

## The Effect of Chamomile Mouthwash on the Prevention of Oral Mucositis Caused by Chemotherapy in Children with Acute Lymphoblastic Leukemia

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### Abstract

**Background:** Mucositis is a complex inflammatory response of the digestive system mucous membrane and it is also one of the most common painful side effects following chemotherapy in children with carcinoma. Developing to mucositis affects the patient's life severely and can lead to long – term hospitalization. Therefore, this study was conducted to evaluate the effect of chamomile mouthwash on the prevention of oral mucositis in children with acute lymphoblastic leukemia.

**Materials and Methods:** This double-blinded clinical trial study was done on 31 children with acute lymphoblastic aged 6-15 who were admitted to hospital of 17 Shahrivar Rasht, Iran between 16 July and 8 December 2015. Patients and their parents were instructed to resolve 15 drops of chamomile mouth wash in 10cc water, turn it one minute in the mouth, outpour it, and avoid eating for one hour. After three times tooth brushing a day, the mouth cavity of patients was evaluated one day before chemotherapy, the seventh day and fourteenth day of chemotherapy according to the criteria of world health organization. SPSS (version 11) was used in order to analyze the data and random statistical index and independent t test were run.

**Results:** The severity of oral mucositis on the seventh and fourteenth day after chemotherapy had no significant difference with the first day ( $P = 0.59$ ). The incidence and severity of oral mucositis didn't increase 14 days after chemotherapy in comparison with the seventh day.

**Conclusion:** Chamomile mouthwash can be effective in preventing the incidence and severity of oral mucositis and it can be used as a suitable mouthwash in children undergoing chemotherapy.

**Keywords:** Acute Lymphoblastic Leukemia, Chemotherapy, Mouthwashes, Oral Mucositis

### Introduction

Cancer is a process that begins with changing an unnatural cell that is created by DNA genetic mutation. This unnatural cell with asexual production begins abnormal proliferation and penetrates into cells and reaches to bloody and lymphatic vessels (1). Childhood cancer is the second common reason of death in developing countries. The annual incidence of cancer in children is reported about 0.5% in the United States (2). Among malignant diseases, cancer of hematopoietic cells such as leukemia is the most common childhood cancer which develops to acute lymphoblastic leukemia and reaches to its

peak between the ages of 2 to 5 years old. Pediatric B-cell progenitors have similar prevalence in both sexes; however, all T cell is more common in males (3, 4). Diagnosing cancer and determining the extent of unnatural cell in body, the type of treatment is chosen. Treatment of cancer includes surgery, radiation therapy, and chemotherapy which is done with the aim of providing palliative treatment and improving the life quality of the affected person. Most of chemotherapy drugs generally are anti-proliferation and more effective against tumors that have a quick growth. On the other hand, they have significant side effects on healthy tissues

that proliferate quickly such as bone marrow and gastric mucosa (5).

Oral mucositis refers to erythematous and ulcerative lesions of the oral mucosa observed during the treatment of cancer such as transplantation of hematopoietic fundamental cells, and chemotherapy (6) and generally is caused due to the consumption of some drugs such as 5-fluorouracil, methotrexate and cytarabine. Mucositis can cause soreness in all parts of the digestive tract from oral cavity to outlet. The incidence and severity of mucositis is different from patient to patient and depend on the treatment type. However, it is estimated that the incidence of mucositis in patients under treatment is 40% (7).

The incidence of mucositis endangers the treatment and nutrition status of patients and washing mouth with chlorhexidine, topical anesthetic such as lidocaine and antistheroidanti inflammatory drugs including paracetamol three times a day is recommended to these patients (8, 9).

Chamomile is a plant which is increasingly used for many years in traditional and herbal medicine for its special properties such as anti-inflammatory, antispasm, calming, antibacterial, and antifungal (10, 11).

## Materials and Methods

### Study design

This clinical trial study was conducted without any control group (RCT without control). The ID code of register dedicated to this research with number IRCT2015040821658N1 from Iranian Registry of Clinical Trials. The study design was double blinded since the person evaluated the oral mucosa (one day before chemotherapy and on the seventh and fourteenth days following the chemotherapy) and also statistical analysts were unaware of the type of used mouthwash.

### Participants

The study population were children aged 6-15 years old admitted to oncology ward

of 17 shahrivar hospital in Rasht, Iran. These children were underwent chemotherapy with BFM 2002 protocol of developing acute lymphoblastic leukemia. Methotrexate and cytarabine were also used in some parts of this protocol (13).

### Ethical considerations

ID code of ethics (IR. MUI. REC. 1394.4.38) was dedicated to this study. Acknowledging the safety of chamomile mouthwash and the goals of the study for the children and their parents, written and informed consent was obtained from their parents.

Inclusion criteria were as follows:

1. Suffering from acute lymphoblastic leukemia
2. Aged 6-15 years
3. The same treatment regimen
4. Lack of getting gum disease and tooth
5. No oral ulcer occurrence and oral mucositis one day prior to chemotherapy.

Exclusion criteria were as follows:

1. Unwillingness to continue the study.
2. History of infection or neutropenia.
3. The necessity of antibiotic use during chemotherapy.

### Procedures

Participants were given toothbrush special to children. The correct ways of brushing and using chamomile mouthwash were explained to them at the beginning of the study. The parents were asked to write down the times of using chamomile mouthwash according to the presented protocol in the study.

The participated were given 30 cc chamomile mouthwash built by Chamomile mouthwash (barjessans/kashan-Iran) (dilute 15 drops of solution in 10 cc of water). They were asked to wash their mouth with it for 14 days and three times a day. They should avoid eating one hour after using mouthwash while the previous standard treatment of physician was continued. Demographic information questionnaire was completed one day before chemotherapy. The patients' status of oral cavity was evaluated, according to the

protocol, one day before chemotherapy and 7 days and 14 days following the chemotherapy by ward nurse. Moreover, the oral mucositis was examined according to the checklist of the world health organization (Table I).

