the investigator at the hospital; III) the individual application of at home by patients. The patients in the control group (n=35) received standard care. Additionally, "Patient Information Form ", "Edmonton Symptom Assessment Scale", "World Health Organization Mucositis Scale (OTS)", and "Visual Analog Scale (VAS)" were conducted. **Results:** OTS and VAS scales, the OC group was significantly more effective than the GCW and control groups throughout the beginning 21-day period. During the 1st 16 days of evaluating the OTS and VAS conditions, the GCW groups showed significantly more effectiveness than the control group. **Conclusion:** OC alone was effective and safe for treating OM. The results of this study showed the clinical applicability of OC in the management of OM. OC and GCW significantly reduced the pain and toxicity scale in the first 16 days. There was no significant difference between the GCW and control groups between the 16-21 days.

Keywords: Adjuvant chemotherapy; breast cancer; nursing; oral cryotherapy; oral mucositis

ÖZET Amaç: Kemoterapi gören meme kanserli hastalarda oral mukozitin (OM) önlenmesi ve semptom yönetiminde oral kriyoterapi (OK) ve soğuk suyla gargara (SSG) yapmanın etkisini belirlemek. **Gereç ve Yöntemler:** Bu paralel gruplu, üç-kollu, randomize ve değerlendiricinin kör olduğu araştırmada müdahale gruplarına OK ve SSG uygulandı. Meme kanseri olan 105 uygun hasta 3 gruba ayrıldı. Müdahale grupları için OK (n=35) ve SSG (n=35) 3 aşamada gerçekleştirildi: I) Hastanedeki araştırmacı tarafından verilen talimatlar; II) hastanede araştırmacı eşliğinde uygulama; III) Hastaların evde bireysel uygulaması. Kontrol grubundaki hastalar (n=35) standart bakım aldı. Ayrıca hastalara "Hasta Bilgi Formu", "Edmonton Semptom Değerlendirme Ölçeği", "Dünya Sağlık Örgütü (DSÖ) Mukozit Ölçeği [World Health Organization Mucositis Scale (OTS)]" ve "Görsel Analog Skala (VAS)" uygulandı. **Bulgular:** OTS ve VAS ölçeklerinde, OK grubu, başlangıç 21 günlük süre boyunca SSG yapan grup ve kontrol gruplarına göre anlamlı düzeyde daha etkiliydi. OTS ve VAS ölçeklerinin değerlendirilmesinin ilk 16 günü boyunca SSG grupları, kontrol grubuna göre önemli ölçüde daha fazla etkinlik gösterdi. **Sonuç:** OM tedavisinde tek başına OK etkili ve güvenlidir. Bu çalışmanın sonuçları, OM tedavisinde OK'nin klinik olarak uygulanabilirliğini gösterdi. OK ve SSG yapan bireylerde, ilk 16 günde ağrı ve toksisite ölçeğini önemli ölçüde azalttı. SSG ve kontrol grupları arasında 16-21 gün arasında anlamlı bir fark yoktur.

Anahtar Kelimeler: Adjuvan kemoterapi; meme kanseri; hemşirelik; oral kriyoterapi; oral mukozit

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Correspondence: Berna KURT
Hacettepe University Faculty of Nursing, Department of Internal Medicine Nursing, Ankara, Türkiye
E-mail: bernacolakoglu85@gmail.com

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Chemotherapy is one of the treatments used in cancer.[1] Chemotherapy, which is frequently used in the treatment of breast cancer, impacts cancer cells as well as intestinal and oral mucosal epithelium, which have the potential to increase rapidly in the body, bone marrow hematopoietic cells, and hair follicle cells.[2] One of the most common symptoms chemotherapy patients observe is oral mucositis (OM). Erythema and ulcerative lesions in the oral cavity, mucous membrane, and lateral sides of the tongue are symptoms of OM.[3] In particular, Deoxyribo Nucleic Acid sequencing and specific chemotherapy drugs disproportionately contribute to the development of mucositis. Because of their strong mitotic activity, chemotherapeutic drugs induce mucosal irritation. The chemotherapeutics include Adriamycin (Doxorubicin), 5-Fluorouracil (5-FU), and Vinblastine (Velban). Although the frequency of mucositis in chemotherapy patients changes according to the treatment strategy, it is estimated to be between 15% and 50%.[4]

