Effect of 0.12% Chlorhexidine Oral Rinse on Preventing Hospital-Acquired Pneumonia in Nonventilator Inpatients

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ABSTRACT

Background: Nonventilator hospital-associated pneumonia (NV-HAP) is a nosocomial infection with a multifactorial etiology that is particularly prevalent in individuals with poor oral health.

Purpose: This study was designed to determine the effect of a 0.12% chlorhexidine gluconate oral rinse intervention on oral health and on reducing NV-HAP in inpatients.

Methods: A randomized, double-blind, and triple-arm clinical trial was conducted on a sample of 103 patients aged ≥50 years. Using the blocking sample method, patients were randomly assigned into three groups. These included Group A, using an oral rinse solution of 0.12% chlorhexidine; Group B, using Listerine; and Group C, using a standard saline oral rinse. In addition to routine hospital-associated pneumonia preventative nursing care, the participants used the oral rinse solutions twice a day with a period of at least 9 hours between each use. Oral health, the degree of bacterial exposure, and the clinical pneumonia index scale were evaluated in each of the groups at baseline (first day), on Intervention Days 3 and 7, and at discharge. The clearance rate was calculated by dividing the number of bacteria cleared by the total frequency of oral bacteria in the collected culture × 100%.

Results: Each arm of the study was composed of 34–35 participants, with an average hospitalization duration of 7.5 days. There was no incidence of NV-HAP or any changes in clinical pulmonary infection score among the three groups. Group A achieved a more significant improvement in oral health assessment tool scores between baseline and discharge than either Group B or C (p = .03), particularly in the tongue, gums, and tissues; saliva; and oral cleanliness subscales. In addition, Group A reported higher clearance rates for Staphylococcus (100.00% vs. 66.67% vs. 66.67%, respectively), Escherichia coli (100.00% vs. 60.00% vs. 66.67%, respectively), and Pseudomonas aeruginosa (75.00% vs. 46.30% vs. 25.00%, respectively) than Groups B and C.

Conclusions/Implications for Practice: Although the results do not provide evidence supporting the use of a 0.12% chlorhexidine oral rinse as better in terms of preventing NV-HAP in middle-aged and elderly inpatients, nursing supervision was found to have an overall positive effect on oral health. The use of oral rinse with 0.12% chlorhexidine for nonventilated patients with poor oral health may be recommended.

KEY WORDS:
oral rinse, chlorhexidine, nonventilator hospital-associated pneumonia, pneumonia-associated bacteria.

Introduction

Nonventilator hospital-acquired pneumonia (NV-HAP), a type of hospital-acquired pneumonia (HAP), is strongly associated with longer hospital stays and increases mortality rates among affected patients (Giuliano et al., 2018). A large veteran-based database in the United States found an incidence of NV-HAP in veteran admission acute care settings between 2016 and 2020, with a rate of 1.26 cases per 1,000 patient-days (Carey et al., 2022). Fortunately, NV-HAP may be prevented through the application of basic oral care

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Older adults are at a particularly high risk of developing neurological-disorder-related pneumonia that results in changes to the oral milieu, with symptoms including swallowing abnormalities and decreased salivary production, among others (Palmer et al., 2001). Arnold et al. (2020) conducted a population-based cohort study to observe 102,264 older adults over 2 years. The results showed that 4.7% older adults were hospitalized for community-acquired pneumonia. The incidence of community-acquired pneumonia was 1,786 per 100,000 population among patients aged 65–84 years and 3,948 per 100,000 population among those aged 85 years or older (Arnold et al., 2020). Recently, Ewan et al. (2017) suggested that preventative strategies such as swallowing assessments and improvements to oral hygiene should be considered to prevent HAP (Ewan et al., 2017).

