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ORIGINAL ARTICLE

Effect of Green Tea Mouthwash on Chemotherapy - Induced Oral Mucositis in Cancer Patients

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ABSTRACT: Oral mucositis presents a significant challenge for cancer patients undergoing chemotherapy for cancer. Mouth rinses such as normal saline or sodium bicarbonate solutions are commonly used to enhance oral health, and various treatment strategies are employed to manage oral mucositis during chemotherapy. Therefore, this study aimed to determine the effectiveness of green tea mouthwash in preventing and treating oral mucositis in cancer patients undergoing chemotherapy. A true experimental research design was utilized. Thirty participants meeting the inclusion criteria were selected using simple random sampling and were assigned to an experimental group (n=15) and a control group (n=15). Demographic and clinical variables were assessed, followed by a pre-test assessment of oral mucositis using the Oral Mucositis Assessment Scale for both groups. The experimental group received 5% solution of green tea mouthwash, while the control group received a sterile water mouthwash. A post-test assessment was conducted for both groups using the same tool at the end of the 14-day intervention. Out of 15 participants in the experimental group in the pre-test, 7 participants (46.67%) had lesions smaller than 1 cm^2, 5 (33.3%) had no lesions, and 2 (13.3%) had lesions sized 1 – 3 cm^2. In the control group, 6 (40%) had lesions smaller than 1 cm^2, and 1 (6.6%) had a lesion larger than 3 cm^2. The pre-test revealed that in the experimental group, 1 participant (6.67%) had severe erythema, 8 (53.3%) had mild erythema, and 6 (40%) had no erythema; in the control group, 4 (26.67%) had severe erythema, and 10 (66.6%) had mild erythema. A paired t-test revealed a significant change in ulceration and erythema in the experimental group after the intervention ($p<0.001$). A significant difference was also found between the experimental and control groups ($p<0.001$). The findings of this study suggest that administering green tea mouthwash to cancer patients undergoing chemotherapy is an effective method to prevent and treat oral mucositis.

INTRODUCTION

Cancer encompasses a wide range of potentially fatal diseases marked by abnormal cell growth and spread. Either adjuvant or neoadjuvant chemotherapy, which uses one or more anti-cancer drugs as part of a standardized regimen, has been a cornerstone in cancer treatment for decades. Its primary goals are to kill or slow the growth of rapidly dividing cancer cells, shrink tumors for easier surgical removal, eliminate any remaining cancer cells after surgery, prevent metastasis, and palliatively reduce symptoms associated with cancer Although effective in

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treating cancer, chemotherapy can cause several side effects, including oral mucositis. This condition develops in about 20% to 40% of patients with solid tumors undergoing chemotherapy, typically within five to fourteen days of initiating treatment [1]. It involves painful swelling due to inflammation and sores in the mucous membranes lining the digestive tract and can significantly affect nutritional intake, mouth care, and quality of life [2, 3]. Oral mucositis initially presents as redness in the mucosal lining, which then progresses to erosion and ulceration. These ulcerations may be covered by a white fibrinous pseudomembrane. Generally, these ulcers are found on the non-keratinized areas of the mouth, including the inner cheek lining (buccal mucosa), sides and underside of the tongue, and the soft palate [2]. The incidence and severity of mucositis vary between chemotherapeutic agents, the number of chemotherapy cycles, the dose of chemotherapy, and from patient to patient [4,5]. Patients who receive myeloablative preparations for hematopoeitic stem cell transplant have a higher incidence of oral mucositis [6]. Chemotherapeutic agents that affect DNA synthesis (S-phase), e.g., 5-fluorouracil, methotrexate, and cytarabine, have a high incidence of oral mucositis [4]. Anthracyclines, mTOR inhibitors, alkylating agents, and antimetabolites also have an increased risk of oral mucositis [7, 8]. Typical symptoms of oral mucositis encompass discomfort, bleeding, ulceration, and challenges in swallowing liquids or solids and speaking. Furthermore, it can lead to serious complications like secondary infections and notable weight loss. These issues have the potential to hinder the treatment and prognosis of the primary disease [9-11]. Various treatment strategies are employed to manage oral mucositis in the course of chemotherapy treatment [12]. Alternative and complementary therapies can play a supportive role in managing chemotherapy-induced oral mucositis. These therapies are not replacements for conventional medical treatment but can be used to alleviate symptoms and improve quality of life. For example, cryotherapy [13, 14] and keratinocyte growth factor [13, 15] demonstrated some benefits in preventing mucositis. Zinc [16, 17] and vitamin E [17, 18] were effective in reducing the severity of oral mucositis. However, the evidence supporting the benefits of Aloe vera [19], and honey [19-23] is less substantial. Green tea-based mouthwashes can be considered effective in maintaining oral health, potentially comparing favorably to medicated mouthwashes [24]. The increasing interest in green tea mouthwash as a potential remedy for oral mucositis, particularly in patients undergoing chemotherapy, is largely due to its natural anti-inflammatory, antioxidant, and possibly antimicrobial properties, which may protect the oral mucosa against the harmful effects of chemotherapeutic agents [25]. This has led to research aimed at determining the effectiveness of green tea mouthwash as a preventative measure against chemotherapy-induced oral mucositis.

