

Cryotherapy as A Prophylaxis of Mucositis in Children with Cancer Undergoing Chemotherapy at Dr. M. Djamil General Hospital

Hidayatul Hasni ^{1*}, Mayetti ², Dwi Novrianda ³

¹ Department of Pediatric-Maternity Nursing, STIKes Mercubaktijaya, Padang, Indonesia

² Department of Pediatric Dr. M. Djamil General Hospital, Padang, Indonesia

³ Faculty of Nursing, Andalas University, Padang, Indonesia

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*Corresponding author:

Hidayatul Hasni

Department of Pediatric-Maternity Nursing, STIKes Mercubaktijaya, Padang, Indonesia
hidayatul36@gmail.com

ABSTRACT

Background: Mucositis is one of the side effects of chemotherapy, which can be a severe problem for children with cancer. Cryotherapy can cause vasoconstriction and decrease blood flow to the oral mucosa, resulting in lower concentrations of chemotherapy agents to prevent mucositis. This study aims at determining the effectiveness of oral cryotherapy as prophylaxis mucositis in children with cancer undergoing chemotherapy.

Methods: This quasi-experiment study with a pretest-posttest control-group design involved 45 respondents (22 in the intervention group and 23 in the control group) selected using consecutive sampling. The data collection instrument was the WHO mucositis scale.

Results: Of the 45 children undergoing chemotherapy, 24 (53.3%) were of school age, 25 (55.6%) were male, 33 (73.3%) had good nutritional status, and 17 (37.8%) had mild neutropenia before undergoing chemotherapy. All respondents (100%) did not experience mucositis, but after chemotherapy, 9 children (40.9%) in the intervention group had mucositis, and 19 children (82.6%) experienced mucositis in the control group. The data were analyzed using the Wilcoxon test to see the difference between the intervention group and the control group and the Chi-Square test with Yates's correction to see the effect of cryotherapy on the prevention of mucositis. The results showed that there was a difference in the incidence of mucositis between before and after intervention in the intervention group ($p = 0.003$) and the control group ($p = 0.000$), and cryotherapy was effective in preventing mucositis ($p = 0.01$).

Conclusions: Cryotherapy is effective against the prevention of mucositis. Nurses and families need to be able to apply oral cryotherapy and other evidence-based treatment as a method to prevent mucositis.

INTRODUCTION

Cancer is one of the most common causes of death in children under 14 years of age. One of the most common cancers in children is leukemia. One-third of children are diagnosed with this cancer [1]. Leukemia treatment can be done in a supportive and curative way. Supportive treatment is intended to treat and prevent further complications from leukemia while curative treatment is intended to cure leukemia by chemotherapy [2]. Chemotherapy is one of the cancer treatments with a high cure rate and improves the survival of children with cancer [3,4].

Continuous chemotherapy in children will cause side effects. These side effects include infection, bleeding, lethargy, hair loss, mucositis, nausea, vomiting, fatigue, diarrhea, constipation, and sleep disturbances [5,6]. The most common side effect of children undergoing chemotherapy is mucositis developing on days 5–7 after chemotherapy, which causes difficulty in eating and drinking [7,8].

The prevalence of mucositis varies from 20 to 100% [9,10]. Children are at a higher risk for mucositis than adults. The incidence of mucositis in children due to chemotherapy reaches 52%–80% [11] and 75% during chemotherapy procedures [12]. The prevention and

treatment of mucositis in adults have been evaluated in Cochrane [13]. Some tested and recommended preventions for oral mucositis include oral care, cryotherapy [14,15] palifermin [16] growth factor mouthwash, sucralfate, and chlorhexidine [17].

In cryotherapy, oral cooling, ice is applied during chemotherapy, which is initially for adults receiving the 5-FU chemotherapy process [18]. Oral cryotherapy causes vasoconstriction and decreases blood flow to oral mucosa resulting in a lower concentration of chemotherapy agents [19-21]. The advantage of this therapy is in its low-cost budget natural treatment to minimize the occurrence of side [9,14]. The use of oral cryotherapy has been proven to prevent mucositis in adults undergoing chemotherapy [9,20,22].

There is much research on the use of cryotherapy in adults. The study by Marchesi et al. [22] on multiple myeloma patients showed that cryotherapy given during high-dose chemotherapy was effective in reducing mucositis. Johansson et al. [7] in their study on 94 respondents diagnosed with myeloma (18-70 years old) who underwent hematopoietic stem cell transplantation also found that cryotherapy was effective in reducing mucositis. Several meta-analyses showed that oral cryotherapy is a viable nursing intervention and significantly prevents the occurrence of oral mucositis [8,18,15]. Meanwhile, in an article obtained, the research on oral cryotherapy for children with cancer undergoing chemotherapy showed oral cryotherapy does not reduce the severity of mucositis [23]. In Indonesia, the application of oral cryotherapy for children with cancer has not been found, so this research needs to be done to see the effectiveness of oral cryotherapy in preventing mucositis in children with cancer undergoing chemotherapy.