Chlorhexidine (CHX) is a broad-spectrum cationic biocide that is effective against both gram-positive and gram-negative bacteria (Block, 2001). Previous studies have reported that using CHX reduces the incidence of ventilator-associated pneumonia (VAP) significantly (Kes et al., 2021; Rabello et al., 2018; Veitz-Keenan & Ferraiolo, 2017). A systematic review conducted by Rabello et al. (2018) concluded that oral hygiene care with CHX, ranging from CHX concentrations of 0.05% to 0.20%, has a protective effect against HAP and VAP. In addition, 0.12% CHX is the most common concentration of CHX currently used in oral hygiene care. However, the evidence in the literature regarding the effect of CHX on NV-HAP prevention is limited and inconsistent. Hollaar et al. (2017) conducted a multicenter study covering 17 nursing homes to examine the effectiveness in preventing NV-HAP of an oral hygiene care intervention using 0.05% CHX, finding no significant reduction in infection rate. Similar results were reported by Deschepper et al. (2018), who observed 82,274 inpatients in a single hospital over 3 years. These results indicate that oral hygiene interventions using CHX do not reduce risk of mortality and that interventions using CHX with a cumulative dose of less than 300 mg may significantly increase the risk of death by 2.61-fold (Deschepper et al., 2018). An abstract in a European respiratory journal by Ogbac and Arquiza (2018) summarized their experience conducting a randomized open-labeled parallel study in the Philippines among 160 patients without ventilator use. Their results showed the benefit of oral CHX not only in preventing NV-HAP but also in shortening hospital stays compared with oral hygiene without CHX, particularly in patients with malignancy, chronic obstructive pulmonary disease, and bronchial asthma (Ogbac & Arquiza, 2018).

In this study, a randomized triple-arm trial was conducted to investigate the effect of oral CHX on reducing the risk of contracting NV-HAP in middle-aged and older adults during hospitalization.

Methods

Study Design

This study was a double-blind, randomized, placebo-controlled trial conducted between May and December 2020. The participants were allocated randomly to one of three groups using a blocking sample method, with each group receiving a different intervention. One researcher generated the random allocation sequence, the leaders in the medical wards enrolled participants, and another researcher assigned participants to the interventions. This study was registered in the U.S. Registry of Clinical Trials on May 21, 2020, with IRCT ID NCT04403971. The study protocol was approved by the institutional review board of National Cheng Kung University Hospital (NCKUH No. A-ER-108-397). After institutional ethics board clearance, participants were blinded to their received treatment and subjected to a standardized study protocol. Pneumonia-associated oral bacteria counts and hospital-acquired infection status were assessed 4 times during the study: at admission (baseline), on the third and seventh day of hospitalization, and at discharge. In this study, the patients and the investigator of the outcomes were blinded.

Sample and Sampling

This study was conducted on patients attending a general medicine ward in southern Taiwan. The inclusion criteria were as follows: patients who were admitted to a general ward, aged 50 years or older, and able to rinse orally and communicate. The exclusion criteria were as follows: admission for routine examination or quick screening (e.g., for cardiac catheterization, unconsciousness, acute psychiatric syndromes, CHX allergy). The required sample size was determined using statistical software G*Power 3.1.9.2. The current evidence regarding the effect of oral hygiene care with 0.12% CHX on HAP among nonventilated patients is inconsistent. Although a prospective randomized controlled trial conducted by Ogbac and Arquiza (2018) found that using 0.12% oral CHX in nonintubated patients reduced the risk of developing HAP twofold in the intervention group compared with the control group (6.25% vs. 12.5%), the effect size was found to be small (0.25). On the basis of a repeated measurement method using effect size = 0.25, α = .05, and power = 0.85, a sample size sufficient to assign at least 30 participants to each arm of this study was needed for this study.

Intervention

Participants were divided randomly into three groups. Group A was given a 0.12% CHX solution (Aseptic Innovative Medicine Co., Ltd., Taipei, Taiwan), Group B received a Listerine-based oral rinse solution (without CHX), and Group C received oral rinse with normal saline (control/placebo; Figure 1). The participants were observed until hospital discharge or to the onset of nosocomial infection.
Outcome Measures

**Nonventilator hospital-acquired pneumonia**

NV-HAP was diagnosed in patients who were not on ventilators and contracted a pulmonary parenchymal acute infection > 48 hours after hospital admission. Pulmonary parenchymal infection was defined as a new or progressive infiltration on the chest x-ray with at least two of the following conditions: fever, increased white blood cell count, and purulent sputum (Chou et al., 2019). The clinical pulmonary infection scale (CPIS) results of the participants were also collected. CPIS is measured using six indicators, including temperature, white blood cells, sputum, oxygenation, and chest x-ray, and is used to evaluate HAP severity. Each indicator is scaled from 0 (normal) to 3 (abnormal) points, with a total score of 6 or higher indicating pneumonia. The sensitivity and specificity of the CPIS have been previously assessed as 93% and 100%, respectively (Pugin, 2002).