Mucositis affects with both the patient's everyday activities, nutrition, and quality of life. Patients whose activities of daily life are disrupted may find it difficult to adhere to the scheduled therapy, and treatment may generate conditions in which dosages are skipped or reduced.[5] OM increases mortality by 40%, prolongs hospital stays and raises treatment costs. Although there is no conventional therapeutic strategy for mucositis prevention, there are several non-pharmacological options that exist most regularly utilized treatments for mucositis.[6,7] Oral cryotherapy (OC) is one of the practical, side-effect-free, easy-to-apply, and low-cost applications that include freezing the oral mucosa to prevent the distribution of chemotherapeutic drugs to the oral mucosa through vasoconstriction of the mucosa.[6,7] Cascinu et al. used OC and the rate of mucositis was significantly reduced by cryotherapy considering both the first cycle of therapy (the mean toxicity score for cryotherapy was 0.59) and all the chemotherapeutic courses (the mean toxicity score for cryotherapy was 0.36).[8] Dumont et et al. investigated the impact of cryotherapy and discovered that 20% of patients receiving just melphalan developed mucositis.[9] Karagözoğlu and Ulusoy studied 60 patients and started cryotherapy 5 minutes before intravenous injection of chemotherapy cycles. According to Patient-Judged Mucositis Grading the rate of mucositis is 36.7% in the study group and 90.0% in the control group.[10]

OC studies have often used ice chips for brief infusions and short half-life studies have been evaluated. Moreover, trials that included information and the whole treatment regimen but looked at a particular treatment were determined to be insufficient. Even so, no research in the scientific literature compares the efficiency of cooling ice chips with trials employing cold water and intraoral cooling. As a result, it is anticipated that this study will be beneficial to cancer patients in the management of mucositis, and the effectiveness of a practical strategy that is simple to apply to health practitioners will be assessed and adapted to the clinic. In the literature review, no other study was found in which OC and gargling with cold water (GCW) were applied together in the management of mucositis and their results were evaluated.

MATERIAL AND METHODS

STUDY DESIGN

This parallel-grouped, three-arm, assessor-blinded randomized control trial consisted of two intervention groups (OC) and GCW and a control group (CG). The enrollment CONSORT flow diagram is shown in Figure 1.

PARTICIPANTS

Patients undergoing adjuvant chemotherapy at the Oncology Chemotherapy Unit between September 2019- March 31, 2020 were included.

The inclusion criteria are: I) 18-65 years, II) planning to receive adjuvant chemotherapy first, III) without OM before treatments, IV) and any oral, dental, or neck operations in the prior 3 months who have not passed, V) nonsmokers and non-drinkers who have not undergone radiotherapy.

SAMPLE SIZE CALCULATION

15 patients were randomized into the OC (5 patients), GCW (5 patients), and CG (5 patients), the width of influence was calculated because it covers all tests. Power analysis was calculated using the G*Power

