

Effects of Probiotics on Clinical Appearance of Oral Mucositis in Children with Leukemia during Chemotherapy

Research Article

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Abstract

Introduction: Mucositis is one of the side effects induced by chemotherapy. It results in pain, discomfort, difficulties in talking, swallowing, eating, drinking, poor nutrition, systemic weakness and life-threatening infections. Probiotics contain nonpathogenic live microorganisms that give benefit to our health and help in preventing inflammation in the oral cavity. Several studies have reported the use of probiotics for oral health purposes.

Objectives: The aim of this study was to analyze the effect of probiotic to oral mucositis in children with hematology cancer that underwent the chemotherapy process before gargling, 7 days after gargling, and 14 days after gargling with probiotic.

Materials and Methods: The study was held in National Cancer Hospital. Eleven patients were meet the criteria. One day after the chemotherapy started, the researcher checked the patient's oral health condition using Oral Assessment Guide (OAG). Then the patient started to gargle the probiotic twice a day for 7 days and the researcher rechecked the score of oral mucositis after 7 days and 14 days.

Results: There was a significance decreasing OAG score between before gargling with 7 days and 14 days after gargling probiotics.

Conclusions: Probiotics gave effects in children with leukemia during chemotherapy and could be an alternative therapy for oral mucositis.

Keywords: Chemotherapy; Children; Leukemia; Oral Assessment Guide; Oral Mucositis; Probiotic.

Introduction

Hematologic cancer is the most common types of cancer that is found in children and the treatment option is chemotherapy. One of the unexpected complication and mostly seen due to chemotherapy is oral mucositis, start from the inflammation and ulcerated in oral mucous then cause the pain, uncomfortable and systemic weakness [1-4]. Eighty percent of children that have chemotherapy will get various levels of mucositis, depends on the types of cancer and medical treatment [5]. Children with hematologic malignancies have the mucositis more often than children with tumor, and they who have the chemotherapy are more frequently to get mucositis than adults, mostly seen in 90% of children below than 12 years [6, 7].

Oral mucous is easily broken because of chemotherapy. Inflam-

mation in oral mucous can cause pain, infected ulceration and disability to eat, drink, even swallow. There are many assessment scale that can be used to evaluate the oral mucositis. Each of them use the same criteria but has different levels, so it is hard to compare the accuracy of study result [5]. Oral Assessment Guide (OAG) can be trusted and legal, it can be used and sensitive with the changing condition [8]. OAG scores mucous in 8 different area to see the extension of mucositis better than the other scoring method, and according to some researchers, OAG is easily used, especially for children [5]. Saliva is a complex media in the oral cavity that contains various bactericidal, bacteriostatic and inhibitor protein, which if they were combined, will destroy some plankton species. Probiotics that are swallowed will expose with the saliva protein and effect to adhesion, morphology, metabolism activity and viability of probiotic microorganism. After the adhesion with oral cavity, probiotic helps in preventing inflam-

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Received: October 13, 2020

Accepted: November 18, 2020

Published: November 24, 2020

Citation: Hans Christian, Margaretha Suharsini, Eva Fauziah. Effects of Probiotics on Clinical Appearance of Oral Mucositis in Children with Leukemia during Chemotherapy. *Int J Dentistry Oral Sci.* 2020;7(11):1032-1036. doi: <http://dx.doi.org/10.19070/2377-8075-20000204>

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mation in the oral cavity and oral tissue destruction because of the oral pathogen. Probiotics also activate and regulate immune system [9].

Based on the study, oral mucositis is one of the most common condition seen in children with cancer who take chemotherapy and weakening them, it is found in 52-80% children that are being treated [10, 11]. Oral mucositis causes inflammation and ulcer in oral cavity, begin with tissue depletion in the oral, erythema then become ulcer [6, 12]. Usually probiotics study is in digestive system and there is a new study about the benefit of probiotic in oral health, by manipulating oral microflora that significantly reduce the inflammation in the oral [13]. Probiotics containing *Lactobacillus* spp. are known as an effective new pharmacotherapy in intervene mucositis [14]. Based on this information, researcher interested to study about the effect of probiotics to oral mucositis in children with cancer who are having chemotherapy. The aim of this study was to analyze the effect of probiotic to oral mucositis in children with hematology cancer who underwent the chemotherapy process before gargling, 7 days after gargling, and 14 days after gargling with probiotic.