MATERIALS AND METHODS

A quantitative approach utilizing a true experimental pre-test and post-test design was adopted to conduct the study in the Oncology ward of Saveetha Medical College and Hospital in May 2023, after obtaining formal permission from the head of the department. The study sample consisted of cancer patients receiving chemotherapy with oral mucositis who met the inclusion criteria. A total of 30 samples fulfilling the inclusion criteria were selected using a simple random sampling technique. They were randomly assigned into an experimental group (n=15) and a control group (n=15). Both male and female patients aged 20-60 years with oral mucositis from the first cycle of chemotherapy, no allergy to green tea, hemodynamic stability, willingness to participate, and ability to follow instructions were included in the study. The exclusion criteria included patients who were unconscious or critically ill, those unable to open their mouths more than 1 cm, and those with severe oral cancer or harmful oral lesions. The study's purpose was explained to participants in their regional language, and any doubts were clarified. Written informed consent was obtained from all participants, ensuring confidentiality. Demographic and clinical variables were collected using a multiple-choice questionnaire, followed by a pre-test assessment using the Oral Mucositis Assessment Scale [26]. This scale is a

standardized and objectively measuring the appearance of erythema and ulceration in the oral cavity. In the Oral Mucositis Assessment Scale, scores are interpreted as follows: 0=no lesion; 1=<1 cm², 2=1-3 cm², and 3=>3 cm² and Erythema is interpreted as 0=none, 1=not severe, and 2=severe. Participants were instructed to use the Bass brushing method with a soft, small-headed toothbrush for at least five minutes, twice a day to optimize oral health by improving gum health and preventing bad breath. The bass brushing technique involves positioning the toothbrush at an angle where the bristles face the gum line and performing brief back-and-forth motions, then gently sweeping the brush from beneath the gum towards the outer edge of the tooth. Green tea mouthwash was administered from the day before chemotherapy until the fourteenth day for the experimental group. Green tea was freshly prepared each time, using 5g (1 teaspoon) of green tea powder dissolved in 100ml of boiled water to produce a 5% solution. Additionally, 1-2 ice chips, each measuring the size of one inch by one inch, prepared in a sterile manner using distilled water, were added. These ice chips aid in preventing the onset of oral mucositis and promoting comfort by minimizing pain associated with oral mucositis. The control group received the sterile water mouthwash. A post-test assessment was conducted at the end of the intervention on the fourteenth day using the same tools. Confidentiality was maintained throughout the procedure. Participants were monitored for progress and any adverse effects during the intervention. Data were analyzed using descriptive and inferential statistical methods with IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). The background variables and pre-test and post-test levels of oral mucositis in participants were described in terms of frequency and percentage. The effectiveness of the intervention within and between the groups was determined using paired and unpaired t-tests. A p-value of <0.05 or less was considered statistically significant.