METHODS

Population

This research was conducted in the Non-Infectious Room of the Obstetrics and Pediatrics Installation at Dr. M. Djamil General Hospital on 48 children with leukemia undergoing consolidation phase chemotherapy and chemotherapy through intravenous. However, 3 children did not accomplish the process; 2 children experienced nausea during the intervention; 1 control group did not take the post-test as the initial agreement. All respondents in this study did not experience malnutrition. The inclusion criteria for this study were children with cancer undergoing chemotherapy aged 6-18 years who had no oral cavity problems and parents who were willing to have their children as research subjects. The children with cancer who had a history of sensitive teeth received chemotherapy agent oxaliplatin and did not accomplish the intervention were

excluded. This research has obtained official written permission from the Health Research Ethical Committee of Dr. M. Djamil General Hospital number 187/KEPK/2019. The researcher explained to the children and their families about the research to be carried out and asked for written consent before conducting the study.

Oral cryotherapy

Oral cryotherapy causes vasoconstriction and decreases blood flow to the oral mucosa, so it makes a lower concentration of chemotherapy agents to prevent the development of mucositis. The materials used were ice chips of 2 x 1 cm, toothbrushes, penlights, and tongue spatels (tongue depressor). After preparing the material and oral cryotherapy device, the researcher prepared the children for chemotherapy. Thirty minutes before cryotherapy intervention, the children were instructed to clean their mouths by brushing their teeth with a soft toothbrush provided. Then, they were required not to eat or drink for 5 minutes before chemotherapy. The researcher gave the children ice chips to be sucked into the mouth and instructed them to move the ice chips within the oral cavity to reach the entire mucosal layer of the mouth. If less than 5 minutes the ice chips have melted, the researcher gives new ice chips (and so on for 5 minutes). During the chemotherapy process, ice chips were given again in the first 15 minutes; then the children rested for 10 minutes and continued for another 15 minutes and so on until the chemotherapy was finished. These ice chips were given while chemotherapy drugs were administered until chemotherapy was finished. Five minutes after the chemotherapy drugs were administered; the children were required to suck the ice chips for 3 minutes. The control group only received standard care provided by the hospital.

Research flow

Figure 1 shows that the number of subjects has changed from 70 to 22 people because they did not meet the criteria set. Therefore, 48 respondents were involved as the research subject. Subsequently, the randomization system was used to divide the respondents into the intervention and control groups. The result of randomization showed that 24 respondents were categorized to the intervention group and 24 to the control group. There was a change in the number of samples in the intervention group where 2 respondents did not complete the intervention because they experienced nausea. In the control group, 1 respondent did not take the post-test based on the initial agreement. As a result, the total of samples analyzed was 45 people.

Instruments

The questionnaire consists of two parts. The first part contains questions related to the characteristics of the respondent included age, nutritional status, and

