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Impact of oral care modalities on the incidence of ventilator-associated pneumonia in the intensive care unit

A meta-analysis

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Abstract

Background: At present, evidence of the role of oral hygiene in ICU-related pneumonia is rare. The study aimed to evaluate the effectiveness of toothbrush-based oral care in preventing ventilator-associated pneumonia (VAP) in patients with mechanical ventilation in the ICU.

Methods: Ten databases were searched for randomized controlled trials (RCTs) evaluating toothbrush-based oral care for preventing VAP in patients with mechanical ventilation in ICU. Quality assessment and data extraction were independently performed by 2 researchers. The meta-analysis was performed using RevMan 5.3 software.

Results: Thirteen RCTs with 657 patients were included. Tooth brushing + 0.2%/0.12% chlorhexidine was associated with reduced incidence of VAP compared to chlorhexidine (OR = 0.63, 95% confidence interval [CI]: 0.43–0.91, *P* = .01) or tooth brushing + placebo (OR = 0.47, 95% CI: 0.25–0.86, *P* = .02) in patients with mechanical ventilation in ICU, but was similar to cotton wipe with 0.2% or 0.12% chlorhexidine (OR = 1.33, 95% CI: 0.77–2.29, *P* = .31).

Conclusions: Tooth brushing combined with chlorhexidine mouthwash can prevent VAP in patients with mechanical ventilation in ICU. There is no advantage of tooth brushing combined with chlorhexidine mouthwash over cotton wipe with chlorhexidine mouthwash for preventing VAP in these patients.

Abbreviations: CI = confidence interval, OR = odds ratio, RCTs = randomized controlled trials, VAP = ventilator-associated pneumonia.

Keywords: intensive care unit, mechanical ventilation, meta-analysis, randomized controlled trial, tooth brushing, ventilator-associated pneumonia

1. Introduction

Ventilator-associated pneumonia (VAP) refers to the development of pneumonia in patients with mechanical ventilation, occurring at least 48 hours after admission.[1] The increased need for mechanical ventilation increases VAP risk from 9% to 40%.[2] A previous study found that more than 90% of cases of ICU-related pneumonia occurred during mechanical ventilation, and nearly 50% of these cases occurred during the first 4 days of mechanical ventilation. The condition correlates with high morbidity and mortality rate (20%–70%),[3,4] making it the leading cause of death in this population. VAP can prolong the duration of mechanical ventilation and increase the average length of hospital stay by approximately 7 days, which leads to higher medical costs.[5–7] Therefore, the prevention of VAP is a key priority in critical care medicine. A large body of evidence suggests an association between inadequate oral care leading to colonization of oral bacteria and the development of pneumonia in patients with mechanical ventilation.[8,9] Reducing oral bacterial load is one of the key measures for the prevention of VAP. Recent years have witnessed a gradual increase in research on reducing oral bacterial accumulation through toothbrushing to prevent VAP. However, there is no clear consensus regarding the role of toothbrushing in preventing VAP.[10] Our study aimed to explore the effectiveness of toothbrushing in preventing the occurrence of VAP in ICU patients with mechanical ventilation. By synthesizing the available evidence, our study may help inform the development of clinical practice guidelines for oral care of patients with mechanical ventilation.

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study does not require consent statement and Ethics Committee ethics approval.

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2. Methods

The systematic evaluation was implemented following the PRISMA statement[11] and the Cochrane Handbook for Systematic Reviews of Interventions.[12]

2.1. Search strategy

A comprehensive search strategy was developed to retrieve relevant studies from online biomedical databases. Mesh terms, keywords, and free words were used. The English search terms were "oral nursing," "oral care," "oral decontamination," "oral hygiene," "chlorhexidine," "toothbrush," "ventilator-associated pneumonia," and the Chinese search terms were "ventilator-associated pneumonia," "hospital-acquired pneumonia," "pneumonia," "mechanical ventilation," "tracheal intubation," "oral care," and "toothbrushing." Ten electronic databases, including PubMed, Ovid Medline, The Cochrane Library, EMBASE, Web of Science, CENTRAL, CINAHL, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Wanfang Database, were searched to identify randomized clinical trials (RCTs) evaluating toothbrush-based oral care for preventing VAP in patients with mechanical ventilation in ICU. The references in the included literature were also manually screened. The search time frame was from inception of the database to May 2021. The specific search strategy was based on Ovid Medline as an example (Supplementary file, Supplemental Digital Content, http://links.lww.com/MD/I733).