Materials and Methods

The research project was approved by the Dental Research Ethics Committee. Clinical experimental study was performed to evaluate the clinical appearance of oral mucositis. The subjects were children patients in National Cancer Hospital that were having chemotherapy and agreed to take part in this study. The children were diagnosed by the pediatrician and having chemotherapy in induction and consolidation phase, also they had to be able to follow instructions for gargling.

Measurement of oral mucositis had to be determined clinically in children. The instrument that was used to assess oral mucositis had a standard. In this study, the researcher used Oral Assessment Guide to control the oral health patient that underwent chemotherapy and scoring the level of oral mucositis. There were eight components in OAG: voice, swallow, lips, saliva, tongue, mucous membrane, gums, and teeth. The total of these eight components would be calculated to see the oral health condition. A normal mouth would receive a score of 8 (Table 1).

Eleven children patients in National Cancer Hospital agreed to take part in this study. One day after the chemotherapy started, the researcher checked the patient's oral health condition using Oral Assessment Guide (OAG). Then the patient started to gargle the probiotic twice a day for 7 days and the researcher rechecked the score of OAG. Patients continued gargling and researcher did the scoring of OAG 14 days later. OAG showed eight categories from oral cavity, those were voice, swallow, lips, saliva, tongue, mucous membrane, gums, and teeth.

The score were totaled; which increasing of the score indicated the severity of oral mucositis, whereas decreasing of the number meant improvement to the normal condition. Friedman test was performed to compare the score of Oral Assessment Guide before, after 7 days, and after 14 days gargling with probiotics since the data distribution was not normal.

Results

There were 11 patients that fulfilled the criteria and joined the program. The OAG scores for each measurement were analyzed with SPSS. The normality test with Shapiro-Wilk showed that the data distribution was not normal with $p\text{-value} < 0.05$, therefore Friedman test was used to see the difference between before, after 7 days and 14 days of the oral health condition by using OAG (Table 2).

After the analysis had come out, the Wilcoxon post-hoc analysis was done to see the significance between each experimental time (Table 3).

Discussion

This study was undertaken to see the patients' oral health condition that were taking chemotherapy and their response in the oral mucositis after short-term exposure to probiotic in ALL children during the induction and consolidation phase of chemotherapy treatment. The main finding showed that there was a decrease in Oral Assessment Guide score after 7 days and 14 days gargling with probiotic for 1 minute twice a day for 14 days.

Figure 1. Day 1 after chemotherapy before gargling probiotic, the tongue area had lesions.



Figure 2. Day 7 after gargling probiotic, the tongue lesion was getting better.



Figure 3. Day 14 after gargling probiotic, the tongue lesion was healed.



Table 1. Oral Assessment Guide (Adapted from Eilerset al.,1988).

Category	Method of observation	Rating 1	Rating 2	Rating 3
Voice	Converse with patient. Listen to crying	Normal	Deeper or raspy	Difficulty talking or crying, or painful.
Ability to swallow	Ask patient to swallow	Normal swallow	Some pain on swallowing	Unable to swallow
Lips	Observe and feel tissue	Smooth, pink and moist	Dry or cracked	Ulcerated or bleeding
Saliva	Insert depressor into mouth, touching center of tongue and floor of the mouth.	Watery	Thick or ropy. Excess salivation due to teething.	Absent
Tongue	Observe appearance of tissue	Pink, moist and papillae present	Coated or loss of papillae with a shiny appearance with or without redness. Fungal infection.	Blistered or cracked
Mucous membrane	Observe appearance of tissue	Pink and moist	Reddened or coated without ulceration. Fungal infection.	Ulceration with or without bleeding
Gingiva	Gently press tissue	Pink and firm	Edematous with or without redness, smooth. Edema due to teething.	Spontaneous bleeding or bleeding with pressure
Teeth (if no teeth, score 1)	Visual. Observe appearance of teeth.	Clean and no debris	Plaque or debris in localized areas (between teeth)	Plaque or debris generalized along gum line

Table 2. Analysis of OAG score before gargling probiotic, after 7 days and 14 days gargling probiotic. There are statistically significant difference before and after gargling probiotic.

