

Ventilator-associated pneumonia with or without toothbrushing: a randomized controlled trial

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Abstract Certain guidelines for the prevention of ventilator-associated pneumonia (VAP) recommend oral care with chlorhexidine, but none refer to the use of a toothbrush for oral hygiene. The role of toothbrush use has received scant attention. Thus, the objective of this study was to compare the incidence of VAP in critical care patients receiving oral care with and without manual brushing of the teeth. This was a randomized clinical trial developed in a 24-bed medical-surgical intensive care unit (ICU). Patients undergoing invasive mechanical ventilation for than 24 h were included. Patients were randomly assigned to receive oral care with or without toothbrushing. All patients received oral care with 0.12% chlorhexidine digluconate. Tracheal aspirate samples were obtained during endotracheal intubation, then twice a week, and, finally, on extubation. There were no significant differences between the two groups of patients in the baseline characteristics. We found no statistically significant differences between the groups regarding the incidence of VAP (21 of 217 [9.7%] with toothbrushing vs. 24 of 219 [11.0%] without toothbrushing; odds ratio [OR]=0.87, 95% confidence interval [CI]=0.469–1.615; $p=0.75$). Adding manual toothbrushing to

chlorhexidine oral care does not help to prevent VAP in critical care patients on mechanical ventilation.

Introduction

Ventilator-associated pneumonia (VAP) remains a major cause of morbidity, mortality, and increased cost of care in critically ill patients [1–5]. Different pharmacological and non-pharmacological measures have been proposed for the prevention of VAP [6, 7].

Oral care with chlorhexidine solution has been found to reduce the risk of VAP, according to some meta-analyses [8–13]; however, the role of toothbrushing has received scant attention [14–18]. Some cohort studies have indicated that oral care with an antiseptic agent and toothbrushing could reduce the incidence of VAP compared with no oral care [14–16]; however, a limitation of these cohort studies is that it is not possible to discriminate the influence of toothbrushing per se, since the intervention group received both the antiseptic agent and toothbrushing. In a randomized study published by Pobo et al. in 2009, including a total of 147 patients, toothbrush use did not reduce the incidence of VAP [17]. In another randomized study published by Munro et al. in 2009, including 471 patients mechanically ventilated for a period of more than 24 h assigned into four groups (119 patients received chlorhexidine oral care, 113 patients toothbrushing, 116 patients toothbrushing and chlorhexidine oral care, and 123 patients usual care only), toothbrush use did not reduce the incidence of VAP [18].

Certain guidelines on the prevention of VAP make no reference to the question of oral care with chlorhexidine [19], while others recommend its early use [20–22]. However, none of them refer to the use of a toothbrush for oral care. Some care bundles proposed for VAP prevention in

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Europa and the USA did not refer to the use of a toothbrush for oral care [23, 24]. Oral care was perceived to be of a high priority in mechanically ventilated patients in a questionnaire survey in 59 European intensive care units (ICUs) and it was found that oral cavity cleaning was considered to be difficult by 68%, 63% of cases have insufficient supplies, and about 37% are under the impression that oral health worsens despite their efforts to keep the mouth healthy [25]. Given the potential benefit of toothbrushing and the absence of evidence, we designed this study.

We tested the hypothesis that adding toothbrush use to oral care with 0.12% chlorhexidine could reduce the incidence of VAP, by reducing the presence of endogenous oropharyngeal flora. The study was designed to compare the incidence of VAP using oral care with and without brushing the teeth with a manual brush in patients undergoing invasive mechanical ventilation for more than 24 h. The new aspects of our randomized controlled trial in comparison with the previous randomized controlled trials are the larger sample size and the surveillance of throat flora to explore the effect of toothbrushing on endogenous VAP.

Methods

Study design

A randomized clinical trial was performed in a 24-bed medical-surgical ICU of the Hospital Universitario de Canarias (Tenerife, Spain), a 650-bed tertiary hospital, from 1 August 2010 to 25 August 2011. The study was approved by the Institutional Review Board and informed consent from the patients or from their legal guardians was obtained.