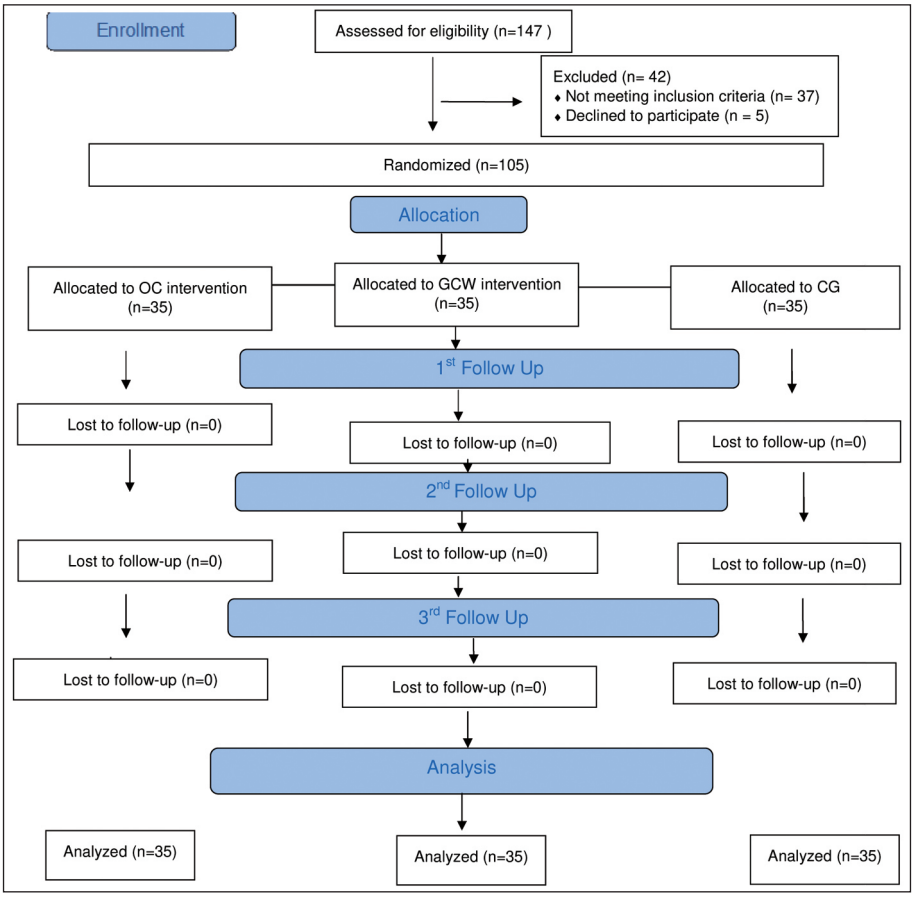

FIGURE 1: The process of the study according to the CONSORT flow diagram (2010).
OC: Oral cryotherapy; GCW: Gargling cold water; CG: Control group.

G*Power 3.0.10. (Franz Faul, Universität Kiel, Kiel, Germany) package program, and the effect size was 0.9. The power of the study was 95% (β:0.05, and α:0.05); at least 30 patients were to be included in each group. Understanding that there may be patients who may request based on the assumption of attrition, 105 patients (35 patients each) were recruited.

Randomization and Blinding

A stratified allocation was conducted to investigate the effect of patients' ages and surface area of the body (BSA) on OM. During the stage of blinding the practitioner, the statistician (www.random.org) was requested to contribute the randomization table for the study, and the randomization results were classified as Group 1, Group 2, and Group 3 and sent to the second author. This information was not shared with the 1st author. All applications were completed by experienced 2nd and 3rd authors who had been nurses at the clinic. Subsequently, the 1st author's communication with patients was avoided. Moreover, because of the characteristics of intervention trials, participants could not be blinded as patients. The data collecting tools were administered by a 1st author who was blinded to the study groups.

Measures

Participants in the OC, GCW, and CG groups received follow-up care at the hospital during their 21-day Adriamycin-Cyclophosphamide treatment and at home, on the days they did not attend treatment. Data was collected using the "Patient Information Form", "World Health Organization Mucositis Scale (OTS)", "Visual Analog Scale (VAS)", and "Edmonton Symptom Assessment Scale (ESAS)" during face-to-face interviews with all patients on the 1st cycle (T0=Baseline data=day 0) of adjuvant chemotherapy before commencing treatment. The VAS, OTS, and

ESAS were re-administered during a face-to-face interview done on the 1st and 2nd cycles (T1= day 21) for patients in the OC, GCW and CG groups undergoing adjuvant chemotherapy.