Oral Assessment Guide Score	n	Mean (Standard Deviation)	p
Before	11	13.18 (1.328)	0.002*
After 7 days	11	10.91 (2.023)	
After 14 days	11	10.27 (1.849)	

* Statistically significant difference compared before and after ($p < 0.05$, Friedman test)

Table 3. Significance (p-value) using Wilcoxon post-hoc analysis. There are statistically significant difference before – after 7 days gargling and before – after 14 days gargling.

OAG score	After 7 days	After 14 days
Before	0.005	0.007
After 7 days		0.368

* Statistically significant difference ($p < 0.05$, Wilcoxon test)

One of the treatment option for children with leukemia is chemotherapy. Methotrexate and cytarabine are used for leukemia which have side effects in oral mucositis [15]. Chemotherapy destroys the basal cell when drugs get into the cell through blood vessel of submucous connective tissue. The progress of mucositis is complex and dynamic, it can be described in five stages: initiation, primary damage response, signal amplification, ulceration, and healing [12, 16].

Oral status monitoring in patients with chemotherapy is important in the treatment and prevention of inflammatory lesions or ulcers [15]. This study showed a decrease in OAG score before gargling with after gargling probiotics for 7 days and 14 days. Probiotics contain mostly *Lactobacillus* species and *Lactobacillus casei* is used in this study. Probiotic organisms can compete with potential pathogens for nutrients and growth factors, disintegration of toxins, local and systemic immunomodulation, develops a mucosal barrier, and activates immune system [17]. Probiotic can prevent mucositis not only in oral but also gastrointestinal, with symptoms as nausea, vomiting, and abdominal pain [18]. A previous study showed that oral and intestinal could be relevant to mucositis development and treatment but no specific probiotic formula has found to human clinical trial [4]. Other studies reported that probiotic reduced oral and intestinal inflammation in immunosuppressed experimental rats, also prevent mucositis symptoms [18, 19]. Some patients showed improvement in mucous membrane, saliva, lips, and tongue area in this study. Figure 1 to figure 3 showed the improvement of tongue lesion in one of the patients. The tongue had a lesion because of the chemotherapy effect (figure 1) and the lesion healed after gargling probiotics for 7 days (figure 2) and 14 days (figure 3).

A study showed that probiotic reduced oral mucositis by improving the immunity of patients and it reduced the incidence of oral mucositis induced by chemoradiotherapy in patients with nasopharyngeal carcinoma [20]. An initial treatment with chemotherapy cause damage and death of basal epithelial cells, whereas progressive mucosal destruction results in ulceration [4]. In this study, OAG score in leukemia patients showed nonparametric data (Table 2), and there was a statistically significant decrease of OAG score between before with 7 days and 14 days after gargling probiotic (Table 3). It meant that the probiotic gave effect in decreasing OAG score after gargling but no statistically significant changes was found between after 7 days with 14 days. It maybe because of the probiotics that had already taken for 7 days and after 14 days the OAG score was decreased but not significant. The result is similar to some research that showed probiotics can reduce inflammation in oral and intervene to mucositis [13, 14].

The obstacles in this study were in the sample size, limited time and patients that fulfilled the criteria. As we know that the chemotherapy caused systemic weakness, so not all leukemia patients could follow the method. We recommend that future studies with same approach consider to increase in sample size, provide more time and maybe can do it in another types of cancer.

Conclusion

This study showed that there was a statistical score difference of OAG before and after gargling with probiotics in children pa-

tients with leukemia that are having chemotherapy. Mostly chemotherapy drugs give same side effects and they act not only in cancer cells but also in healthy cells. Therefore, probiotics could be an alternative therapy and prevention for oral mucositis.

Acknowledgement and Declarations

The researcher would like to thank the patients and parents who were willing to take part in this research, doctors from the hospital and those who participated in this study. The authors confirmed that there was no conflict of interest in this research.

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