

**COMPARISON EFFECTS OF CHLORHEXIDINE GLUCONATE AND
POVIDONE IODINE MOUTHWASHES TO CHEMOTHERAPY-INDUCED ORAL
MUCOSITIS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA**

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ABSTRACT

Oral mucositis is one of a common, debilitating complication of cancer chemotherapy. Mucositis causes severe pain and distress, and may limit the tolerability of chemotherapy. The aim of this study was to compare the efficacy of chlorhexidine gluconate and povidone iodine mouthwashes on oral mucositis in children receiving chemotherapy for acute lymphoblastic leukemia (ALL).

A total of 18 children age 2 to 10 years were participated a clinical trial with pre-post test design and single blinded system. Subjects were divided into three groups, using chlorhexidine gluconate, povidone iodine, and alkaline saline as a control group, respectively. Clinical measurements to assess mucositis and pain using General Mucositis Scale from WHO and Wong-Baker Faces Rating Scale, respectively. Children in all groups received daily oral hygiene instructions, and were examined daily until the mucositis heals.

Data were analyzed by ANAVA and Newman-Keuls methods with significance value $\alpha = 0.05$. The results showed that mucositis and its related pain were disappeared after 5 to 7 days, 8 to 14 days, and 13 to 14 days using chlorhexidine gluconate, povidone iodine, and alkaline saline (control), respectively.

It is concluded that chlorhexidine gluconate was more effective on the healing of oral mucositis than povidone iodine.

Key words : Mucositis, chlorhexidine, povidone iodine

INTRODUCTION

Mucositis is an inflammatory-like process of the oral mucosa due to chemotherapy. It occurs in up to 40% patients undergoing chemotherapy and it develops more often in nonkeratinized mucosa like buccal and labial mucosa and ventral tongue. It occurs most often between the seventh and fourteenth day after chemotherapy, especially VP16, epotomide, and methotrexate, when the effects of the drugs produce an extremely low WBC count.¹

The earliest signs and symptoms include erythema and edema, a burning sensation, and an increased sensitivity to hot or spicy food. Erythematous areas may develop into elevated white desquamative patches and subsequently into painful ulcers.² Mucositis may produce severe discomfort and pain which interfere with oral feeding, delays of dosage limitation of antineoplastic treatment, and in some patient life-threatening septicaemia.³

The management of mucositis is aimed to maintain the mucosal integrity and oral hygiene.¹ Oral hygiene of hospitalized children suffering from ALL is generally poor.⁴ They

should be considered as patients who need a supervised oral hygiene care such as daily oral hygiene instructions and the use of conventional antimicrobial agents.

Antimicrobial mouthrinse may be useful in treating chemotherapy-induced mucositis.¹ A variety of chemical substances has been used for the treatment of mucositis such as chlorhexidine and povidone iodine.^{1,5}

Chlorhexidine mouthwash has been widely used for the aforementioned purpose. It is most active against vegetative bacteria and mycobacteria and has moderate activity against fungi and viruses. Oral toxicity is low because chlorhexidine is poorly absorbed from the alimentary tract.⁶ The limitation of this agent is that it has a side effect of discoloration in the teeth in the long term usage.^{6,7}

The wide antiseptic effects including antiviral, antibacterial, and antifungal efficacy and good tolerability have resulted in the frequent use of povidone iodine as a preventive and therapeutic drug in chemotherapy induced oral mucositis.²

The aim of this study was to compare the efficacy of chlorhexidine gluconate and povidone iodine mouthwashes on oral mucositis in children receiving chemotherapy for acute lymphoblastic leukemia (ALL).

MATERIALS AND METHODS

This study has been approved by the Ethics Committee of Health Research, Faculty of Medicine/Hasan Sadikin Hospital, Padjadjaran University, Bandung – Indonesia. Subjects were children with diagnosis of ALL and suffer a chemotherapy-induced oral mucositis.

Twenty three children, three to ten years of age receiving intensive chemotherapy in the induction phase for treatment for acute lymphoblastic leukemia were evaluated. These children were admitted to Hasan Sadikin Hospital, Bandung, West Java, Indonesia. They receive an identical chemotherapy regimen for the induction phase (six week periode). The

regimen consisted of methotrexate (an intrathecal dose on days 1, 14, and 42), dexamethasone (an oral dose of 6 mg/m²/day for 5 weeks), vincristine (an intravenous dose of 1,5 mg/m² in infusion in 5 minutes on days 7, 14, 21, 28, 35), and L-Asparaginase (an intravenous dose of 6000 µ/m² on weeks 4 and 5).

No children had any clinical signs of oral complications on the mucosa before initiating the intensive chemotherapy. Children received an oral hygiene care every day (including twice a day teeth brushing with identical tooth brushes for every children, supervised by dentist) and evaluated every day for the sign of mucositis. Eighteen children develop mucositis and they were divided into three groups with randomized technique.