Patient Information Form

This form was conducted in face-to-face interviews.[3-7] Eight questions are the characteristics of the patient such as age, BSA, occupation, educational status, marital status, history of other diseases, drugs used other than chemotherapy, and oral care status. The collection of data took approximately 10 minutes for each patient.

WHO Mucositis Scale (OTS)

This diagnostic tool is commonly used to identify toxicity caused by cytostatic agents, especially in clinical studies. In this assessment, anatomical changes of oral mucosa and severity of mucositis are graded between 0 and 4. Although grade 0 means that there is no mucositis, grade 1 is mild, grade 2 is moderate, grade 3 is severe, and grade 4 indicates a life-threatening level.[11] The blinded evaluator (BK) via telephone interviews on days 1, 6, 11, 16, and 21.

Visual Analog Scale

The scale represents a possible solution. Patients mark a point on a 10 line that represents a continuum from "no pain" to the worst pain imaginable.[12] Applying this scale, participants were given instructions to indicate the severity of their pain in the mouth and when swallowing caused by mucositis. VAS underwent interviews conducted by the BK via telephone interviews on days 1, 6, 11, 16, and 21.

Edmonton Symptom Assessment Scale (ESAS)

The assessment is an analog scale used to assess the severity of nine common chemotherapy symptoms in cancer patients (pain, fatigue, nausea, sadness, anxiety, sleeplessness, anorexia, feeling bed, drowsiness and other problems). The scale ranks symptoms between 0 and 10 (0 is not a symptom and 10 is a very severe symptom). The investigators who performed the scale's Turkish validity and reliability study added 3 symptoms (mouth ulcers, change in the skin and nails, and numbness in the hands) to the "other problems" category. The Cronbach Alpha coefficient for our study was 0.83. The collection of ESAS data lasted approximately 10 min for each patient.[13] Every single individual needs approximately 10 minutes to obtain the ESAS data. ESAS underwent interviews conducted by the BK 10 days 0, 11, and 20.

Implementation

Intervention Group-1 (The Implementation of Oral Cryotherapy)

The researcher carefully prepared the ice cubes for cryotherapy as individual ice bags intended for one-time usage. The ice cubes are fragmented into little portions (15 ml) to facilitate their movement within the oral cavity, minimizing potential patient discomfort. These ice cubes were delivered from the start of Adriamycin therapy and were replaced regularly along with the chemotherapy treatment during the whole therapy period. Patients were given directions to do the oral ice application at 30-minute increments. It is advisable to submit application ice cubes intra-orally in the clinic with the 2nd and 3rd researchers, as well as at home, for a minimum of 21 days, at least 6 times a day, and up to 10 times, for an extended period of 30 minutes.

Intervention Group-2 (Gargling with Cold Water)

GCW consist of disposable water bottles used for cooling purposes. The researchers meticulously prepared it and kept it in the treatment room's refrigerator. This included receiving cold water from the refrigerator once a day at the start of the treatment. The researchers will provide 10-15 ml of water to the patients, as indicated in the literature, which will be cooled at 2-8 °C.[3-7] Patients were given directions to do the GCW in 30-minute increments. It is advisable to submit an application GCW intra-orally in the clinic with the 2nd and 3rd researchers, as well as at home, for a minimum of 21 days, at least 6 times a day, and up to 10 times, for an extended period of 30 minutes.

Control Group-3

The patients in the trial had a standard therapy program and no further interventions were conducted. Patients received instruction on specific oral health methods and their performance was assessed until they demonstrated proficiency.

