



Comparative Evaluation of the Efficacy of Ice Cubes Versus Sodium Bicarbonate Mouthwash both as Prophylactic Measure and as Treatment of Oral Mucositis Induced by Systemic Anticancer Therapies

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Oral mucositis is a complication of systemic anticancer therapies. This study aimed at investigating the use of ice cubes and sodium bicarbonate mouthwash as a preventive and a treatment measure for oral mucositis in patients receiving systemic anticancer therapies. The two measures were given to 50 patients, 24 of whom already had oral mucositis at Oncology Department in Rizgary Teaching Hospital in Erbil/ Iraq. Patients' grades for oral mucositis were recorded before and after receiving the two measures. After treatment of the 24 patients with Oral Mucositis, the number decreased to 9 patients. The grades of patients' oral mucositis also decreased to lower grades. The two measures were effective but sodium bicarbonate mouthwash was more significant effective as a treatment and preventive measure for oral mucositis ($p=0.044$) than ice cubes ($p=0.022$).

Keywords: Ice Cubes, Sodium Bicarbonate Mouthwash, Oral Mucositis, Treatment Chemotherapy.

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Introduction

Oral mucositis (OM) can be defined as the inflammation of the epithelial oral cavity; it is clinically characterized by existence of erythematous areas that later become ulcerations [1]. The cause of oral mucositis is destruction of the oral mucosal epithelium and constriction of its growth secondary to antineoplastic treatment in the form of chemotherapeutic drugs or radio therapy, and OM is also characterized by severe ulcers and pain that can hinder the person's ability to eat, swallow, and talk [2-4].

Systemic anticancer therapies are widely used as a treatment for cancer in different anatomic sites. The incidence of mucositis caused by high doses of

antineoplastic drugs is about 20% – 50% in all tumor sites; however, these treatment drugs lead to collateral drug effects in different organic systems such as gastrointestinal system. Some of most common symptoms of these effects are nausea, vomiting, lack of appetite and mucositis [5]. Moreover, in addition to these effects, it can also cause dry mouth which in turn can lead to secondary infections mainly by fungi and bacteria. Other potential effects include changes in the sense of taste which may result in low fluid and food intake, dehydration and malnutrition [6].

Oral mucositis clinically appears about 4-5 days after the start of chemotherapy when it becomes evident with emergence of erythematous areas in the oral cavity, and after 7-10 days it develops to ulcers which gradually increase in number and size, and tend to form large ulcerated zones. The lesions are very painful and need

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approximately two weeks to heal after the chemotherapy is ceased [7].

There are several classifications of oral mucositis stages, but the World Health Organization (WHO) has the most widely used system which is presented below [8].

0: no subjective or objective evidence of mucositis.

I: pain with or without erythema, no ulcers

II: erythema and ulceration, but the patient can swallow solid foods.

III: erythema and ulceration, the patient can only swallow liquids but not solid foods

IV: erythema and ulceration, the patient cannot swallow liquids or solids foods.

Sodium bicarbonate mouthwash has been used in many studies which have proven it to be very effective and convenient as a treatment and as a preventive measure because it deodorizes, refreshes, cleans the mouth; helps to neutralize the production of acid in the mouth; prevents infections from occurring, and besides health effectiveness, Sodium Bicarbonate mouthwash is known to be very cost effective and inexpensive; and according to some recommendations in guidelines the preparation is done by mixing one tea spoon of baking soda with a glass of water [9]. The patients were instructed to rinse mouth with this sodium bicarbonate mouthwash by using 20 ml every six hours during receiving intravenous chemotherapy until it was finished Mouthwash containing sodium bicarbonate has also been used in preventing radiotherapy-induced oral mucositis in patients with locally advanced head and neck cancer; according to a study conducted on 29 patients (21 men and 8 women with age ranging 44-68) with stage III to IV head and neck cancer and the results of the study revealed a significance difference in mucositis scoring between the intervention group and placebo group, and the oral care by mouthwash containing sodium bicarbonate for head and neck cancer patients undergoing radiotherapy is an effective interventional option to prevent oral mucositis [10]. Choi & Kim (2012) investigated the difference and comparison in efficacy between sodium bicarbonate and chlorhexidine mouthwash in oral care of acute leukemia patients under induction chemotherapy: the two researchers studied 48 patients who were over 18 years old, patients who had never been treated with chemotherapy, patients who were under induction chemotherapy, and patients with grade 0 oral mucositis, and their study results found that oral care by sodium bicarbonate was an effective intervention for their patients undergoing chemotherapy. The researchers recommend using sodium bicarbonate mouthwash instead of