The mouthwash was given in the day the children develop mucositis. Children in the group A received chlorhexidine, group B received Povidone iodine, and group C received alkaline saline as control group. This is a double blind clinical trials. The mouthwashes were to be rinsed twice a day (in the morning and in the evening).

Each group were evaluated daily by the same pediatric dentist for the course of mucositis severity and the pain complain. The severity of mucositis was measured by WHO's General Mucositis Scale and the pain was measured by Wong-Baker Faces Rating scale. These procedures were performed every day until the mucositis heals or for maximum of 2 weeks.

Table 1. Criteria used to measure severity of mucositis⁸

Scale	Clinical Appearances
0	No mucositis
1	Soreness/erythema
2	Erythema/ulcers/can eat solids
3	Ulcers/requires liquid diet only
4	Alimentation not possible

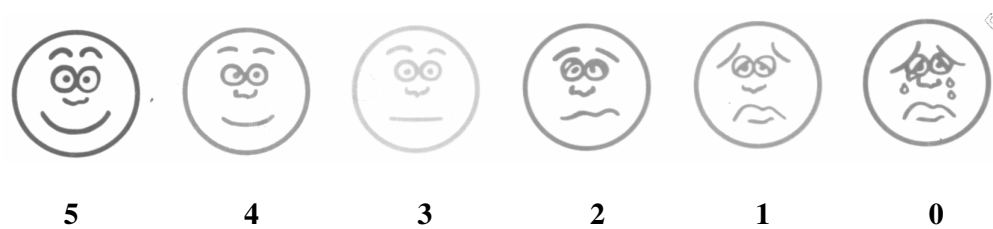


Figure 1 *Wong-Baker Faces Rating Scale*⁹

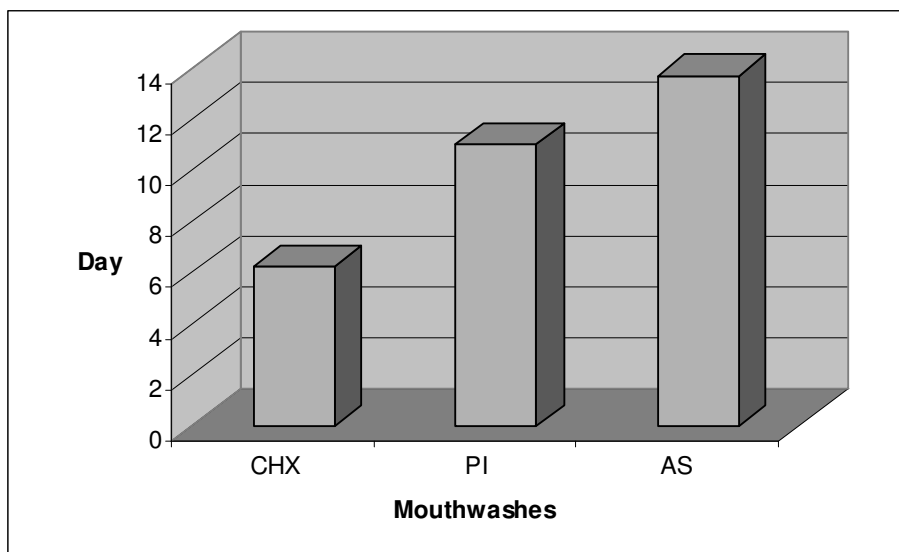
Statistical analysis

The data were analyzed statistically by means of ANAVA and Newman-Keuls test. A p value < 0.05 was considered significant.

RESULT

Eighteen children out of 23 were included in the experimental period. The 5 rest of it was excluded because they did not develop mucositis. A significant decrease in the severity of mucositis and its related pain in the children who received chlorhexidine mouthrinse were observed. It showed that the mucositis and its related pain healed in days 5 to 7 for chlorhexidine group, 8 to 14 day for povidone iodine, and 13 to 14 days for control group.

The ANAVA test for this clinical trial showed the difference of duration of healing in oral mucositis to be significant. Further more, the data was test by Newman-Keuls test to show the sequence of duration of healing, which was chlorhexidine followed by povidone iodine, and alkaline saline which appear to be the longest duration.