Patients

Consecutive patients undergoing invasive mechanical ventilation were randomly assigned to one of two oral care groups, using a list of random numbers generated with Excel software (Microsoft, Seattle, WA), to discriminate the benefit of toothbrushing in VAP incidence. In group A, the oral cleansing was performed with 0.12% chlorhexidine-impregnated gauze and oral cavity injection only; in group B, the oral cleansing was performed with 0.12% chlorhexidine-impregnated gauze and oral cavity injection, followed by manual brushing of the teeth with a brush impregnated with 0.12% chlorhexidine.

Exclusion criteria were as follows: edentulous, age < 18 years, pregnancy, human immunodeficiency virus (HIV), white blood cell (WBC) count <1,000 cells/mm³, solid or hematological tumor, immunosuppressive therapy, and mechanical ventilation duration less than 24 h.

Oral care groups

In both groups, nurses performed oral cleansing every 8 h, as follows: first, the endotracheal cuff pressure was tested and oropharyngeal secretions were aspirated, then gauze impregnated with 20 mL of 0.12% chlorhexidine digluconate was used to cleanse the teeth, tongue, and mucosal surfaces, followed by the injection of 10 mL of 0.12% chlorhexidine digluconate into the oral cavity, and, finally, after 30 s, the oropharyngeal area was suctioned.

In the interventional group, after the application of oral chlorhexidine in the same way, the nurses used a manual toothbrush to brush the patient's teeth (tooth by tooth, on the anterior and posterior surfaces), the gum line, and the tongue for a period of 90 s.

Measures to prevent VAP

Before the study was started, the following measures to prevent VAP in both groups of patients were established: no routine change of ventilator circuits, tracheal suction when necessary by an open system, respiratory secretion suctioning performed with barrier measures (hand washing, use of gloves and face masks), semi-recumbent body position to maintain a head elevation $\geq 30^\circ$, periodic verification every 8 h of intracuff pressure to maintain a pressure of 25 cm H₂O, endotracheal tube with a separate dorsal lumen for subglottic secretion drainage (performed intermittently during 1-h periods with a 10-mL syringe), nasogastric tube and periodic verification of the residual gastric volume every 6 h (residual gastric volume lower than 250 cc was considered as acceptable), and no selective digestive decontamination. The sedation drugs were adjusted to achieve a level 3–4 Ramsay score [26]. The weaning of mechanical ventilation started by pressure support ventilation at a pressure support of 20 cm of water, after which, the pressure support is progressively reduced to zero and, finally, a T-tube circuit is used. The types of endotracheal tubes used were as follows: (1) TaperGuard Evac™ (Mallinckrodt, Athlone, Ireland), which incorporates a dorsal separate lumen ending in the subglottic area for subglottic secretion drainage and (2) Hi-Lo™ (Mallinckrodt, Athlone, Ireland), which does not incorporate the lumen for subglottic secretion drainage. Several months after the start of the study, we followed a national project for the control of the VAP, but this did not affect the measures that had been selected at the beginning of the study.

Microbiological vigilance

Tracheal aspirate samples were obtained during endotracheal intubation, then twice a week, and, finally, on extubation.

A throat swab was taken at admission to the ICU, twice a week thereafter, and at discharge from the ICU, for the study of bacterial flora to classify pneumonia as being of endogenous or exogenous origin.

Definitions

The diagnosis of pneumonia was based on the fulfillment of all the following criteria: (a) new onset of bronchial purulent sputum, (b) body temperature >38 °C or <35.5 °C, (c) white blood cell count $>10,000/\text{mm}^3$ or $<4,000/\text{mm}^3$, (d) chest radiograph showing new or progressive infiltrates, (e) significant quantitative culture of respiratory secretions by tracheal aspirate ($>10^6$ cfu/mL).