**Pneumonia-associated oral bacteria**

On the days when data were collected, all of the patients were instructed to rinse 20-ml normal saline according to a standard protocol, which was rinse up, rinse down, rinse left, and rinse right at least twice in each direction for 30 seconds. The participants were then instructed to spit the rinse solution into a sterilized collection box. The samples were cultured for 2 hours, and bacterial colonies were quantified (colony-forming unit per milliliter [CFU/ml]). To observe the variation because of the different rinse solutions, the number of bacteria was determined again after the intervention. Degree of bacterial clearance was assessed based on comparison with the baseline.

**Oral health assessment tool**

The oral health assessment tool (OHAT) is widely recommended as an aid to the clinical judgment of healthcare providers and in the diagnosis of poor oral health. OHAT may be used with different patient groups, including with older patients who are unable to reliably self-report and require a clinical assessment. OHAT incorporates the eight subscales of lips, tongues, gums and tissues, saliva, natural teeth, dentures, oral cleanliness, and dental pain, all of which are scored using a Likert scale (0 = health, 1 = oral changes, or 2 = unhealthy). The intraclass correlation coefficient for
the OHAT total score has been reported as .78 (Chalmers et al., 2005).

**Demographic data**
The demographic information collected in this study included age, gender, educational level, consciousness, cause of hospitalization, intensive care unit (ICU) history, hospital days, comorbidities (i.e., dementia, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, heart failure, cerebral vascular disease, cancer, liver cirrhosis, and chronic renal failure), types of antibiotic used, and caregiver information.

**Study Procedure**
After approval of the proposal, all of the hospitalized patients in the general ward who met the inclusion criteria were randomly assigned to three groups. Before the oral rinse intervention, patients’ demographic data, oral health scores, CPIS scores, and oral bacteria were collected and used to calculate baseline values. Oral bacteria were collected in the early morning after the participants awoke and before they had eaten. Oral rinse solutions were placed in standard, cloudy containers for all three groups. The solutions were administered twice a day (at 9:00 a.m. and 6:00 p.m.) by nurses. The participants rinsed for 30–60 seconds with 10 ml of one of the three types of oral rinse solutions and were required to fast for 30 minutes afterward.

**Data Analysis**
Chi-square tests (for dichotomous variables) and one-way analysis of variance (ANOVA; for continuous variables) were used to compare the variances in the demographic data. The differences in the changes in oral health and clinical pulmonary infection between admission and discharge among the three groups were compared using one-way ANOVA with a post hoc test. Paired t tests were used to assess the changes on the eight subscales of oral health between admission and discharge. The differences in the clearance rate of pneumonia-associated oral bacteria among the three groups were compared using one-way ANOVA, as applicable. Baseline bacteria and the oral bacteria results were compared at each time point. For example, one participant’s oral bacteria results showed at baseline to be > 10,000 CFU/ml, with negative results for *Staphylococcus* at all three subsequent time points. Therefore, this participant had successfully cleared *Staphylococcus* across the three time points in comparison with the baseline. The clearance rate was calculated by the sum of successful clearance divided by the total frequency of oral bacteria culture collected multiplied by 100%. In the above example, the clearance rate of *Staphylococcus* was 100%. A p value < .05 was defined as statistically significant in a two-tailed test. Intention-to-treat analysis was used in this study to prevent attrition bias. The analyses were conducted using SPSS v.22.2 (IBM Corp., Armonk, NY, USA).

**Results**

**Demographic Data**
The 103 participants were assigned randomly into three groups, with 35 in Group A, 34 in Group B, and 34 in Group C (Figure 1). Randomization ensured that the baseline characteristics of the three groups were comparable in terms of average days of hospitalization, age, gender, level of education, ICU history, number of comorbidities, and caregiver status. The major diagnoses among the participants were infectious diseases (44.1%) such as fever, cellulitis, and pneumonia, followed by gastrointestinal diseases (32.4%; Table 1).