2.2. Study inclusion and exclusion criteria

2.2.1. Literature inclusion criteria.

(1) Study design: Randomized-controlled trials (RCTs).
(2) Participants: Adult patients eligible for ventilator therapy.
(3) Interventions: The experimental group used toothbrushing or a combination of toothbrushing and chlorhexidine mouthwash solution.
(4) Control: The control group used chlorhexidine mouthwash alone, tooth brushing combined with placebo mouthwash, or cotton ball scrubbing combined with chlorhexidine mouthwash.
(5) Outcome: Primary outcomes: incidence of VAP.

2.2.2. Literature screening and data extraction. The titles and abstracts of all retrieved studies were independently screened by 2 researchers according to the inclusion and exclusion criteria using literature management software (NoteExpress), followed by a full-text review of the included literature to establish the final inclusion. Similarly, 2 researchers independently extracted the data from the selected studies using a predesigned extraction form. Data pertaining to the following variables were extracted: title of the study, authors, year of publication, and study population; study area; study design; study population and sample size; intervention and control groups; outcomes; methodological quality of the study (e.g., randomization sequence generation, allocation concealment); and conclusions. Any inconsistency in the extracted information was resolved by consensus with participation of a third investigator.

2.3. Evaluation of literature quality

The methodological quality of the included studies was independently evaluated by 2 researchers using the Cochrane Collaboration Network Risk Assessment Tool.[12] The assessment items consisted of random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; selective reporting; other biases. The risk of bias was classified as "high risk of bias," "low risk of bias," and "unclear." Any inconsistency in the assessment was resolved by discussion with a third investigator.

2.4. Data analysis methods

Meta-analysis was performed using the Review Manager (RevMan) software (version 5.3, Nordic Cochrane Centre). Heterogeneity among the included studies was assessed using the Q-test. In case of no significant heterogeneity among the included studies ($P > .1$ and $I^2 < 50\%$), the study used fixed-effects model for analysis. In case of significant heterogeneity ($P \geq .1$ or $I^2 \leq 50\%$), the study used random-effects model for meta-analysis. Besides, subgroup analysis was performed to identify factors causing heterogeneity.

3. Results

3.1. Literature search

A total of 1268 studies were retrieved from the databases, including 689 in English and 579 in Chinese. After the literature management and manual screening, 111 duplicate publications were excluded. After reviewing the titles and abstracts, one hundred twenty-nine studies were excluded due to duplicated publications, non-RCTs, or incomplete data. After reviewing the full text of the remaining articles, 13 papers were finally included.

3.2. Basic characteristics of the included studies and evaluation of methodological quality

Thirteen studies[9,13–24] published between 2008 and 2018 and performed in 8 countries were included. Ten of them,[9,13–16,18–20,22,23] with 657 patients, were eventually subjected to the meta-analysis. The maximum sample size for a single study was 145 cases. The specific steps of the intervention strategy were described in detail. The characteristics of the included studies are shown in Table 1.

All the included studies were RCTs. Of these, 12 (92%) described appropriate randomization (e.g., use of a random number table), 6 (46%) described allocation concealment, 4 (31%) implemented blinding of study subjects and interventionists, and 11 (85%) implemented blinding of outcome assessors; no incomplete data, selective reporting, or other biases were identified. The evaluation of the quality of the included studies is shown in Figure 1.