chlorhexidine for patients with acute leukemia [11]. Another study Turhal et al (2000) wanted to determine the efficacy of a mouthwash that contained (sodium bicarbonate) in relieving mucositis-induced discomfort in patients receiving chemotherapy, the number of patients consisted of 31 (16 male, 15 female) with their age ranging from 16 to 80, and the results revealed patients' relief throughout the duration of mucositis and relief during the worst stage of each mucositis episode [12]. The other preventive and treatment measure used was ice cubes. It is also called Cryotherapy which is defined by Meriam-Webster online dictionary as "therapeutic use of cold." It has been investigated by many researchers as a good measure, the medical explanation is that when ice is applied to the oral cavity, it results in vasoconstriction which helps decrease blood flow to the oral mucosa, this reduces cytotoxic medication reaching the cells which means lowering the incidence of mucositis. A good advantage of ice is that it is non-costly [13]. The patients holding ice cubes in their mouth before receiving chemotherapy infusion 10 minutes, and during infusion for 15 minutes, and after infusion for 15 minutes. This method is used by Batlle with his Co-investigators in his research [14]. The use of ice cubes has been proven to be effective in treating and preventing oral mucositis by many studies. Askarifar et al (2016) conducted a clinical trial on the effects of oral cryotherapy on chemotherapy-induced oral mucositis in patients, in their study on 29 patients who were undergoing stem cell transplantation in Iran were randomly selected and assigned to control group (13 patients) and intervention group (16 patients) [15]. The researchers used mouthwash and cryotherapy in their study, and their results showed cryotherapy was more effective than saline mouthwash. The effect of cryotherapy on oral mucositis in patients with head and neck cancers receiving radiotherapy was studied in a randomized controlled trial with 40 head and neck cancer patients who were divided into control and experimental groups of 20 each, although their study results showed no significance differences between the control group and the experimental group, the patients using ice cubes felt more comfort in their oral cavity during radiotherapy [16]. Katranciet al (2012) carried out a randomized controlled trial for the evaluation of the effect of cryotherapy in preventing oral mucositis associated with chemotherapy, specifically of 5-fluororocil with leucovorin, and in their study, 60 patients were included, thirty patients in study group and 30 in control group. The patients in the study group were instructed to hold ice cubes in their mouth shortly before, during, and shortly after infusion of 5-DU

with leucovorin, the results showed that the incidence of oral mucositis in the experimental group were quite lower than of the control group [17]. The present study aimed at investigating the efficacy of Ice Cubes versus Sodium Bicarbonate mouth wash both as a preventive measure and as treatment of OM induced by systemic anticancer therapies and drugs.