Note : CHX = chlorhexidine, PI = povidone iodine, AS = alkaline saline

Figure 2. Day of healing of mucositis and its related pain

DISCUSSION

The result of this result showed that there was a difference effect of chlorhexidine and povidone iodine mouthwashes as a treatment for chemotherapy-induced mucositis in children with acute lymphoblastic leukemia. This result is consistent with the findings of Ferreti *et al* and (1987) and de Brito Costa *et al* (2003), the severity of mucositis was reduced after using chlorhexidine mouth rinse.⁶

Study which evaluate the effect of povidone iodine to chemotherapy-induced mucositis was done by Hasenau *et al.* (1998) and Rahn *et al* (1997) which showed that povidone iodine can reduce both incidence and the severity of mucositis.^{10,11}

Chlorhexidine gave a better result compared to povidone iodine according to rate of healing the patient experience the mucositis and its related pain. These occur since chlorhexidine was absorbed at the tooth surface, plaque, and oral mucosa, thus slowly released in 24 hours period when the saliva concentration decreased. Povidone iodine is not absorbed at tooth surface, plaque, and oral mucosa.¹²

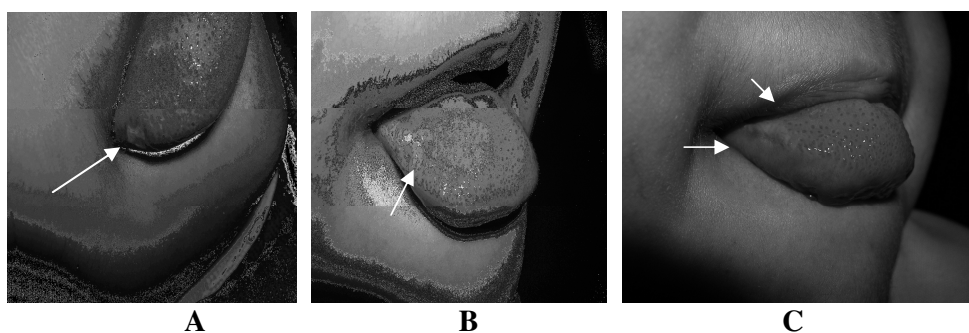


Figure 3. Scale 3 mucositis in the tongue border. 2 days after initial administration of intrathecal dose methotrexate (A). Three days after administration of chlorhexidine (B). Mucositis healed five days after chlorhexidine administration.

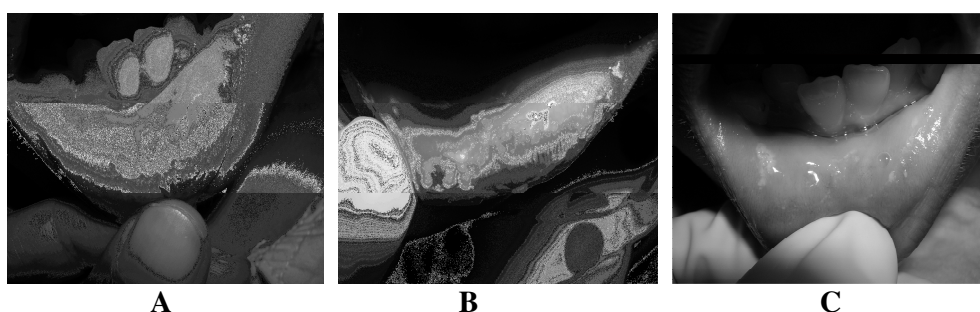


Figure 4. Scale 2 mucositis in the lower labial mucosa, four days after initial administration of intrathecal dose of methotrexate (A). Four days after being administered by povidone iodine mouthwash (B). Mucositis healed in the tenth day (C)

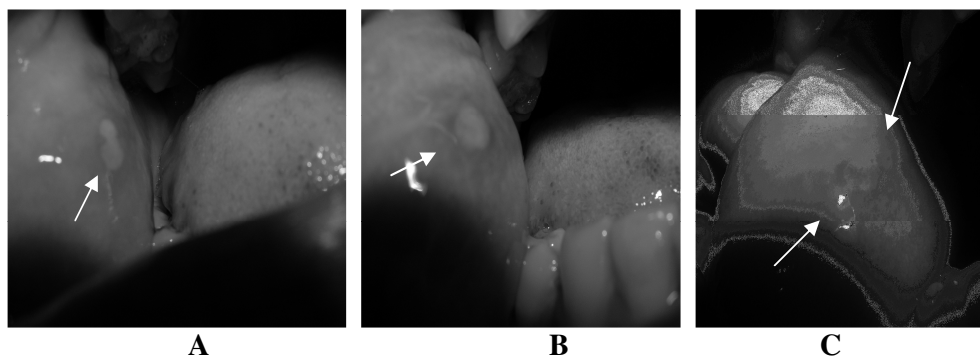


Figure 5. Scale 2 mucositis in the buccal mucosa, two days after initial administration of intrathecal dose of methotrexate (A). Seven days after being administered by alkaline saline (B). In the 14th days, the mucositis still showed the scale 1 mucositis. (C).

CONCLUSIONS

The results obtained in this limited number of patients are promising. The result showed that chlorhexidine gave better effect in treating chemotherapy-induced mucositis. Mouthwash administration is recommended to treat oral mucositis and its related pain for patients who undergo chemotherapy. It is important to have a teamwork which include pediatrician and pediatric dentist in preventing and treating oral complication prior, during, and after chemotherapy.

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