Five[13,17,18,22,24] studies defined the clinical onset of VAP by using the clinical pulmonary infection score (CPIS) more than 6; 6 studies[9,14–16,20,23] applied the modified version of CPIS which has been recommended for the detection and management of VAP by the American Thoracic Society. In 1 study, the diagnosis of suspected VAP was based on the colonization of supragingival dental plague.[19]

3.3. Meta-analysis

3.3.1. Toothbrushing + chlorhexidine mouthwash vs chlorhexidine mouthwash. Four[9,13,18,20] studies (with 413 cases in toothbrushing plus chlorhexidine mouthwash arm and 414 cases in chlorhexidine mouthwash alone arm) were included to analyze the incidence of VAP. Owing to the lack of significant heterogeneity among these studies ($P = .32$, $I^2 = 15\%$), the study used fixed-effects model for analysis. The results showed a significantly reduced incidence of VAP in the toothbrushing plus chlorhexidine mouthwash arm (odds ratio [OR]: 0.63; 95% confidence interval [CI] 0.43–0.91; $P = .01$) (Fig. 2). These results indicate that toothbrushing combined with chlorhexidine

Table 1

Baseline characteristics of the included studies.

Studies	Area	No. (E/C)	Sex (female, E/C)	Age	Frequency of intervention (E/C)	Intervention		Outcomes
						E	C	
Atashi et al[13]	Iran	40/40	13/11	E = 52.44 ± 14.88 C = 45.55 ± 17.06	E: 3/d C: 2/d	Toothbrush brushing + cotton ball wiping + 0.2% chlorhexidine solution	Cotton ball wipe + 0.2% chlorhexidine solution	Incidence of VAP, Clinical pulmonary infection score
Chacko et al[14]	India	104/102	57/34	E = 41.02 ± 17.78 C = 45.91 ± 18.38	E: 3/d C: 3/d	Suction toothbrush + 0.2% chlorhexidine solution rinse	Cotton ball wipe + 0.2% chlorhexidine solution	Incidence of VAP
de Lacerda Vidal et al[15]	Brazil	105/108	54/54	E = 59.4 ± 14.5 C = 63.2 ± 14.5	E: 2/d C: 2/d	Toothbrush brushing + 0.2% chlorhexidine solution	Cotton ball wipe + 0.2% chlorhexidine solution	Incidence of VAP, duration of mechanical ventilation, length of hospital stay, ICU mortality
Lorente et al[9]	Spain	217/219	71/74	E = 61.0 ± 15.6 C = 60.4 ± 16.6	E: 3/d C: 3/d	Manual brushing + rinsing and suction with 0.12% chlorhexidine solution	Flushing and suction with 0.2% chlorhexidine solution	Incidence of VAP
Meinberg et al[16]	Brazil	28/24	Unclear	E = 40.1 ± 14.6 C = 41.0 ± 19.0	E: 4/d C: 4/d	Toothbrush brushing + 0.2% chlorhexidine solution	Brushing + placebo solution	Incidence of VAP
Munro et al[17]	USA	E1 = 49 E2 = 48 C1 = 44 C2 = 51	Unclear	47.9 ± 17.5	E1: 3/d E2: 3/d C1: 2/d C2: Unclear	E1:toothbrush E2:toothbrush brushing + 0.12% chlorhexidine solution	C1: 0.2% chlorhexidine solution + cotton ball wipe C2: Routine care	Incidence of VAP
Nasiriani et al[18]	Iran	84/84	28/27	E = 44.9 ± 13.9 C = 44.2 ± 14	E: 2/d C: 2/d	Toothbrush brushing + cotton ball wiping + 0.2% chlorhexidine solution	Chlorhexidine solution + cotton ball wipe	Incidence of VAP
Needleman et al[19]	UK	23/23	9/10	E = 42.7 ± 12.8 C = 53.0 ± 12.5	E: 2/d, 2 min C: 2/d, 2 min	Toothbrush + 0.2% chlorhexidine solution for rinsing and suction	0.2% chlorhexidine solution + sponge and toothpick scrubbing	Plaque colonization number
Pobo et al[20]	Spain	74/73	25/27	E = 52.6 ± 17.2 C = 55.3 ± 17.9	E: 3/d C: 3/d	Toothbrush + oral care	0.12% chlorhexidine solution + routine oral care	Incidence of VAP, duration of mechanical ventilation, length of hospital stay
Prendergast et al[21]	USA	25/31	Unclear	E = 51 ± 19 C = 52 ± 19	E: 2/d C: 2/d	Electric toothbrush + tongue scraping	Manual toothbrush	Oral hygiene
Scannapieco et al[22]	USA	47/49	15/23	E = 44.8 ± 19.9 C = 50.0 ± 22.5	E1: 2/d E2: 1/d C: 2/d	E1: toothbrush brushing + 0.12% chlorhexidine E2: toothbrush brushing + 0.12% chlorhexidine + placebo	Toothbrush + placebo	Incidence of VAP
Tantipong et al[23]	Thailand	102/105	52/54	E = 56.5 ± 20.1 C = 60.3 ± 19.1	E: 4/d C: 4/d	Toothbrush brushing + 0.12% chlorhexidine solution	Toothbrush + placebo	Incidence of VAP