RESULTS

Table 1 illustrates that within the experimental group, the majority of participants, six (40%), were aged between 41-50 years, nine (60%) were female, ten (66.7%) were married, and 80% resided in rural areas. Furthermore, 13 (86.7%) were employed in the private sector, and 4 (26.7%) engaged in both smoking and alcohol consumption. In the control group, 6 (40%) were aged between 41-50 years, 8 (53.3%) were female, 10 (66.7%) resided in rural areas, and 11 (73.3%) were private employees.

Table 1. Background Information of Cancer Patients Receiving Chemotherapy.

Demographic variables	Experimental groupfrequency (%)	Control group frequency (%)
Age in Years		
21 – 30	3 (20%)	2 (13.3%)
31 – 40	2 (13.3%)	3 (20%)
41 – 50	6 (40%)	6 (40%)
51 – 60	4 (26.7%)	4 (26.7%)
Gender		
Male	6 (40%)	8 (53.3%)
Female	9 (60%)	7 (46.7%)
Marital Status		
Unmarried	3 (20%)	2 (13.3%)
Married	10 (66.7%)	13 (86.7%)
Widow	2 (13.3%)	-
Residence		
Rural	12 (80%)	10 (66.7%)
Urban	3 (20%)	5 (33.3%)
Occupation		

Demographic variables	Experimental groupfrequency (%)	Control group frequency (%)
Government employee	1 (6.7%)	2 (13.3%)
Private employee	13 (86.7%)	11(73.3%)
Unemployed	1 (6.7%)	2 (13.3%)
Habits		
Smoking	2 (13.3%)	3 (20%)
Alcoholism	3 (20%)	2 (13.3%)
Smoking & Alcohol consumption	4 (26.7%)	2 (13.3%)
Betal / Tobacco Chewing	2 (13.3%)	3 (20%)

Table 2 indicates that among the 15 participants in both the experimental and control groups, the majority (>40%) had gastro-intestinal tract cancer. Over 60% were in stage I and undergoing their 1st or 2nd chemotherapy cycle. Additionally, 50% were receiving methotrexate, and more than 90% had neither a past history of chemotherapy or radiation therapy nor a family history of cancer.

Table 2. Clinical Variables of Cancer Patients Receiving Chemotherapy.

Clinical variables	Experimental group frequency (%)	Control group frequency (%)
Site of cancer		
Breast	4 (26.7%)	3 (20%)
Gastro – intestinal	6 (40%)	8 (53.3%)
Reproductive	5 (33.3%)	4 (26.7%)
Duration of illness		
< 1 year	13 (86.7%)	11(73.3%)
2 - 3 years	2 (13.3%)	4 (26.7%)
Chemotherapeutic agents prescribed		
Methotrexate	8 (53.3%)	7 (46.7%)
5 Fluorouracil	4 (26.7%)	3 (20%)
Cyclophosphamide	1 (6.7%)	2 (13.3%)
Cisplatin	1 (6.7%)	1 (6.7%)
Doxorubicin	1 (6.7%)	2 (13.3%)
Cycle of chemotherapy		
1- 2 cycles	12 (80%)	10 (66.7%)
3 - 4 cycles	3 (20%)	5 (33.3%)
Stage of cancer		
Stage I	9 (60%)	10 (66.7%)
Stage II	3 (20%)	2 (13.3%)
Stage III	2 (13.3%)	3 (20%)
Stage IV	1 (6.7%)	-
Past history of chemotherapy or radiation therapy		
Yes	1 (6.7%)	-
No	14 (93.3%)	15 (100%)
Family history of cancer		
Yes	2 (13.3%)	1 (6.7%)
No	13 (86.7%)	14 (93.3%)

In the pre-test, among the 15 participants in the experimental group, 7 (46.67%) had lesions smaller than 1

cm², 5 (33.3%) had no lesions, and 2 (13.3%) had lesions sized 1 – 3 cm². After the intervention, 9 (60%) had no lesions, 5 (33.3%) had lesions smaller than 1 cm², and none had lesions larger than 3 cm². In the control group, during the pre-test, 6 (40%) had lesions smaller than 1 cm², and 1 (6.6%) had a lesion larger than 3 cm². In the post-test, 6 (40%) had no lesions, while 1 (6.6%) still had a lesion larger than 3 cm² as depicted in Table 3.