The mean age at enrollment was 65.9 ± 11.8 years, and the average length of hospital stay was 7.5 ± 5.0 days. Over half (59.2%) of the participants were male, and 76.7% had less than a junior high school education. The sample had an average of 1.6 comorbidities (Table 1).

**Nosocomial Infection**
No cases of NV-HAP were observed during the study period, and no significant differences were observed in CPIS scores among the three groups (Table 2).

**Oral Health**
Analyses of the changes in the oral health of the three groups using one-way ANOVA showed an obvious improvement in OHAT in all three between admission and discharge (−1.20 in Group A, −0.75 in Group B, and 0.25 in Group C). The variance of oral health had improved significantly more in Group A than Group C (p = .03). However, in terms of CPIS scores, no significant differences were found among the three groups (Table 2).

**The Differences in the Eight Subscales of Oral Health Among the Three Groups**
On the basis of the eight subscales of oral health, Group A had achieved significantly improved scores for the tongue (p < .01), gums and tissues (p = .03), saliva (p < .01), and oral cleanliness (p < .01) subscales between admission and discharge. In addition, oral health had increased significantly for the lips (p = .04) and oral cleanliness (p < .01) subscales in Group B. However, Group C did not record any improvement in oral health (Table 3).

**Differences in the Clearance Rates of Pneumonia-Associated Bacteria Among the Three Groups**
No significant differences in the clearance rates of microbes, including unidentified gram-negative bacteria, gram-positive cocci, enterobacteria, aquatic bacteria, or others, were found among the three groups. A detailed examination of each microbe type found a higher average clearance rate in Group A (0.12% CHX oral rinse) of pneumonia-associated bacteria.
such as *Staphylococcus aureus* (75.0%), *E. coli* (100%), and *P. aeruginosa* (75.0%) than in Groups B and C (Table 4).

**Side Effects**

No side effects of the interventions were detected in this study. A few patients who smoked or had been treated with chemotherapy described uncomfortable conditions, specifically mild irritation of the mucosa and an unpleasant taste. Symptoms were minimal and disappeared after suspending use of the oral rinse solutions.

**Discussion**

Oral hygiene practices that include the use of CHX in ICU patients have been a standard prophylaxis for the prevention

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**Table 1**

Demographic Data of Participants ($N = 103$)

| Variable                                | Overall | Group A ($n = 35$) | Group B ($n = 34$) | Group C ($n = 34$) | $p$  |
|-----------------------------------------|---------|-------------------|-------------------|-------------------|------|
|                                        | $n$ | %     | $n$ | %     | $n$ | %     | $n$ | %     |
| Average hospitalized days (mean and SD) | 7.5 | 5.0   | 6.6 | 4.4   | 7.6 | 5.0   | 8.3 | 5.7   | .38  |
| Age (years; mean and SD)                | 65.9 | 11.8  | 66.7 | 13.5  | 65.0 | 9.4   | 66.2 | 12.3  | .83  |
| Gender                                  | .39    |
| Male                                    | 61    | 59.2  | 23   | 65.7  | 21  | 61.8  | 17  | 50.0  |      |
| Female                                  | 42    | 40.8  | 12   | 34.3  | 13  | 38.2  | 17  | 50.0  |      |
| Major diagnoses of admission            | .56    |
| Gastroenterological diseases            | 33    | 32.4  | 8    | 22.9  | 14  | 42.4  | 11  | 32.4  |      |
| Infectious diseases                     | 45    | 44.1  | 18   | 51.4  | 10  | 30.3  | 17  | 50.0  |      |
| Renal diseases                          | 16    | 19.6  | 7    | 20.0  | 8   | 24.2  | 5   | 14.7  |      |
| Cardiovascular disease                  | 3     | 2.9   | 1    | 2.9   | 1   | 3.0   | 1   | 2.9   |      |
| Fracture                                | 1     | 1.0   | 1    | 2.9   | 0   | 0.0   | 0   | 0.0   |      |
| Level of education                      | .36    |
| Less than junior high school            | 77    | 76.7  | 27   | 77.1  | 27  | 79.4  | 25  | 73.5  |      |
| Less than college                       | 18    | 17.5  | 4    | 11.4  | 6   | 17.6  | 8   | 23.5  |      |
| Master’s degree or above                | 6     | 5.8   | 4    | 11.4  | 1   | 2.9   | 1   | 2.9   |      |
| Intensive care unit history             | 20    | 19.4  | 8    | 22.9  | 7   | 20.6  | 5   | 14.7  | .68  |
| Number of comorbidities                 | .16    |
| Mean and SD                             | 1.6   | 1.2   | 1.7  | 1.2   | 1.4 | 1.0   | 1.9 | 1.3   |      |
| Range                                   | 0–5   | 0–4   | 0–3  | 0–5   |      |      |      |      |
| Main caregiver                          | .11    |
| None                                    | 9     | 8.7   | 1    | 2.9   | 6   | 17.7  | 2   | 5.9   |      |
| Family                                  | 84    | 81.6  | 30   | 85.7  | 27  | 79.4  | 27  | 79.4  |      |
| Assistance                              | 10    | 9.7   | 4    | 11.8  | 1   | 2.9   | 5   | 14.7  |      |