C = control group, d = day, E = experience group, VAP = ventilator-associated pneumonia.

mouthwash for ICU patients with mechanical ventilation may reduce VAP incidence compared to chlorhexidine mouthwash alone.

3.3.2. Toothbrushing + chlorhexidine mouthwash vs cotton ball wipe + chlorhexidine mouthwash. Three studies[14,15,19] compared the intervention toothbrushing plus chlorhexidine mouthwash with cotton ball/gauze wiping plus chlorhexidine mouthwash in patients with mechanical ventilation (235 cases in the intervention arm and 230 cases in the control arm). Owing to lack of significant heterogeneity among these studies (P = .27, I^2 = 23%), the fixed effects model was used for meta-analysis. There was no significant difference in the incidence of VAP between the 2 groups (OR: 1.33; 95% CI 0.77–2.29; P = .31) (Fig. 3). This suggests that toothbrushing plus chlorhexidine rinse was not superior to cotton ball wiping plus chlorhexidine rinse in reducing the incidence of VAP in patients with mechanical ventilation in the ICU.

3.3.3. Toothbrushing + chlorhexidine mouthwash vs toothbrushing + placebo mouthwash. A total of 3 studies[16,22,23] compared toothbrushing plus chlorhexidine rinse and toothbrushing plus placebo rinse (184 in the intervention arm and 192 in the control arm). Owing to no significant heterogeneity, (P = .93, I^2 = 0%), the fixed effects model was used for meta-analysis. The incidence of VAP was significantly lower in the toothbrushing plus chlorhexidine arm (OR: 0.47; 95% CI 0.25–0.86; P = .02) (Fig. 4). The results indicated that toothbrushing plus chlorhexidine mouthwash was significantly better than toothbrushing plus placebo mouthwash in reducing the incidence of VAP in patients with mechanical ventilation in the ICU.

4. Discussion

4.1. Quality of the included studies

Thirteen studies were included in this study, and the quality of the studies was moderate or above. Twelve studies described specific randomization grouping methods, 6 described allocation concealment, 4 involved blinding of the study population, eleven involved blinding to the outcome measure,