Table 3. Pre-test and Post-test levels of Ulceration.

Level of Ulceration	Experimental Group				Control Group			
	Pretest		Post Test		Pretest		Post Test	
	F	%	F	%	F	%	F	%
No lesion	5	33.3	9	60	4	26.7	6	40
<1 cm²	7	46.7	5	33.3	6	40	4	26.7
1 – 3 cm²	2	13.3	1	6.7	4	26.7	4	26.7
>3 cm²	1	6.7	0	-	1	6.6	1	6.6

Out of 15 participants in the experimental group, the pre-test revealed that 1 (6.67%) had severe erythema, 8 (53.3%) had mild erythema, and 6 (40%) had no erythema. However, in the post-test after the intervention, 9 (60%) had no erythema, and 6 (40%) had mild erythema. In the control group, during the pre-test, 4 (26.67%) had severe erythema, 10 (66.6%) had mild erythema, and 1 (6.7%) had no erythema. Similarly, in the post-test, 1 (6.67%) had severe erythema, 8 (53.3%) had mild erythema, and 6 (40%) had no erythema as shown in Table 4.

Table 4. Pre-test and Post-test levels of Erythema.

Level of erythema	Experimental group				Control group			
	Pretest		Post test		Pretest		Post test	
	F	%	F	%	F	%	F	%
None	6	40	9	60	4	26.7	6	40
Not severe	8	53.3	6	40	10	66.6	8	53.3
Severe	1	6.7	0	-	1	6.7	1	6.7

Table 5 illustrates that the pre-test mean score for ulceration was 2.13±0.74, which was reduced to a post-test mean score of 0.53±0.63. The mean difference was 1.60. The calculated paired 't' test value of t = 12.220 was statistically significant at the p<0.001 level. Similarly, a comparison of pre-test and post-test mean scores using the paired t-test revealed a calculated value of t = 11.000, also statistically significant at the p<0.001 level. These findings indicate that after administering green tea mouthwash, there was a significant reduction in the levels of ulceration and erythema, thereby effectively decreasing chemotherapy-induced oral mucositis among the cancer patients receiving chemotherapy.

Table 5. Within the group comparison of oral mucositis.

Variables	Experimental Group				Mean difference score	Paired 't' test & p-value
	Pretest		Post test			
	Mean	S.D	Mean	S.D		
Ulceration	2.13	0.74	0.53	0.63	1.60	t = 12.220, p=0.0001, S***
Erythema	1.86	0.35	0.40	0.50	1.46	t = 11.000, p=0.0001, S***

***p<0.001, S – Significant

Table 6 shows that the post-test mean score for ulceration, along with the standard deviation, in the experimental

group was 0.53±0.63, compared to 2.31±0.41 in the control group, yielding a mean difference of 1.78. An unpaired t-test was used to compare these post-test scores, and the calculated t-value of 14.31 was statistically significant at the p<0.001 level. Additionally, the post-test mean score for erythema was 0.40±0.50 in the experimental group and 1.96±0.32 in the control group. Comparison using an unpaired t-test revealed a calculated t-value of 12.214, also statistically significant at the p<0.001 level. These findings indicate a significant difference in the reduction of ulceration and erythema levels between the experimental and control groups.

Table 6. Comparison of oral mucositis between the groups.

Variables	Experimental group		Control group		Mean difference score	Unpaired 't' test & p-value
	Post-test		Post test			
	Mean	S.D	Mean	S.D		
Ulceration	0.53	0.63	2.31	0.41	1.78	t = 14.310, p=0.0001, S***
Erythema	0.40	0.50	1.96	0.32	1.56	t = 12.214, p=0.0001, S***

The demographic variable of age demonstrated a statistically significant association with the post-test level of erythema among cancer patients receiving chemotherapy, as evidenced at the p<0.05 level. Other demographic variables did not show a statistically significant association, as detailed in Table 7.

Table 7. Association of post-test level Erythema with selected demographic variables in Experimental Group.