Note. Group A = chlorhexidine; Group B = oral solution without chlorhexidine; Group C = normal saline.

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**Table 2**

The Effect of 0.12% Chlorhexidine Oral Rinse on Oral Health and Clinical Pulmonary Infection Scores

| Variable                                | Group A (CHX) ($n = 35, 34.0\%$) | Group B (Without CHX) ($n = 34, 33.0\%$) | Group C (N/S) ($n = 34, 33.0\%$) | $p$/Post Hoc |
|-----------------------------------------|----------------------------------|------------------------------------------|----------------------------------|--------------|
|                                        | Admission | Discharge | Changes | Admission | Discharge | Changes | Admission | Discharge | Changes | Admission | Discharge | Changes | $p$/Post Hoc |
| OHAT score (mean and SD)                | 3.67      | 2.46      | 2.39    | 1.73      | −1.20     | 3.29      | 1.62      | 2.61      | 1.73      | −0.71     | 2.91      | 1.23      | 2.66      | 1.75      | −0.25     | .03         |
| CPIS score (mean and SD)                | 0.77      | 0.77      | 0.51    | 0.78      | −0.26     | 1.00      | 1.04      | 0.82      | 1.00      | −0.18     | 1.21      | 1.12      | 0.74      | 1.11      | −0.47     | .45         |

Note. Bold font indicates statistical significance. CHX = chlorhexidine; N/S = normal saline; OHAT = oral health assessment tool; CPIS = clinical pulmonary infection score.
of VAP (Rabello et al., 2018). However, the preventive effect of oral CHX on NV-HAP in middle-aged and elderly inpatients has not yet been determined. This randomized, double-blind study was the first to evaluate the effect of oral rinsing with CHX on reducing the risk of contracting HAP in Asia. In this study, it was difficult to determine the effect of 0.12% CHX on NV-HAP risk, as no cases of NV-HAP were diagnosed during the study period. Although the findings show that a 0.12% CHX oral rinse seems to have a slight effect on enhancing the clearance rate of pneumonia-associated bacteria such as S. aureus, E. coli, and P. aeruginosa in nonventilated middle-aged and elderly inpatients, this effect was not significant. The results of this study are consistent with those of Hollaar et al. (2017) and Deschepper et al. (2018). In addition, the findings are similar to previous randomized, double-blind trial studies conducted by Scannapieco et al., with the results further confirming the mechanism of using a 0.12% CHX oral rinse to decrease the concentration of respiratory pathogens such as S. aureus (Scannapieco et al., 2009). However, the findings of this study are at odds with a randomized, open-label study conducted in the Philippines (Ogbac & Arquiza, 2018). However, further exploring the differences is difficult, as the Philippine study is available in abstract form only. However, our findings could not further determine the benefit of oral rinsing with 0.12% CHX on the prevention of NV-HAP because of the lack of cases of HAP. Nevertheless, oral rinsing with CHX likely promotes the prevention of NV-HAP in inpatients based on its observed reduction effect on oral pneumonia-associated bacteria. Oral rinsing is a patient-friendly, minimally invasive way to maintain good periodontal health and proactively control the inflammatory cycle. This study found favorable results regarding the use of oral rinse solutions, regardless of whether that rinse was CHX or Listerine, in improving oral health compared with the control group. The effects were particularly notable in terms of lips and oral cleanliness. This finding is consistent with previous studies (Brookes et al., 2020; James et al., 2017). A narrative review showed adjunctive, short-term use of CHX to be effective in managing gingivitis and dry socket and in reducing anaerobic bacteria counts (Brookes et al., 2020). James and colleagues’ systematic review found using CHX mouth rinse to be effective in reducing gingivitis