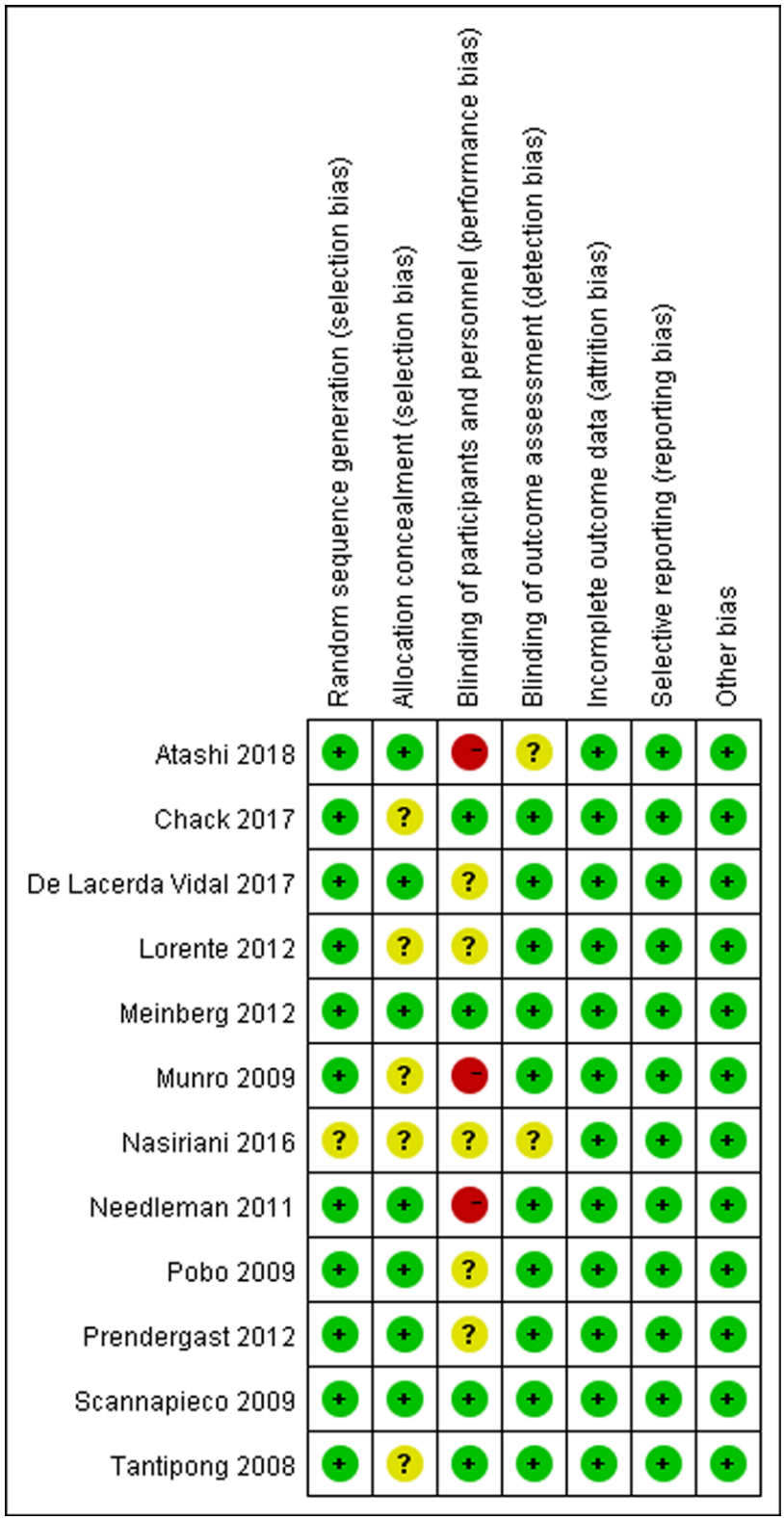

Figure 1. Quality of the included studies.

and 4 were double-blinded. All studies reported the loss of follow-up and baseline information, including age, sex, and type of disease. The results showed comparable baseline information between the intervention and control groups ($P > .05$). Therefore, the quality of the studies included in the meta-analysis was high.