Materials and Methods

The design of this study was a cross-sectional prospective research. The setting was clinical study. After the protocol of the current research was presented to the KBMS (Kurdistan Board of Medical Specialties), it was approved by the research committee. Concerning Ethical Clearance, it was obtained from the Kurdistan Board of Medical Specialties' Ethical Committee. Fifty patients were randomly selected and approved by Oncology Department at Rizgary Teaching Hospital in the city of Erbil, Kurdistan- Iraq. The patients were receiving various systemic anticancer therapies such as Cisplatin, Gemzar, Cyclophosphamide, Adriamycin, 5 Fluorouracil, Taxoter, Everolimus. The starting date for taking the patients' medical records was January 2018. The end date for taking notes was July 2018. The patients were asked to give their consent to participate in the study. The fifty patients were divided into two groups of 25 each in sequence according to the measure given to them. That is, first group consisted of patients from 1 to 25 and were given ice cubes and the second group consisted of patients from 26-50 and were given sodium bicarbonate mouthwash. Among the fifty patients, 29 were men and 21 were women with their ages ranging from 24 to 80 years old. The patients included in this study all suffered from different stages of cancer with solid tumors, they were taking chemotherapy intravenously in different cycles at the above-mentioned hospital. Patients who had received any preventive measures such as mouthwash, received cryotherapy or laser therapy, and had allergy for sodium bicarbonate were excluded from the study. After checking the medical records of the patients, it was revealed that out of the 50 patients, 24 patients had Oral Mucositis. In the group giving ice cubes, 9 patients had Oral Mucositis, 16 did not have it. In the group giving sodium bicarbonate mouthwash, 15 patients had oral mucositis, 10 patients did not have it. The two measures used for the patients were sodium bicarbonate mouthwash and ice cubes the first measure used was ice chips which were given to another group of 1-25 patients. Ice cubes are a

cryotherapy measure. The patients were given oral ice cubes before taking chemotherapy infusion 10 minutes, and during infusion for 15 minutes, and after infusion for 15 minutes. The patients were instructed to chew and suck the ice chips during the three phases [14]. The second measure was sodium bicarbonate mouth rinse was given to 26-50 patients taking chemotherapy. According to some recommendations in guidelines the preparation is done by mixing one teaspoon of baking soda with a glass of water [9]. The patients were instructed to rinse mouth with this sodium bicarbonate formula by using 20 ml every six hours during receiving intravenous chemotherapy until it was finished [10]. Patient's record was observed and reported from the day of treatment with ice cubes and sodium bicarbonate mouthwash, and the oral mucositis was graded. Observation was done every three days by checking the patients for oral mucositis and grading it severity for 16 days duration. After the two groups were completed, the data was reported and entered into SPSS (version 23 software for statistical analysis).

Results

Table 1 shows that among the fifty patients, 29 were men and 21 were women with their ages ranging from 24 to 80 years old, and most of the patient had breast cancer followed by gastric, colon, lung, prostate, ovarian cancer, and chondrosarcoma.

Table 1. Patients Demography

| Gender | Age Range | Frequency | Type of Cancer | Frequency |
|--------|-----------|-----------|-----------------|-----------|
| Male | 21 | 24-29 | Breast Cancer | 15 |
| Female | 29 | 30-39 | Gastric Cancer | 12 |
| | | 40-49 | Colon Cancer | 9 |
| | | 50-59 | Lung Cancer | 7 |
| | | 60-69 | Prostate Cancer | 2 |
| | | 70-79 | Ovarian Cancer | 3 |
| | | 80 | Chondrosarcoma | 2 |

As shown in table 2 out of the 50 patients, 24 patients had oral mucositis. In the group receiving ice cubes, 9 patients had oral mucositis, 16 did not have oral mucositis. In the group receiving sodium bicarbonate mouthwash, 15 patients had oral mucositis, 10 patients did not have oral mucositis, totally twenty six (52 percent) patients were reported to have grade 0. The other 24 (48 percent) had different grades of mucositis. Three patients had grade 1, nine patients had grade 2, nine other patients reported grade 3, the last three patients had grade 4.

Table 2. Oral mucositis grade before and after treating by the ice cubes and sodium bicarbonate mouthwash

| Oral mucositis grades | Total (n=24) | | | | 1st group (n=9) Ice cubes | | 2nd group (n=15) Sodium bicarbonate | | | | | |
|-----------------------|--------------|----|-------|----|------------------------------|----|--|----|--------|----|-------|----|
| | Before | | After | | Before | | After | | Before | | After | |
| | no. | % | no. | % | no. | % | no. | % | no. | % | no. | % |
| 0 | 26 | 52 | 41 | 82 | 16 | 64 | 21 | 84 | 10 | 40 | 20 | 80 |
| 1 | 3 | 6 | 7 | 14 | 1 | 4 | 3 | 12 | 2 | 8 | 4 | 16 |
| 2 | 9 | 18 | 2 | 4 | 3 | 12 | 1 | 4 | 6 | 24 | 1 | 4 |
| 3 | 9 | 18 | 0 | 0 | 3 | 12 | 0 | 0 | 6 | 24 | 0 | 0 |
| 4 | 3 | 6 | 0 | 0 | 2 | 8 | 0 | 0 | 1 | 4 | 0 | 0 |
| +ve cases | 24 | 48 | 9 | 18 | 9 | 36 | 4 | 16 | 15 | 60 | 5 | 20 |