| Variable/OHAT Score         | Group A (CHX) (n = 35) | Group B (Listerine) (n = 34) | Group C (N/S) (n = 34) |
|-----------------------------|------------------------|------------------------------|------------------------|
|                             | M          | SD     | p       | M       | SD   | p       | M       | SD  | p       |
| Lips                        |            |        |         |            |       |         |            |       |         |
| Admission                   | 0.16       | 0.37  | .49     | 0.21     | 0.42 | .04     | 0.06     | 0.25 | .42     |
| Discharge                   | 0.10       | 0.30  |         | 0.07     | 0.26 |         | 0.13     | 0.34 |         |
| Tongue                      | < .01      |        |         | 0.50     | 0.58 |         | 0.56     | 0.51 |         |
| Admission                   | 0.13       | 0.34  |         | 0.46     | 0.58 |         | 0.50     | 0.62 |         |
| Gums and tissues            | .03        |        |         | 0.14     | 0.36 |         | 0.09     | 0.30 |         |
| Discharge                   | 0.03       | 0.18  |         | 0.07     | 0.26 |         | 0.06     | 0.25 |         |
| Saliva                      | < .01      |        |         | 0.48     | 0.63 |         | 0.39     | 0.57 | .48     |
| Admission                   | 0.13       | 0.34  |         | 0.39     | 0.60 |         | 0.29     | 0.60 |         |
| Natural teeth               | .75        |        |         | 0.94     | 0.85 |         | 0.79     | 0.88 | .91     |
| Dentures                    | .33        |        |         | 0.97     | 0.84 |         | 0.79     | 0.88 | .88     |
| Oral cleanliness            | < .01      |        |         | 0.19     | 0.60 |         | 0.29     | 0.71 | .13     |
| Natural teeth               | < .01      |        |         | 0.23     | 0.62 |         | 0.21     | 0.63 | .13     |
| Dental pain                 | .57        |        |         | 1.13     | 0.76 |         | 0.96     | 0.79 | .81     |
| Oral cleanliness            | < .01      |        |         | 0.77     | 0.72 |         | 0.61     | 0.69 | .59     |
| Natural teeth               | .16        |        |         | 0.06     | 0.25 |         | 0.04     | 0.19 | .03     |
| Natural teeth               | .10        |        |         | 0.03     | 0.18 |         | 0.11     | 0.32 | .16     |

Note. Bold font indicates statistical significance. OHAT = oral health assessment tool; CHX = chlorhexidine; N/S = normal saline.
and dental plaque in individuals with mild gingival inflammation or dental plaque (James et al., 2017). A systematic review by Alshehri (2018) that included 26 studies showed that an essential oil (Listerine) mouth rinse may be used as an adjunctive method to improve oral health (Alshehri, 2018). The results of this study support the oral health improvement effects of using an oral rinse under supervision during short-term hospitalization. Interestingly, we found that CHX oral rinse increased saliva secretion significantly more than either the Listerine or control rinse. Possible explanations for the improvement in oral health because of the CHX oral rinse may be attributable to changes in the oral environment such as increased saliva secretion because of higher pH levels. Saliva plays a significant role in maintaining oral health, as saliva contains bicarbonate, phosphate, and urea. Bicarbonate and urea help reduce plaque by neutralizing oral acidic substances and improve the oral pH value (Miletic & Baraba, 2011). Similar results were presented in Kalyani and Leelavathi (2019), who recruited 30 Indian students in a university department of dentistry. The students were evaluated for effect on oral pH after they had rinsed with water, tea, or CHX. The results showed that the average pH value in the CHX group was higher than in the water and tea group both after 5 minutes and after 1 hour (Kalyani & Leelavathi, 2019). Therefore, the authors of this study propose that oral rinsing with CHX improves xerostomia via CHX-related changes to the oral pH environment, especially in hospitalized middle-aged and older adults. Further research is necessary to evaluate the effect of the CHX mouth rinse intervention on the relationship between saliva secretion and oral environment pH level.

