Journal of Dental Sciences 20 (2025) 248–253

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Original Article

Oral care methods to reduce salivary bacteria in infants undergoing cardiac surgery: A randomized controlled trial

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Received 2 July 2024; Final revision received 21 July 2024
Available online 10 August 2024

KEYWORDS
Infant;
Cardiac surgery;
Oral care;
Povidone iodine;
Bacterial count

Abstract *Background/purpose:* Complications, such as postoperative pneumonia, can occur after pediatric cardiac surgery; however, studies on related changes in perioperative oral bacterial counts are scarce. Herein, we investigated the changes in oral bacterial counts before and after surgery in infants who underwent cardiac surgery, as well as after oral care using an antiseptic mouthwash.
Materials and methods: A total of 102 infants who underwent congenital heart disease surgery were enrolled in this study. Preoperative oral care was provided using water and a sponge brush. Bacterial cultures were used to determine salivary bacterial counts before and after oral care. Postoperatively, the infants were randomized into a water group (WA group), benzethonium chloride mouthwash group (BZ group), or povidone-iodine mouthwash group (PV—I group), and their salivary bacterial counts, before and after oral care, were measured.
Results: The preoperative salivary bacterial colony counts did not change after oral care; however, the postoperative bacterial counts were significantly lower, possibly because of the use of systemic antibiotics. Bacterial counts before and after oral care were not significantly different between the WA and BZ groups; however, bacterial counts were significantly decreased in the PV-I group after oral care.
Conclusion: Overall, the results of this study show that systemic administration of antibiotics reduces postoperative salivary bacterial counts in infants undergoing cardiac surgery, and oral care with PV-I can further reduce bacterial counts.

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https://doi.org/10.1016/j.jds.2024.07.035

Introduction

Approximately 1 in 100 newborns are born with congenital heart diseases such as ventricular septal defects, atrial septal defects, or patent ductus arteriosus.[1] Some diseases resolve spontaneously, but many require surgery during infancy. Surgical site infection occurs in pediatric cardiovascular surgery at a rate of 1.7—8.0%.[2] Regarding postoperative pneumonia, Ja'como et al. reported ventilator-associated pneumonia (VAP) in 16.9% of infants who underwent cardiac surgery,[3] whereas Roeleveld et al. reported that VAP occurred in 14.4% of infants who were intubated for >24 h.[4]

Postoperative pneumonia is known to be caused by the aspiration of oropharyngeal fluid containing pathogenic microorganisms in the lower respiratory tract of immunocompromised individuals. However, studies on the perioperative bacterial counts in the oropharyngeal fluid of pediatric patients undergoing cardiac surgery are lacking. This study therefore aimed to determine the salivary bacterial count of infants undergoing cardiac surgery before and after surgery, and to compare the effects of oral care with water, benzethonium chloride mouthwash, and povidone-iodine mouthwash on the salivary bacterial count. Although it is necessary to identify the pathogenic microorganisms of postoperative pneumonia after cardiac surgery in children and to examine the perioperative changes in the species of these organisms, we decided to examine the perioperative changes in total bacterial counts and the suppression effect of mouthwash solution without identifying the organisms in this preliminary study.

Materials and methods

Study design

This was a randomized, open-label, phase II study, which complied with the requirements of the 2010 Consolidated Standards for Reporting Trials Statement. The study was conducted from July 2022 and December 2023 and in a single-center setting. The study protocol was approved by the Ethics Review Committee of our institution (approval number: 21—40) and registered in the University Hospital Medical Information Network Center (UMIN-CTR Unique Trial Number: UMIN000047838). All study participants provided written informed consent. After explaining the study, written informed consent was obtained from the parents.

Participants

The inclusion criteria were as follows: (1) From one week old to under 20 years old, (2) infants undergoing thoracotomy for congenital heart disease, (3) visited the Pediatric Dentistry Department for a preoperative oral examination.