Demographic variables	Frequency	Chi-Square test P-value
Age in years		
21 – 30	5	χ^2=7.917
31 – 40	5	d.f=3
41 – 50	3	p=0.048
51 – 60	2	S*

DISCUSSION

Oral mucositis presents major challenges such as the inability to eat and drink, pain, and an increased risk of infections, all of which significantly impact the overall quality of life for patients undergoing chemotherapy for solid tumors. Mouth rinses are commonly used to enhance oral health. While some remedies, including oral cryotherapy, topical application of honey, and Benzydamine mouthwash have shown potential in reducing chemotherapy-induced mucositis, there is a lack of sufficient evidence in designing the intervention protocol for many, highlighting the need for further research. Recent studies suggest that mouthwashes with anti-inflammatory properties are particularly effective in mitigating mucositis induced by cancer therapy, especially in patients with head and neck cancer [27]. The current study conducted a thorough analysis of oral mucositis, specifically focusing on ulceration and erythema, in patients undergoing chemotherapy from cycle 1 to cycle 3. Additionally, it examined the effects of green tea mouthwash on oral mucositis. The findings revealed that over 40% of patients experienced oral mucositis, with lesion sizes varying from less than 1 cm² to more than 3 cm², and the severity of erythema ranging from not severe to severe. The study also demonstrated that green tea mouthwash was effective in reducing and preventing the occurrence of oral mucositis. In the experimental group, the proportion of participants

with no lesions increased from 30% to 60%, and none had lesions larger than 3 cm². Furthermore, the percentages of lesions less than 1 cm² and those between 1-3 cm² decreased from 47% to 33% and from 13% to 6%, respectively, after 14 days of intervention. Similarly, the severity of erythema also decreased, shifting from severe to not severe, and in some cases, to none. A significant difference was also observed between the experimental and control groups. This study's findings are strongly supported by Liao YC et al, 2021 who reported that the continuous use of green tea mouthwash can improve oral health status and maintain it over an extended period [28]. Their study intervention lasted for 6 months, in contrast to the duration in the present study. Based on this, the current study recommends continuing this intervention until the completion of the chemotherapy treatment course, followed by an additional 2 weeks. In another study, found that green tea extract mouthwash had promising effects on reducing radiation-induced mucositis in patients with head and neck cancers during 8 weeks of radiation therapy; however, it did not significantly reduce the severity of pain and burning [29]. The current study lacks an assessment of pain and the associated problems with swallowing ability linked to mucositis. Sant Ana G et al, 2020 conducted a systematic review of randomized clinical trials and reported that natural, topical agents are effective in reducing the severity of oral mucositis lesions and pain intensity in patients undergoing chemoradiotherapy, although the effects vary depending on the type of agent used [30]. A study demonstrated that the oral intake of honey during radiotherapy is effective in reducing the severity of oral mucositis [31]. Similarly, it was reported that the use of a 0.1% curcumin mouthwash significantly delayed the onset of radiation-induced oral mucositis [32]. Many studies have been conducted to analyze the impact of natural and herbal products on oral mucositis, and they have shown that these agents can help in preventing and treating mucositis caused by radiotherapy. However, there are limited studies on chemotherapy-induced oral mucositis, particularly involving green tea mouthwash. The current study has shown that green tea is an effective non-pharmacological measure to prevent and treat oral mucositis, even with a small sample size. Therefore, this study recommends further evaluation of chemotherapy-induced oral mucositis in various settings to confirm these results.

CONCLUSIONS

The current study's findings suggest that administering green tea mouthwash to cancer patients undergoing chemotherapy effectively prevents the occurrence and treatment of oral mucositis. This indicates that green tea mouthwash could be considered as non-pharmacological measure, given its simplicity, natural composition, effectiveness, and safety. This approach would provide more robust evidence regarding the efficacy of green tea mouthwash in managing chemotherapy-induced oral mucositis, thus offering valuable insights for clinical practice and patient care. However, further investigation through randomized controlled trials in various settings, with a larger sample size, is required to corroborate these results and generalize the findings.

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Conflict of interests

NO conflict.

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