DATA ANALYSIS

Analyses of the IBM SPSS Statistics 26 (IBM Corp., Armonk, NY, USA) software package. When we look at the mod and median values of the data, these values are coincident in normal distribution. To the extent these statistics approach each other, the distribution approaches the normal distribution. Frequencies (number, percentage) have been provided for categorical variables, while descriptive data (mean, standard deviation) came out for numerical variables. Derived averages for the OC, GCW, and CG were analyzed separately. Comparative analysis of three distinct groups (interventions, control) was conducted using the Mann-Whitney U test. A significance level of $p<0.05$ was regarded as statistically significant.

ETHICAL APPROVAL

Ethical committee approval was obtained from the Oncology Training and Research Ethics Committee for the study. Legal permission was obtained from the hospital where the research was conducted, after obtaining ethics permission from the University of Health Sciences Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital Clinical Research Ethics Committee to conduct the study (date: August 7, 2019, no: KA-2019-08/324). All interventions were carried out in accordance with institutional ethical standards and the national research committee, including the 1964 Declaration of Helsinki and subsequent amendments.

TABLE 1: Distribution of descriptive characteristics by groups.

	Study groups							
	OC (n=35)		GCW (n=35)		CG(n=35)		Statistical values	
Characteristic	n	%	n	%	n	%	Chi-square	p value
Age								
<=50	20	57.1	22	62.9	23	65.7	0.565	0.754
>50	15	42.9	13	37.1	12	34.3		
BSA								
1.40-1.59	10	28.6	13	37.1	13	37.1	2.068	0.723
1.50-1.69	17	48.6	17	48.6	18	51.4		
1.70-1.89	8	22.9	5	14.3	4	11.4		
Occupation								
Unemployed	16	45.7	17	48.6	18	51.4	1.118	0.891
Public servant	16	45.7	16	45.7	16	45.7		
Other	3	8.6	2	5.7	1	2.9		
Education status								
Primary school	22	62.9	22	62.9	22	62.9	4.672	0.586
Elementary school	12	34.3	8	22.9	10	28.6		
High school	1	2.9	3	8.6	3	8.6		
Higher education	0	0.0	2	5.7	0	0.0		
Marital status								
Married	26	74.3	24	68.6	22	62.9	1.061	0.630
Single	9	25.7	11	31.4	13	37.1		
History of other diseases								
No	24	68.6	21	60.0	22	62.9	0.577	0.818
Yes	11	31.4	14	40.0	13	37.1		
Additional drugs								
No	24	68.6	21	60.0	22	62.9	0.577	0.818
Yes	11	31.4	14	40.0	13	37.1		
Oral care status								
Yes	23	65.7	22	62.9	24	68.6	0.254	0.966
No	12	34.3	13	37.1	11	31.4		

No statistical differences were found in any patient characteristics between the 3 groups ($p>0.05$). OC: Oral cryotherapy; GCW: Gargling cold water; CG: Control group; BSA: Body surface area.

RESULTS

The chi-square test analysis has shown that 61.9% of the people in the study groups are 50 years of age or younger. Additionally, 49.6% have a VYA between 1.50 and 1.69. The square test was applied to evaluate homogeneity, and there was no statistical difference between the groups (Table 1).

When the chi-square test analysis, a significant correlation was found between the study groups and the findings from 6 to 21-day OTS, with a statistically significant difference p<0.05. The Grade 0 in the OC group for an extended duration of 21 days is significantly higher than that in the GCW and control group. Following a 21-day evaluation comparing the groups with GCW and the control group, it was found that Grade 0 in the GCW group performed a significant increase for 16 days consecutively. No statistically significant difference was seen between the GCW and CG throughout the 16th to 21st day of the treatment (p>0.05, Table 2).

Using One-Way Analysis of Variance, the outcomes were investigated to assess the variations in VAS scores among the OC, GCW, and control groups over a period of 1 to 16 days (p<0.05, Table 3). The analysis stated statistically significant differences in scores among these groups. However, there were also no significant differences in scores between the GCW and control groups for the 16 to 21-day period (p>0.05). The VAS scores obtained from the ice group for days 1 to 16 are significantly less than those of the GCW and control groups. The VAS scores of

TABLE 2: Distribution of mucositis assessment scale by groups.