The exclusion criteria were as follows: (1) could not obtain parental consent, (2) allergies occur with povidone-iodine gargles or Benzethonium chloride gargles, (3) the surgery was cancelled, (4) patients whose doctor or dentist has determined that oral care intervention is not possible.

Intervention

The patients were randomly assigned to the following three groups: water (WA), benzethonium chloride (BZ), and povidone-iodine (PV—I). Using a computer-generated random sequence, the participants were randomly assigned to three groups in a 1:1:1 ratio.

Before the surgery, the oral cavity was wiped with a sponge brush moistened with water, and any ruptured teeth were brushed with a toothbrush. On the postoperative day, oral care was provided according to the assigned group.

Patients in the water group (WA group) were treated with a sponge brush moistened with water to clean their oral cavities. Patients in the benzethonium chloride mouthwash group (BZ group) were treated with 0.2% Neostelin Green Gargle (Nippon Dental Chemical, Shimonoseki, Yamaguchi, Japan), in which the main ingredient was benzethonium chloride. A sponge brush moistened with a 0.02% solution was used to wipe the oral cavity. Patients in the povidone-iodine mouthwash group (PV—I group) were treated with 7% Isodine® Gargle Solution (Mundipharma K.K., Tokyo, Japan), mainly composed of povidone-iodine. The oral cavity was wiped with a sponge brush moistened with a 0.47% solution. The dose of antiseptic gargles used for oral care was determined according to the manufacturer's recommendations.

Outcomes

The following outcomes were assessed pre-operatively: Information regarding sex, age, body mass index (BMI), albumin (Alb), number of erupted teeth, the number of bacteria in saliva before and after oral care performed before surgery.

The following outcomes were assessed before and after the oral care intervention: operative time, blood loss, and number of days prophylactic antibiotics were administered, the number of bacteria in saliva before and after oral care after surgery.

Sample size

From our previous study on intubated infants, we assumed that the logarithm of the number of oral bacteria before

and after oral care would decrease from 5.0 to 3.7 (standard deviation 2.4), with an alpha error of 0.2 and a power of 0.8, resulting in a sample size of 31 patients in each group. We collected 35 cases per group to account for patient dropouts.

Randomization and blinding

In this single-blind study, the assessors were blinded. The study participants were randomly assigned using a stratified block method with that whether teeth have erupted or not; as stratification factors by individuals who were not the assessors.

Sample collection and bacterial culture

Saliva samples were collected preoperatively, the day after surgery, and before and after oral care. For collection, the swab tip was inserted under the tongue using a Transwab ENT (Medical Wire & Equipment Co. Ltd., London, UK) and held for 5 s to allow saliva to enter the swab tip for collection. The tip of the swab was then suspended in 200 μL of saline for 20 s, and the suspended saline was used for culture. Poremedia BHI agar (Eiken Chemical Co., Ltd., Tokyo, Japan) was used as the culture medium. The number of colonies on the medium was counted after 48 h of aerobic incubation at 37 °C.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics (version 23.0; IBM, Tokyo, Japan). For differences in background factors among the three groups, continuous variables were analyzed using a one-way analysis of variance (ANOVA), and categorical data were analyzed using the Kruskal—Wallis test. The number of colonies before and after oral care or surgery was analyzed using paired t-tests.

Results

Patients

Of the 105 patients enrolled in this study, two were excluded because of surgical termination and 1 for withdrawing consent, meaning 102 patients were included in the final analysis (Fig. 1). The study cohort comprised 57 males, and 45 females, with ages ranging from 1 to 81 years (mean, 20.4) months. All patients underwent open chest surgery for congenital heart disease, with a mean operative time of 380 min and mean blood loss of 108 g. Antibiotics were commenced immediately before surgery and were administered for a mean of 4.05 days (Table 1).