### Statistical Analysis

SPSS (version 11) was used in order to analyze the data and random statistical index and independent t test were also run.

### Results

Eighteen boys and 13 girls under going chemotherapy with methotrexate and cytarabine participated in this study. The mean age of the participants was 9.9 with standard deviation equals to 2.9. The participants' age ranged between 6 to 15 years old (Table II). Wilcoxon test showed no significant difference regarding the

severity of oral mucositis 7 and 14 days after chemotherapy ( $z = 0.53$ ,  $P = 0.59$ ) (Table III). Seven days after chemotherapy, 10 patients developed oral mucositis. Out of these 10 patients, 8 were grade 1, 2 people were grade 2, and none of the participants developed grade 3 or grade 4. Fourteen days after chemotherapy, 8 patients developed oral mucositis that 6 patients were grade 1, 1 patient was grade 2, and 1 patient was grade 3 (Figure 1). It means that developing oral mucositis was not significantly different on 14th day in comparison with 7th day ( $P = 0.59$ ). The place which was mostly involved by mucositis was the dorsum of tongue in 3 people and also corners of mouth in 3 people. On the 14th day of evaluation, the upper part of two people and the left corner of mouth of two people were mostly involved (Table IV).

*Table I: Clinical characteristics of oral mucositis of patients using the ratings of World International Organization (WHO1979)*

Clinical characteristics	Grade
Without mucositis	0
Erythema without scar, redness	1
Painfulness, sensitivity	2
Erythema, redness scar, Able to eat solids	3
Ulcer, but require liquid regime	4
Impossibility of food Nutrition	3

*Table II: The frequency distribution of sex and the mean age of participants under study*

Variable		n	%	Mean±SD	Max	Min
Sex	Boy	18	58.1	-	-	-
	Girl	13	41.9	-	-	-
Age		-	-	9.9±2.9	15	6

Table III: The frequency distribution of the severity of oral mucositis 7 days and 14 days after chemotherapy in the group using chamomile mouthwash

The Severity of Mucositis	7 days after chemotherapy		14 days after	
	Percent	number	percent	Number
<b>Without mucositis</b>	67.7	21	74.2	23
<b>grade 1</b>	25.8	8	19.2	8
<b>grade 2</b>	6.5	2	3.3	1
<b>grade 3</b>	0	0	3.3	1
<b>grade 4</b>	0	0	0	0
<b>total</b>	100	31	100	31

Table IV: The frequency distribution of mucositis place on 7th and 14th days 7 following the chemotherapy

The Place of Mucositis	day 14 of evaluation		day 7 of evaluation	
	Percent	Number	Percent	Number
<b>lips</b>	12.5%	1	-	-
<b>left corner of the mouth</b>	25%	2	20%	2
<b>the upper part of the tongue</b>	25%	2	30%	3
<b>lips and corner of the mouth</b>	-	-	10%	1
<b>high palate</b>	12.5%	1	-	-
<b>mouth corners</b>	12.5%	1	30%	3
<b>right corner of the mouth</b>	12.5 %	1	10%	1
<b>Total</b>	100	8	100	10



Figure1. Grade of oral mucositis in patients

## Discussion

According to the obtained results, the severity of oral mucositis on 14th day didn't increase in comparison with 7th day after chemotherapy. However, the most important side effect of methotrexate is bone marrow suppression. Along with mouth mucositis, the most important side effect of cytarabine is bone marrow suppression along with gastrointestinal mucosal injury that appears between the days 5-14 after treatment. (13) that is consistent with Alijani study (2012) (14) conducted to explore the effect of chamomile mouthwash on stomatitis caused by chemotherapy. In this review, he showed that chamomile mouthwash is effective on the incidence and severity of oral mucositis caused by chemotherapy and also can accelerate the healing process.

We believed that reduction of stomatitis was due to other treatment intervention and reduction of the effect of chemotherapy drugs. However, the reduction of stomatitis on 14th day could be due to the efficacy of chommile mouthwash with respect to Adamson's study (13) who holds that harmful effects of chemotherapy drugs appear up to 14 days after treatment. Although, only patients who were undergoing chemotherapy with cytarabine or methotrexate drugs were selected for the current study, none of the patients developed oral mucositis (grade 3 or grade 4) 7 days after chemotherapy and just one person developed grade 3 oral mucositis 14 days following the chemotherapy. Accordingly, we could conclude the positive effect of chamomile month wash on the incidence and severity of oral mucositis that is consistent with the results of Mazokopakis et al., (12). Mazokopakis et al., aimed to investigate the effect of chamomile mouthwash on oral mucositis caused by chemotherapy. According to the aforementioned study, chamomile mouthwash is effective on oral mucositis induced by chemotherapy.

Fidler et al., revealed that chamomile mouthwash is not effective on oral mucositis caused by 5-fluorourcil with the result of this study. We believed that it could be due to the difference in anti-neoplasm drugs and the age of participants in the current study. In Ghadiri's et al., study, the control group just used brush to prevent the oral mucositis. No usage of mouthwash with a suitable treatment method in chemo therapy period increased the developing to oral mucositis (15).

In sum, according to the result of this study, chamomile mouthwash can be effective on the incidence and severity of oral mucositis due to some of its properties such as anti inflammatory, antibacterial, and anti fungal. It's noteworthy to mention that this mouthwash is available with reasonable price and it has good taste.

## Conclusion

Based on the findings of the current study, using mouthwash is recommended to reduce the severity and pain of oral mucositis in patients under chemotherapy.

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## Conflict of Interest

Authors declare no conflic of interest.

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