The following limitations of this study should be addressed in future investigations. First, the small sample size and short duration of hospitalization complicated our ability to detect important associations related to the study outcomes. Second, all of the participants were hospitalized patients aged 50 years or older. Thus, the observed outcomes are limited to the target population and may not be generalizable to other groups. The effect of oral rinses with 0.12% CHX administered under the supervision of a nurse on NV-HAP risk in middle-aged and elderly inpatients could not be assessed in this study because none of the participants contracted this disease during the study period. However, CHX use may still be effective in improving oral health, and oral rinsing with 0.12% CHX may be recommended as safe and beneficial for nonventilated patients with poor oral health.

Table 4
The Clearance Rate of Pneumonia-Associated Oral Bacteria Among the Three Groups

| Bacteria                          | Total Amount of Oral bacteria at the Baseline (CFU/ml) | Clearance Rate (%) | F   | p   |
|----------------------------------|------------------------------------------------------|--------------------|-----|-----|
|                                  |                                                      | Group A (CHX) (n = 83) | Group B (Listerine) (n = 85) | Group C (N/S) (n = 76) |
| Unidentified gram-negative bacteria | 3,230                                               | 58.33              | 75.00 | 79.17 |
| Gram-positive cocci              | > 30,600                                             | 100.00             | 66.67 | 83.33 |
| S. aureus                        | > 30,200                                             | 100.00             | 66.67 | 66.67 |
| Tsukamurella species             | 400                                                  | NA                 | NA   | 100.00 |
| Enterobacteria                   | > 80,400                                             | 57.78              | 51.32 | 64.14 |
| Enterobacter cloacae complex     | 800                                                  | 52.78              | 47.62 | 30.00 |
| E. coli                          | > 37,600                                             | 100.00             | 60.00 | 66.67 |
| Klebsiella pneumoniae            | > 32,900                                             | 61.11              | 59.26 | 64.29 |
| Proteus mirabilis                | 100                                                  | NA                 | 100.00 | NA |
| Serratia marcescens              | 8,500                                                | 50.00              | 50.00 | 100.00 |
| Klebsiella aerogenes             | 500                                                  | 50.00              | 50.00 | 66.67 |
| Aquatic bacteria                 | > 111,160                                            | 34.81              | 54.03 | 55.34 |
| Acinetobacter                    | > 38,100                                             | 40.05              | 55.56 | 66.98 |
| Cupriavidus gilardi              | 300                                                  | 50.00              | 50.00 | 58.33 |
| Citrobacter freundii             | > 10,000                                             | NA                 | NA   | 100.00 |
| Chryseobacterium                 | > 13,600                                             | 16.67              | NA   | 62.50 |
| Elizabethkingia anopolis         | 900                                                  | NA                 | 66.67 | 72.22 |
|Ralstonia mannitolivitica         | 1,200                                                | NA                 | NA   | 100.00 |
| Rothia mucilaginosa              | 1,000                                                | NA                 | 66.67 | 0.00 |
|Stenotrophomonas maltophilia      | > 11,000                                             | 50.00              | 76.67 | 54.17 |
|P. aeruginosa                     | > 41,360                                             | 75.00              | 46.30 | 25.00 |
|Others                            | > 154,500                                            | 72.62              | 80.86 | 69.45 |
|Capnocytophaga                    | > 123,300                                            | 73.81              | 78.47 | 75.00 |
|Haemophilus                       | > 31,200                                             | 95.00              | 100.00 | 100.00 |

Note. CFU = colony-forming unit; CHX = chlorhexidine; N/S = normal saline; NA = not applicable.

* The numbers of samples in each group were not equal because samples were collected multiple times for each individual.
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