Preoperative salivary bacterial counts and the effects of oral care

The preoperative salivary bacterial colony counts ranged from $10^{1.64}$ to $10^{6.66}$ (mean, $10^{4.53}$). The number of colonies after oral care with water and sponge brushes ranged from $10^{1.84}$ to $10^{6.36}$ (mean, $10^{4.44}$). Overall, the difference in bacterial counts before and after oral care was not significant ($P = 0.207$). The logarithm of colony count before oral care was 100%, and the colony count logarithm after oral care was 100.4 ± 1.91%, showing no significant difference (Fig. 2) ($P = 0.848$).

Postoperative salivary bacterial count

The number of bacterial colonies in saliva samples obtained after postoperative systemic administration of antibiotics was $10^{3.76}$, a significant decrease compared with preoperative levels ($P < 0.001$). The logarithm of the preoperative colony count was 100%, and the postoperative count was 88.1 ± 4.46%, showing a significant decrease (Fig. 3) ($P = 0.009$).

Effects of postoperative oral care

The background factors of the WA, BZ, and PV-I groups were not significantly different (Table 2). The mean numbers of colonies were $10^{3.73}$ before oral care and $10^{3.42}$ after oral care in the WA group, $10^{3.73}$ before oral care and $10^{3.35}$ after oral care in the BZ group, and $10^{3.83}$ before oral care and $10^{3.26}$ after oral care in the PV-I group. The values were lower after oral care in all patients. Considering the colony count logarithm before oral care to be 100%, the colony counts after oral care were 94.3% ($P = 0.225$), 92.4% ($P = 0.142$), and 84.7% ($P < 0.001$) in the WA, BZ, and PV-I groups, respectively. The WA and BZ groups did not differ significantly; however, the PV-I group showed significantly lower values than before oral care (Fig. 4).

Discussion

This study revealed that the salivary bacterial count decreased after cardiac surgery in infants because of the perioperative administration of systemic antibiotics. Postoperative oral care with iodine gauze further reduced the bacterial count, while oral care with benzethonium mouthwash or water did not significantly decrease the bacterial count.

Postoperative infectious complications, such as surgical site infection and postoperative pneumonia, may occur during highly invasive surgeries, such as cancer and cardiac and organ transplant surgeries.[2–4] Various preventive measures have been proposed for surgical site infections;[5] however, no effective preventive measures against postoperative pneumonia have yet been established. The risk of postoperative pneumonia is increased by the presence of hypopharyngeal fluid containing pathogenic microorganisms of oral, nasal, or gastrointestinal origin; aspiration into the airways; and systemic immune compromise. Oral care is a simple, low-cost, and preventive method to reduce the number of oral pathogenic microorganisms entering the airways. In adults, the frequency of postoperative pneumonia reportedly decreases when oral care is provided during surgery for esophageal,[6–9] lung,[10] gastric,[9] and colorectal cancers,[9] as shown in past observational studies.

Pediatric cardiac surgery is a highly invasive procedure, and postoperative complications such as surgical site infections and postoperative pneumonia are common.[2–4]