Days	Mucositis Assessment Scale	Study groups			Statistical values	
		OC (n=35)	GCW (n=35)	CG (n=35)	Chi-square	p value
1st days	Grade 0	35 (100)	35 (100)	35 (100)	-	-
6th days	Grade 0	23 (65.7)	14 (40)	10 (28.6)	27.288	**<0.001***
	Grade 1	12 (34.3)	12 (34.3)	8 (22.9)		
	Grade 2	0 (0)	9 (25.7)	16 (45.7)		
	Grade 3	0 (0)	0 (0)	1 (2.9)		
11th days	Grade 0	27 (77.1)	13 (37.1)	4 (11.4)	39.252	**<0.001***
	Grade 1	8 (22.9)	21 (60)	11 (31.4)		
	Grade 2	0 (0)	1 (2.9)	20 (57.1)		
16th days	Grade 0	28 (80)	18 (51.4)	6 (17.1)	61.554	**<0.001***
	Grade 1	7 (20)	16 (45.7)	16 (45.7)		
	Grade 2	0 (0)	1 (2.9)	13 (37.1)		
21st days	Grade 0	28 (80)	17 (48.6)	16 (45.7)	18.883	**<0.001***
	Grade 1	7 (20)	17 (48.6)	11 (31.4)		
	Grade 2	0 (0)	1 (2.9)	8 (22.9)		

*p<0.05; OC: Oral cryotherapy; GCW: Gargling cold water; CG: Control group.

TABLE 3: Distribution of Visual Analog Scale by groups.

Days	Study groups			Statistical values		
	OC (n=35) X±SD	GCW (n=35) X±SD	CG (n=35) X±SD	F	p value	Tukey testing
1st days	0.00±0.00	0.00±0.00	0.00±0.00	-	-	
6th days	1.40±1.29	2.63±1.06	3.29±0.52	31.53	<0.001*	**OC<GCW<CG**
11th days	1.09±1.01	3.31±0.83	4.14±0.36	142.62	<0.001*	**OC<GCW<CG**
16th days	0.31±0.47	1.20±0.58	1.23±0.55	32.90	<0.001*	**OC<GCW**
21st days	0.11±0.32	0.06±0.24	0.00±0.00	2.14	0.122	-

F: One-way Analysis of Variance; *p<0.05. OC: Oral cryotherapy; GCW: Gargling cold water; CG: Control group; SD: Standard deviation.

TABLE 4: Comparison of the chemotherapy symptoms by groups.

Study groups	OC (n=35) X±SD			GCW (n=35) X±SD			CG (n=35) X±SD		
	Zero day	11th day	20th day	Zero day	11th day	20th day	Zero day	11th day	20th day
Pain	0.00±0.00	1.24±0.50	1.66±0.70	0.00±0.00	1.73±0.67	1.76±0.56	0.00±0.00	1.89±0.72	2.26±0.77
Fatigue	0.00±0.00	1.29±0.58	1.91±0.82	0.00±0.00	1.70±0.73	2.35±0.80	0.00±0.00	2.17±0.66	2.45±0.80
Nausea	0.00±0.00	1.27±0.76	0.63±0.55	0.00±0.00	0.38±0.49	1.82±1.42	0.00±0.00	1.71±0.62	2.03±0.71
Sadness	0.43±1.01	1.53±0.56	1.78±0.55	0.11±0.47	1.79±0.86	2.79±1.47	0.17±0.51	2.23±0.81	2.84±1.04
Anxiety	0.31±0.76	1.26±0.51	1.97±0.78	0.06±0.24	1.64±0.82	3.24±1.52	0.06±0.24	2.17±0.75	3.39±1.52
Sleeplessness	0.83±0.95	2.00±0.82	2.34±0.97	0.63±0.94	2.12±1.05	2.64±1.03	0.83±1.07	2.91±0.74	3.13±1.23
Lack of appetite	0.00±0.00	1.41±0.56	1.66±0.55	0.00±0.00	2.09±0.88	2.03±1.07	0.00±0.00	3.09±0.74	3.06±0.93
Feeling bad	0.00±0.00	2.03±0.76	2.28±0.52	0.09±0.28	2.76±0.87	3.09±0.77	0.09±0.28	2.94±1.08	3.71±0.74
Shortness of breath	0.00±0.00	0.52±0.57	0.63±0.69	0.00±0.00	0.85±0.71	0.91±0.88	0.00±0.00	0.88±0.77	0.97±0.69
Change in skin and nails	0.00±0.00	0.26±0.51	0.42±0.50	0.00±0.00	0.26±0.44	0.47±0.51	0.00±0.00	0.66±0.48	0.76±0.50
Mouth ulcers	0.00±0.00	0.44±0.50	0.63±0.55	0.00±0.00	1.09±0.72	1.61±1.09	0.00±0.00	1.71±0.71	2.71±0.59
Numbness in hands	0.00±0.00	0.29±0.46	0.39±0.50	0.00±0.00	0.40±0.50	0.66±0.48	0.00±0.00	0.47±0.51	0.76±0.44