4.2. Effectiveness of tooth brushing plus chlorhexidine mouthwash in preventing VAP

A total of 10 studies were included in the meta-analysis of VAP incidence with different oral care modalities. The results in Figure 2 show that toothbrushing combined with chlorhexidine rinse was superior to single oral care modalities (e.g.,

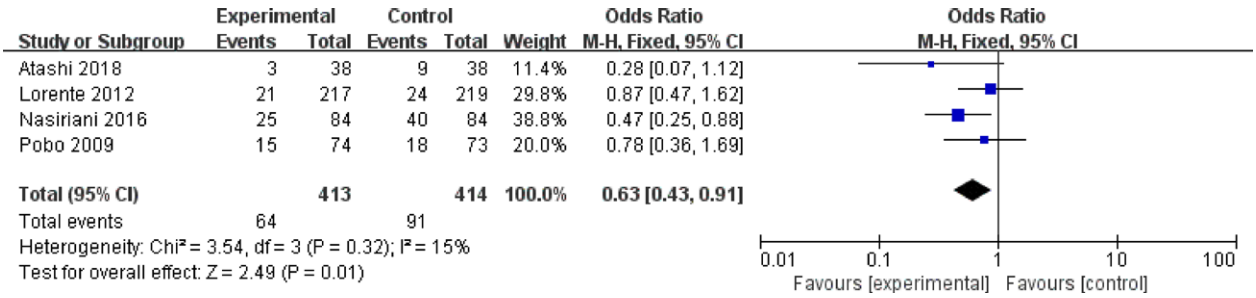

Figure 2. Comparison of the incidence of VAP between toothbrushing plus chlorhexidine mouthwash and chlorhexidine mouthwash alone. VAP = ventilator-associated pneumonia.

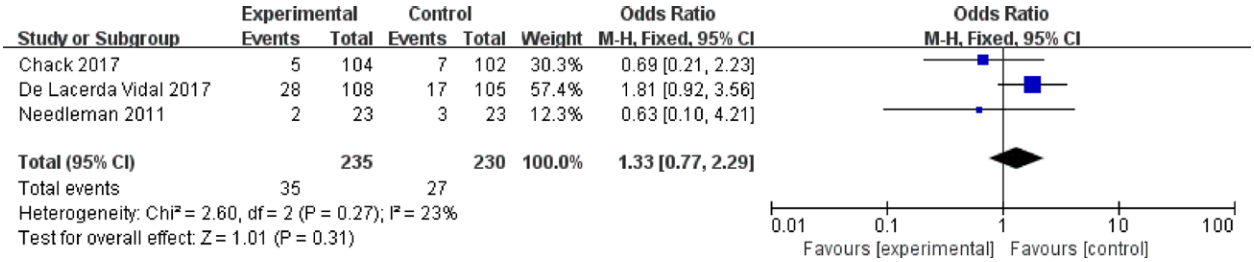

Figure 3. Comparison of the incidence of VAP between toothbrushing plus chlorhexidine mouthwash and cotton ball wipe plus chlorhexidine mouthwash. VAP = ventilator-associated pneumonia.

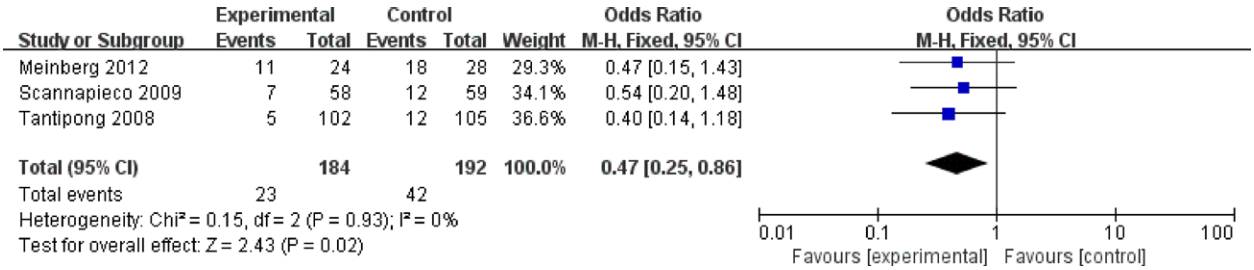

Figure 4. Comparison of the incidence of VAP between toothbrushing plus chlorhexidine mouthwash and toothbrushing plus placebo mouthwash. VAP = ventilator-associated pneumonia.