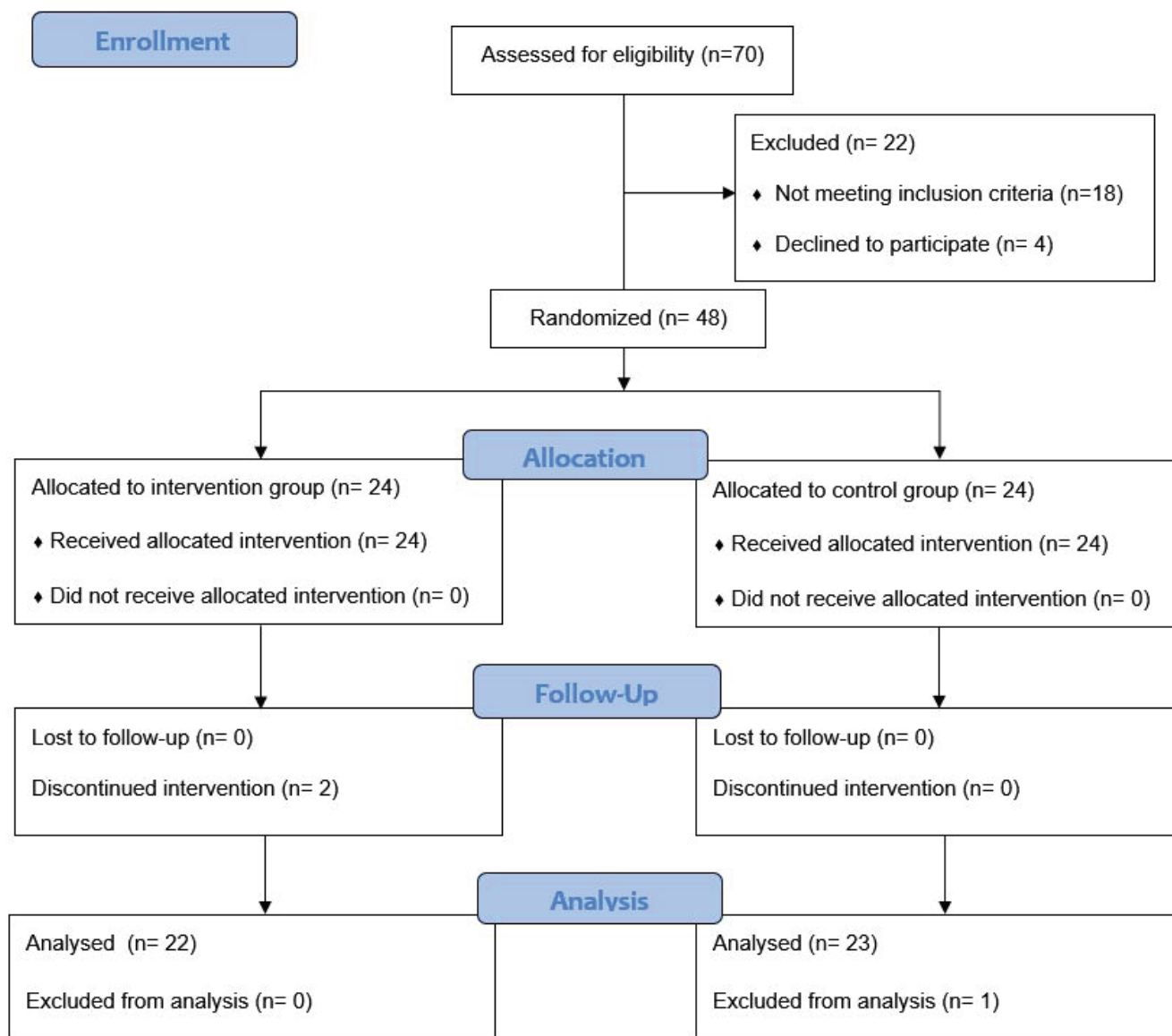


Figure 1. Research flow

neutrophil count. The next part is an assessment sheet of mucositis incidence referenced from a mucositis assessment instrument developed by WHO. WHO mucositis scale was chosen because it is commonly used, the scoring system is objective, and it was easy to use. This instrument was translated into Indonesian in the Language Centre of Andalas University Padang. HH, the researcher observed to assess mucositis incidence in children before and after the cryotherapy intervention. The researcher evaluated for 14 days. The study was stopped if the signs and the symptoms based on the WHO mucositis scale of mucositis appeared before 14 days.

Statistical analysis

The data were processed using SPSS v18 software, a computerized system. Then, they were analyzed using

the Wilcoxon test to see the difference between the intervention group and the control group. The analysis used in this study was the Chi-Square statistical test with Yates’s correction to perceive the cryotherapy effect on mucositis prevention. If the p-value < 0.05, it can be concluded that there is an effect of the oral cryotherapy given.

RESULTS

Table 1 shows the characteristics of the respondents both in the intervention and control groups. More than half of the respondents were school-age children (53.3%) and male (55.6%) and most of them (73.3%) had good nutritional status. The results of the neutrophil count were evenly distributed among normal neutrophils (37.8%), mild neutropenia (37.8%), and severe neutropenia (24.4%).

Table 1. Respondent characteristic distribution

Variable	Intervention (n=22)		Control (n=23)	
	n	%	n	%
Age				
School-age (6–12 years old)	12	54.5	12	52.2
Adolescence (13–18 years old)	10	45.5	11	47.8
Sex				
Male	12	54.5	13	43.5
Female	10	45.5	10	56.5
Nutrition Status				
Sufficient nutrition	16	72.8	17	74
Insufficient nutrition	6	27.2	6	26
Neutrophil				
Normal	8	36.4	9	39.1
Mild neutropenia	9	40.9	8	34.8
Severe neutropenia	5	22.7	6	26.1

Table 2. Differences in the incidence of mucositis before and after giving intervention in the intervention group and the control group

Group	Prevalence								p
	Mucositis				Not mucositis				
	Pretest		Post-test		Pretest		Post-test		
	n	%	n	%	n	%	n	%	
Intervention	0	0	9	40.9	22	100	13	59.1	0.003
Control	0	0	19	82.6	23	100	4	17.4	0.000

Table 3. The effect of cryotherapy on the prevention of mucositis in children with cancer undergoing chemotherapy

Mucositis Incidence	Group of Respondents				Total	p
	Intervention		Control			
	n	%	n	%		
Mucositis	9	20	19	42.2	28	0.01
Non-mucositis	13	28.9	4	8.9	17	

Table 2 shows the differences in the incidence of mucositis before and after chemotherapy in the intervention and control groups. It was found that all respondents in both groups did not experience mucositis before undergoing chemotherapy. After undergoing chemotherapy, 9 respondents (40.9%) in the intervention group had mucositis while 19 respondents (82.6%) in the control group had mucositis. Mucositis is common in children who do not receive oral cryotherapy, which shows that cryotherapy has an effect on mucositis prevention in children with cancer undergoing chemotherapy.