OC: Oral cryotherapy; GCW: Gargling cold water; CG: Control group; SD: Standard deviation.

the GCW, comprising 1 to 16 days, are considerably lower ($p<0.05$, Table 3) compared to the control group.

Upon 1st evaluation of the chemotherapy symptoms in the patients, statistical analysis showed that there was not a significant distinction between the groups ($p>0.05$). The symptom severity reported by patients in the IGs and CG groups was determined to be comparable ($p>0.05$, Table 4). The evaluation of chemotherapy symptoms in the intervention groups and the CG revealed an improvement in symptom severity in the OC group after the 2nd and 3rd evaluates (Table 4).

DISCUSSION

This study will be beneficial used in the treatment of breast cancer in the management of mucositis, and the effectiveness of a practical strategy that is simple to apply to health practitioners will be assessed and adapted. The study investigated the impact of (OC) and (GCW) on taking care of mucositis and levels in breast cancer patients. No comparable study was identified in the literature review that combined the use of OC and GCW in the treatment of OM. When the literature is examined, many studies are confirming the positive effects of only OC on mucositis.[3,4,14-17] Seven randomized controlled trials involving 458 patients found that OC significantly reduced the occurrence of severe OM. Furthermore, the duration of total parenteral nutrition (TPN) administration and the length of hospital stay were significantly decreased.[14] Additional research has demonstrated that the cryotherapy group exhibited notably reduced rates of both OM occurrence and severity. The incidence of mucositis after cryotherapy was 71.4%, but in the no-cryotherapy group it was 95.7%. OM duration and administration of parenteral opioids were also markedly decreased.[15] A study found that OC during high-dose melphalan administration in myeloma patients after autologous stem cell transplant can greatly reduce the incidence of grade 3-4 and all grades of OM, TPN, opioids, and intravenous antibiotic administration.[3] The effectiveness of cryotherapy in preventing OM and OM-related pain. The pain scores of

the patients in the application group were 4-6 and the CG was 7-10, and the difference between the patient groups was statistically significant.[4] The effects of cryotherapy in avoiding OM associated with infusion of 5-Fluorouracil with leucovorin were examined in a randomized, controlled experiment.[16] Another study has shown that cryotherapy is highly efficient in avoiding OM in patients treated with 5-Fluorouracil and melphalan.[17] In a prior study examining the impact of OC autologous transplantation, cryotherapy was shown to be superior to saline mouthwash in mitigating the intensity of mucositis.[5] A comprehensive study conducted by Cochrane found that OC can result in decreases following fluorouracil-based therapy.[18] A meta-analysis conducted by Spivakovsky that OC reduced the risk of OM treated with fluorouracil-based chemotherapy.[19] In our study, the effects of OC application on OM are compatible with the literature. In our opinion, this effect of the mechanism is the promotion of vasoconstriction with ice, which would reduce the delivery of the cytotoxic drug to the at-risk tissues in the mouth.