chlorhexidine rinse only or toothbrushing only) in reducing VAP incidence ($P < .05$). Also, brushing with chlorhexidine was more effective in preventing VAP than toothbrushing with a placebo rinse ($P = .02$). However, toothbrushing combined with chlorhexidine mouthwash was not superior to cotton ball wiping combined with chlorhexidine mouthwash in preventing VAP in patients with mechanical ventilation ($P > .05$). Owing to greater friction between the toothbrush bristles and the tooth surface, and better penetration, oral care using a toothbrush is more effective in preventing oral plaque formation, and removal of residues between the teeth, reducing the risk of pathogen colonization of the oral and respiratory tract.[14] Also, mouthwash with 0.2% or 0.12% chlorhexidine was better at reducing oropharyngeal bacterial growth than placebo. However, no significant difference in the incidence of VAP was observed between toothbrushing plus chlorhexidine mouthwash and cotton ball/gauze wiping plus chlorhexidine mouthwash. It has been shown that cotton ball/gauze wiping is similar to toothbrush scrubbing in that it cleans the mouth by mechanical friction, thereby removing oral residues and plaque.[25] The toothbrush (manual or electric) may only have the added advantage of the ease of handling compared to cotton ball wiping. Compared to using cotton ball wipes for oral care, the toothbrush is relatively convenient to hold and easy to operate.

4.3. Limitations of this study and implications for the future

Although all studies included in the meta-analysis used toothbrushing as an intervention, some of the studies used different oral care modalities and oral rinses, making it difficult to categorize them strictly. Also, due to the volume of literature included, it was not possible to conduct subgroup analyses of the different chlorinated mouthwash concentrations (e.g., i.e., 0.12%, 0.2%, and 2%) and brushing regimens (e.g., 2 times a day, 3 times a day, or 4 times a day) across the studies. Future studies should investigate different mouthwashes, different concentrations, and different brushing frequencies. Secondly, in half of the included studies, the study participants and intervention implementers were not blinded to the intervention. Double-blind clinical trials should be conducted to increase the credibility of the findings. Finally, larger, multicenter, high-quality RCTs are required to provide a more robust evidence base for determining the appropriate oral care modalities for mechanically ventilated patients to reduce the incidence of VAP.

This study suggests that toothbrushing combined with chlorhexidine mouthwash can prevent VAP in patients with mechanical ventilation in the ICU. However, there is no advantage of toothbrushing combined with chlorhexidine over cotton ball wiping combined with chlorhexidine mouthwash in this respect. More rigorous multicenter RCTs are required to support the development of clinical practice guidelines for oral care and prevention in these patients.

4.4. Clinical relevance

4.4.1. Scientific rationale for study. VAP is extremely difficult to define and detect. According to global data, the incidence of VAP in ICU patients with mechanical ventilation is as high as 40% above. VAP is often accompanied by serious complications, such as disability and poor prognosis, resulting in increased medical costs. Oral care is an effective way to reduce the incidence of VAP.

4.4.2. Principal findings. Brushing with chlorhexidine can prevent VAP in ICU patients with mechanical ventilation. However, toothbrushing combined with chlorhexidine mouthwash was not superior to cotton ball wiping combined with chlorhexidine mouthwash in preventing VAP in ICU patients with mechanical ventilation.

4.4.3. Practical implications. The meta-analysis emphasized the importance of toothbrush-based oral care in preventing VAP in patients with mechanical ventilation in the ICU, in order to lower the incidence of VAP and improve the life quality of patients to reduce the economic burden on the health system.

Author contributions

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Formal analysis: Li-Mei Zhu, Yuan-Ping Yang, Li-Qun Yao.
Visualization: Ling Lin.
Writing – original draft: Li-Sang Fu, Yuan-Ping Yang, Li-Qun Yao.
Writing – review & editing: Li-Sang Fu, Li-Mei Zhu, Yuan-Ping Yang, Li-Qun Yao.

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