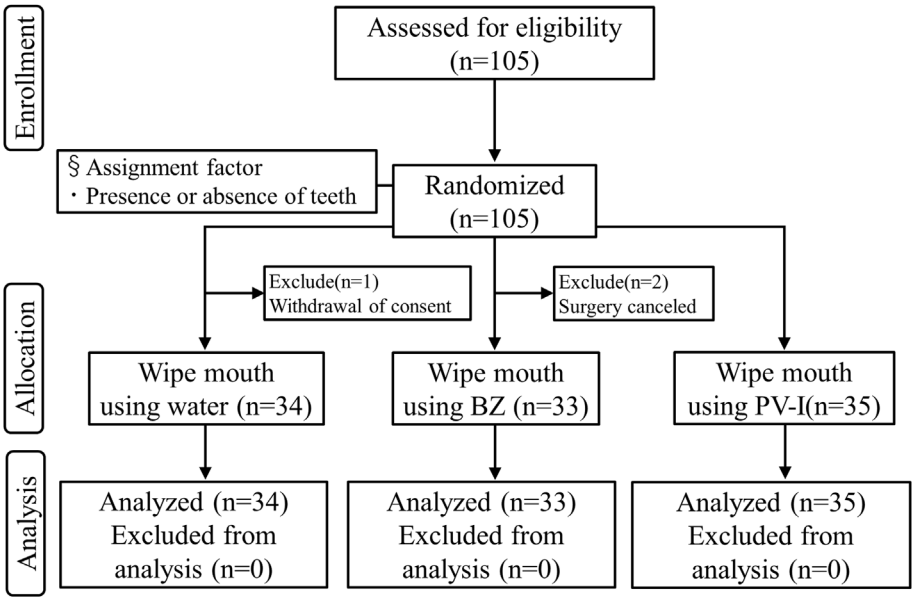

Figure 1 Consort flow diagram. Finally, 102 patients (34 water group, 33 benzethonium group, and 35 povidone-iodine group) were enrolled in the study.

Table 1 Characteristics of participants.

Variable	Number of patients/Minimum - maximum (mean)
Sex	
male	57
female	45
Age (months)	1-81 (20.4)
BMI	12.0–18.8 (15.4)
Number of teeth	0-24 (7.39)
Albumin (g/dL)	3.70–5.50 (4.53)
Operation time (minute)	41-1013 (380)
Blood loss (gram)	0-2169 (108)
Antibiotics administration period (day)	1-14 (4.05)

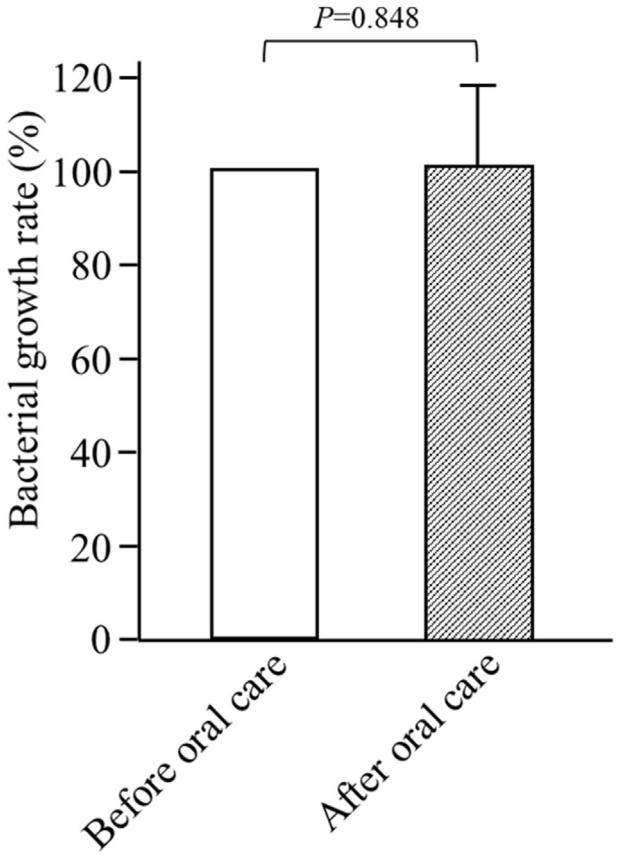

Figure 2 Presurgical salivary bacterial colony counts before and after oral care. There was no significant difference between counts before oral care and those after oral care.

Various studies have been conducted on oral bacteria in children with dental diseases such as dental caries. However, to the best of our knowledge, studies on oral bacteria in the perioperative period in children undergoing cardiac surgery are scarce.