Studies showed that mucositis symptoms develop all through the 3rd to 5th days following chemotherapy. The day starts and the 7th to 10th day continues. According to the conducting studies improvement of symptoms occurs on the 14th day.[20-24] In our study, the oral mucosa of all patients was deliberately injured before chemotherapy and then assessed on the 1st, 6th, 11th, and 16th days after the whole process. On the 21st day, we assessed it using the OTS and VAS. During the 1st 21 days, no patients in the OC group showed grade 2 OM. However, it was found that during the same period, patients in the GCW group accumulated grade 0, grade 1, and grade 2 OM. The CG consisted of 11 to 21 days the rise in levels of grade 2 OM reached its peak within certain days. At this point, the intervention group in our study has similarities to the OC group in the literature studies.

OM assessment is a comprehensive process that includes pain assessment and assessment of functional status through nutritional intake.[6] Patients who develop OM experience varying degrees of pain and loss of function, such as difficulty in speaking and swallowing.[25] In this study, chemotherapy symptoms in the intervention groups and CG showed that after the second and 3rd measurements, there was a decrease in the severity of symptoms in the OC group. While the OC group reported that they experienced less pain in the 2nd and 3rd measurements compared to the GCW group, the patients in the GCW group reported that they experienced less pain than the patients in the control group.

In the literature review, OC was administered around 5 minutes before to chemotherapy, and the ice utilized was supplied using a rounded teaspoon or ice chips to prevent oral injury. Only 2 research provided a description of the specific type of ice utilized. With the exception of one trial that used commercially available popsicles, the ice provided to the patient consisted of clean water with a similar composition to mineral water, stored in a sterile container.[5] The present work provides comprehensive elucidations on the characteristics and configurations of ice and water, as well as their applications, to facilitate future investigations.

To our knowledge, no previously published study has investigated the impact of both OC and GCW use the effects on OM. Only one study stated that chemotherapy treatment caused a decrease in salivary pH and dry mouth and that it was important to keep oral pH at an alkaline level (7.0-7.5) to protect oral health. In a study, it was determined that cryotherapy application decreased the formation of OM at alkaline levels by increasing the oral pH of patients.[10] In our study, it is thought that GCW application prevents pain by preventing dry mouth.

STRENGTHS AND LIMITATIONS

A strength of the study is no previously published study has investigated the impact of both OC and GCW use the effects on OM. However, a potential limitation of this study is it is based on patient statements since the patients perform the applications themselves during home monitoring.

CONCLUSION

The OC group was more effective than the GCW and control groups throughout the beginning

21-day period. During the 1st 16 days of evaluating the OTS and VAS conditions, the GCW groups showed more effectiveness than the control group. OC alone was effective and safe for OM. The results of this study showed the clinical applicability of OC in the management of OM. There was no significant difference between the GCW and control groups between the 16-21 days. Nurses have an important role in supporting them during the administration of chemotherapy. Also, in our study, detailed explanations about the type and shape of ice and water and their use are given for future studies.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

***Idea/Concept:** Berna Kurt; **Design:** Berna Kurt; **Control/Supervision:** Berna Kurt, Berna Ömür Çakmak Öksüzoğlu; **Data Collection and/or Processing:** Berna Kurt, Zeynep Sipahi Karslı, Nurdan Altınöz; **Analysis and/or Interpretation:** Berna Kurt; **Literature Review:** Berna Kurt; **Writing the Article:** Berna Kurt; **Critical Review:** Berna Kurt; **References and Fundings:** Berna Kurt, Berna Ömür Çakmak Öksüzoğlu.*

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