DISCUSSION

This research indicated that oral cryotherapy had a significant effect in preventing mucositis in children with cancer. The oral cryotherapy intervention in this study was by giving ice chips 5 minutes before chemotherapy started, during chemotherapy, and 5 minutes after chemotherapy. The time needed to implement the intervention was 45 minutes. The average time of

effectively giving oral cryotherapy was 30-45 minutes [22,24]. The children were instructed to do oral care using a soft toothbrush and toothpaste provided by the researcher before the oral cryotherapy was given. Essential oral care such as brushing teeth and flossing was recommended to maintain oral health and reduce the negative impact of normal mouth flora [25]. Oral care can be used to prevent and treat complications that arise in the oral cavity in children undergoing cancer [26].

All respondents did not experience mucositis before undergoing chemotherapy, but they did after chemotherapy. Mucositis is an inflammatory response of mucosal epithelial cells to the cytotoxic effects of chemotherapy and radiation therapy characterized by an inflammatory reaction and ulceration of the oral cavity. Chemotherapy also causes cell cleavage, such as mucosal cells in the mouth and throat, so it damages cells during treatment [2,26]. Some respondents in the group receiving oral cryotherapy experienced mucositis. However, mucositis appeared on average on day 9 after chemotherapy. There is a postponement appearance of

mucositis. Oral mucositis was the effect of the epithelial cell damage in the mouth, which usually develops 5-7 days after chemotherapy [27,28].

Several theories can explain delayed mucositis appearance in the group of children receiving oral cryotherapy. Cryotherapy is cooling the mouth using ice to narrow the blood vessels in the mouth and reduce the blood flow containing chemotherapy drugs reaching the mouth [13,27,29]. During the intervention, 2 respondents resigned because they felt painful and nauseous 10 minutes after oral cryotherapy, so the intervention was stopped. However, other respondents tolerated and completed well the oral cryotherapy intervention. We chose 6-year-old children as the respondents in this research because they were able to understand and follow the instructions of the parents and nurses. The respondents followed all the instructions during the intervention to make chemotherapy drug concentration reach the low mucous membrane. There was a narrowing of the blood vessels due to the ice chips given. The respondents liked the interventions because it was their first intervention during chemotherapy. Some control group respondents experienced mucositis because they just received standard care by gargling with saltwater provided in the hospital.

The result of this research in line with Sato et al. [30] found that children undergoing chemotherapy who received oral cryotherapy intervention combined with propantheline administration could reduce mucositis. However, it contradicts the study conducted by Kamsvag et al. [23], in which oral cryotherapy did not decrease the incidence of mucositis, mouth pain, or opioid use.

The results of this research have several advantages and disadvantages in both the method and the results. Cryotherapy is a complementary therapy for mucositis using an intervention that is not difficult, at a low cost, and has no side effects, so it can be received by respondents. Other than that, nurses and parents also want to continue this method; however, it was constrained by the administration of ice chips. Further research related to the use of oral cryotherapy requires further evaluation to assess the healing time of mucositis in children receiving cryotherapy and standard care to increase more additional data. Furthermore, it is necessary to discuss related factors affecting the success of chemotherapy.

This result must be looked at while considering the limitations of this study. This study only involved cancer children with a diagnosis of acute lymphoblastic leukemia who underwent consolidation phase chemotherapy so that the results of the study were not varied and there was still a need for more developmental stages such as cancer children with different diagnoses and different phases of chemotherapy so that the results and discussion were broader.

CONCLUSIONS

The prevalence of mucositis in childhood cancer after chemotherapy in Dr. M. Djamil General Hospital is still high. Further prospective studies are required to explore the risk factors and predictors of mucositis in children with cancer undergoing chemotherapy. This research shows that oral cryotherapy is effective to prevent mucositis in children with cancer undergoing chemotherapy. Oral cryotherapy can be used as a safe and low-cost treatment to prevent the incidence of mucositis in children with cancer undergoing chemotherapy. The results of this study are expected to be used as standard care in preventing mucositis in children.

DECLARATIONS

Ethics Approval

This research has obtained official written permission from the Health Research Ethical Committee of Dr. M. Djamil General Hospital with number 187/KEPK/2019. The researcher explained to the child and family about the research to be carried out and asked for written consent before conducting the study.

Competing of Interest

The author(s) declare no competing interest in this study

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