After taking ice cubes and sodium bicarbonate mouthwash treatment, the patients reported only grade 1 and 2 within two weeks. Therefore, the treatment resulted in eliminating mucositis in 15 patients and alleviating grades of 9 patients. In other words, only 7 patients reported grade 1 and only 2 patients reported grade 2.

The above tables show difference in mucositis scoring before and after receiving ice cubes and sodium bicarbonate mouthwash. The existence of mucositis decreased from 48 percent to 18 percent only over all.

As shown in table 2 before giving ice cubes, 9 (36 percent) patients reported above grade 0 mucositis. After taking was completed, the number decreased to 4 (16 percent) out of 25 patients. Also as shown in table 2 before receiving sodium bicarbonate mouthwash, fifteen patients (60 percent) out of the 25 patients reported to have various grades of mucositis. However, after the measure was delivered to the patients, only 5 patients (20 percent) reported mucositis grade 4 patients (16 percent) grade 1 and 1 patient (4 percent) grade 2. Differences in effectiveness between ice cubes and sodium bicarbonate mouthwash were reported sodium bicarbonate mouthwash is indicated to be had more significant effective ($p=0.044$) than ice cubes ($p=0.022$) in the current study.

Discussion

The idea of this study was stemmed from the fact that chemotherapy causes mucositis in many patients when was observed at the Oncology Department of Rizgary Teaching Hospital in the city of Erbil. This study focused on ice cubes and sodium bicarbonate mouthwash intervention for oral mucositis. These two measures have been widely researched over the years and they were found to be very effective in preventing oral mucositis in patients receiving chemotherapy that is why the decision was made to use them for the first time in Erbil in this study For ice cubes as a preventive and intervention measure, it was effective in this study. Several studies have demonstrated that ice

cubes reduces the severity of oral mucositis in patients receiving chemotherapeutic agents Askarifar et al (2016) , Katranci et al (2012) and the result of above study support the current reported study. A study was done by Choi&Kim (2012) investigated the difference and comparison in efficacy between sodium bicarbonate and chlorhexidine mouthwash in oral care of acute leukemia patients under induction chemotherapy, and their results found that oral care by sodium bicarbonate was an effective intervention for their patients undergoing chemotherapy. Also two studies Djurric M et al (2006), Turhal et al (2000) revealed that using of sodium bicarbonate in preventing and treatment of oral mucositis induced by chemotherapy was more effective than ice cubes and this agrees with our study results. However, both measures had good effect in prevention and treatment of oral mucositis and many studies supported them and the use of sodium bicarbonate mouthwash is very wide in clinical practice. Therefore, the current study did not only acknowledge that sodium bicarbonate mouthwash is a harmless bland rinse that can be helpful for oral hygiene maintenance and patient comfort but it also found that this medical agent is useful for preventing and alleviating oral mucositis. By using the two agents as preventive measures, besides being treatment measures, we wanted to investigate if the agents would intervene and prevent the occurrence of OM because 26, out of 50, patients had grade 0 of OM. But they were prone to OM because of chemotherapy; therefore, using the two agents as preventive measures was important even for grade

Conclusion

This study investigated prevention and treatment of oral mucositis in patients receiving chemotherapy. Two agents, ice cubes and sodium bicarbonate mouthwash, were given to 50 patients. The results showed significant improvement of the number of patients who had oral mucositis. The results also indicated that the sodium bicarbonate mouth wash has better significant effect than ice cubes in prevention and treatment of oral mucositis. In regards to prevention of OM, both agents indicated to be effective in the prevention of OM in patients receiving chemotherapy.

Conflicts of interest

None.

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