In the present study, we found that salivary bacterial counts were significantly lower on the day after surgery than they were preoperatively. In adult cancer surgery, salivary bacterial counts increase postoperatively compared to preoperatively despite systemic antibiotic use, and the rate of increase was distinctly high in patients undergoing postsurgical surgery.[11] We believe that the reason for the difference in salivary bacterial counts before and after surgery between children and adults is that children have few or no teeth or periodontal pockets; thus, their oral bacterial flora and bacterial counts are markedly different from those of adults. However, the present study did not examine bacterial species; therefore, it is unclear whether systemic antibiotic administration reduced the total bacterial count, without reducing pathogenic bacteria, thereby reducing the risk of postoperative pneumonia. In addition to systemic antimicrobial therapy, oral care

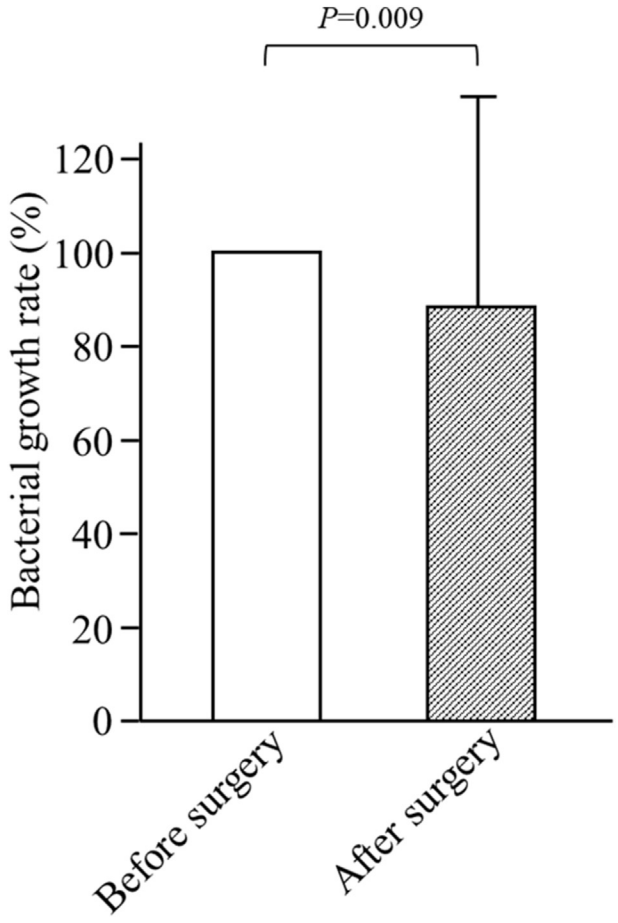

Figure 3 Salivary bacterial counts before and after surgery. A significant reduction of bacterial counts was found after surgery.

should be provided to reduce the pathogenic microorganism count in the oropharyngeal fluid, because postoperative pneumonia occurs frequently after pediatric cardiac surgery.

In Japan, perioperative oral care for cancer and cardiac and organ transplant surgeries has been covered by public insurance since 2012, and many hospitals have implemented this insurance-based care. However, the type of oral care that reduces the risk of postoperative infectious complications remains unclear. Although dental plaque and calculus removal and professional mechanical tooth cleaning (PMTC) are widely used to prevent dental caries and periodontal disease, these oral care methods do not reduce salivary bacterial counts. Tooth brushing diffuses bacteria adhering to the teeth into the oral cavity, temporarily increasing the salivary bacterial count; therefore, mouthwash is essential.[12] In patients who cannot use mouthwash, brushing should be avoided, and oral care, such as mouthwash and suctioning, should be provided.

In this study, we examined whether the use of antiseptic gargles was more effective for oral care than wiping or suctioning the mouth with a sponge brush or wet wipes. The results showed that although wiping with water or benzethonium chloride gargle did not significantly inhibit salivary bacteria, povidone-iodine gargle significantly reduced the salivary bacterial count. Oral care with 0.12% chlorhexidine has previously been recommended to prevent pneumonia in intubated patients;[13] however, in Japan, the use of this drug on mucous membranes is contraindicated because of reported cases of anaphylaxis. By identifying the target organisms of postoperative pneumonia, I think we can effectively promote the implementation of oral care. Although this study did not identify the bacteria that cause pneumonia, povidone-iodine reduces all oral bacteria, both pathogenic and non-pathogenic, and it may be effective in preventing pneumonia. Because this study demonstrated the efficacy of oral care using a povidone-iodine gargle solution, we aimed to increase the number of cases, examine the bacterial flora, and investigate whether oral care using a povidone-iodine gargle can reduce the incidence of postoperative pneumonia in children undergoing cardiac surgery.

This study had several limitations. First, although randomized, the number of participants was small, and unknown biases may exist among the groups; therefore, the

Table 2 Patient characteristics of 3 groups.

Variable	Number of participants/mean ± SD			*p*-value
	WA group	BZ group	PV-I group	
Sex				
male	19	13	17	1.000[a]
female	15	20	18	
Age (months)	17.79 ± 18.75	20.03 ± 20.50	23.17 ± 24.17	0.937[a]
BMI	15.44 ± 1.69	15.36 ± 1.41	15.45 ± 1.32	0.960[b]
Number of teeth	6.18 ± 8.15	8.42 ± 9.07	7.60 ± 8.77	0.550[a]
Albumin (g/dL)	4.56 ± 0.32	4.50 ± 0.34	4.52 ± 0.36	0.905[a]
Operation time (minute)	383.62 ± 144.40	375.82 ± 175.49	381.57 ± 132.11	0.487[a]
Blood loss (gram)	73.79 ± 95.76	91.91 ± 175.468	157.14 ± 383.93	0.485[a]
Antibiotics administration period (day)	3.76 ± 0.96	4.33 ± 2.61	4.06 ± 0.94	0.250[a]

WA group:Groups that used water for oral care.
BZ group: Groups that used benzethonium chloride containing mouthwashes.
PV-I group: Groups that used povidone-iodine containing mouthwashes.
[a] Kruskal—Wallis test.
[b] One-way ANOVA.

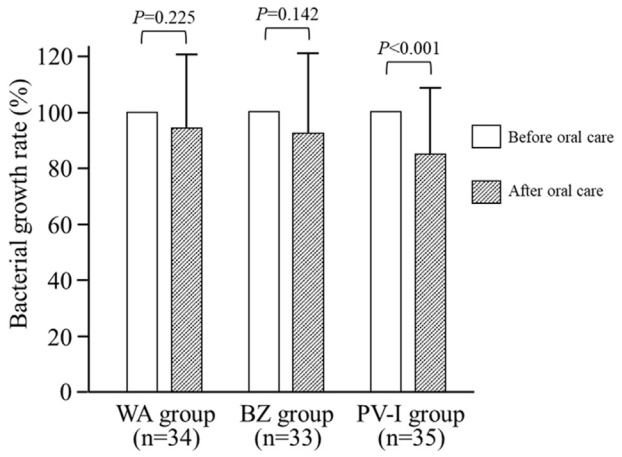

Figure 4 Effects of oral care in the WA, BZ, and PV-I groups. The PV-I group showed significantly lower bacterial counts after oral care. WA group: Groups that used water for oral care. BZ group: Groups that used benzethonium chloride containing mouthwashes. PV-I group: Groups that used povidone-iodine containing mouthwashes.

results obtained cannot be generalized. Second, because the study was conducted using a bacterial culture method, the changes in each bacterial species were unknown, and the organisms responsible for postoperative pneumonia were not identified. However, only a few studies have examined changes in salivary bacterial counts during pediatric cardiac surgery; hence, we believe that this study is highly significant. A future study could be designed and discussed to improve the disadvantages of this study.

Overall, in this study, the bacterial counts in the saliva of 102 pediatric cardiac surgery patients were investigated. The results showed that the bacterial colony count decreased postoperatively compared to preoperatively, probably because of the systemic administration of antibiotics. Furthermore, while wiping with water or benzethonium chloride gargles did not significantly reduce the salivary bacterial count, oral care with povidone-iodine gargles significantly inhibited the salivary bacteria.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

Acknowledgements

This study was supported by J Grants-in-Aid for Scientific Research Grant Number JP 21K10260.

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