Pneumonia was considered as VAP when it was diagnosed during mechanical ventilation and was not present at the time of initiating mechanical ventilation.

VAP was considered as being of early onset when it was diagnosed during the first 4 days of mechanical ventilation, and as late onset when diagnosed after 4 days of mechanical ventilation.

Cases of VAP were classified as endogenous or exogenous according to throat flora analysis [27]: VAP was considered as primary endogenous when caused by microorganisms already present in the patient's oropharyngeal flora on admission to the ICU and as secondary endogenous when caused by microorganisms not found on admission but detected in the patient's oropharyngeal flora during ICU stay. VAP was considered as exogenous when it was caused by microorganisms that were never identified in the patient's oropharyngeal flora.

The diagnosis of VAP was made by an expert panel, blinded to group assignment. The information about the type of oral care (with or without toothbrushing) was removed before the experts read the patient charts. The medical experts in infection control who diagnosed VAP were María Lecuona and María José Ramos.

Variables recorded

The following variables were recorded for each patient: sex, age, diagnosis group, Acute Physiology and Chronic Health Evaluation (APACHE) II score [28], duration of mechanical ventilation, antibiotics prior to VAP onset, use of paralytic agents, tracheotomy, re-intubation, enteral nutrition, duration of ICU stay, and mortality. In addition, the following variables were recorded for each VAP: Predisposition, Insult, Response and Organ dysfunction (PIRO) score for VAP [29], Sepsis-related Organ Failure Assessment (SOFA) score [30], chest X-ray quadrants, and pressure of arterial oxygen/fraction inspired oxygen ($\text{PaO}_2/\text{FiO}_2$).

Statistical analysis

In the year before the study, of the patients undergoing mechanical ventilation for more than 24 h who received conventional oral cleansing without toothbrush use, 15% developed VAP. For a power of 80% and an alpha error of 5%, we required 218 patients per group in order to detect a reduction in VAP incidence from 15% (using conventional care without toothbrushing) to 7.5% (using oral cleansing with manual toothbrushing).

Quantitative variables, described as mean \pm standard deviation, were compared with Student's *t*-test. Qualitative variables, described as percentages, were compared with the Chi-squared test or with Fisher's exact test, as appropriate.

The proportion of VAP between groups was compared with the Kruskal–Wallis test for single-order classification. The incidence density of VAP (number of events/days of mechanical ventilation) between groups was compared using Poisson regression analysis. The probability of remaining VAP-free was represented using the Kaplan–Meier method and comparison between the two groups was performed with the log-rank test.

Differences with a *p*-value of less than 0.05 were considered to be statistically significant. For statistical analyses, we used SPSS 14.0.1 (SPSS Inc., Chicago, IL, USA) and StatXact 5.0.3 (Cyrus Mehta and Nitin Patel, Cambridge, MA, USA).

Results

The present study included 436 ICU patients on mechanical ventilation divided into two groups, one with 217 patients receiving oral care with toothbrushing and the other with 219 patients receiving oral care without toothbrush use. There were no significant differences between the two groups of patients regarding age, sex, diagnosis groups, APACHE II score, use of antibiotics, paralytic agents, reintubation, tracheotomy, enteral nutrition, and duration of mechanical ventilation (Table 1).

We found no statistically significant differences in the incidence of VAP between the groups (21 of 217 [9.7%] with toothbrush use vs. 24 of 219 [11.0%] without; odds ratio [OR]=0.87, 95% confidence interval [CI]=0.469–1.615; *p*=0.75) (Table 2). We also found no statistically significant differences between the two groups in terms of the microorganisms responsible for VAP, early-onset or late-onset VAP, and endogenous or exogenous VAP (Table 2).

We have not found any significant differences in VAP incidence between patients with and without toothbrushing among surgical patients (OR=0.85, 95% CI=0.300–2.440), medical patients (OR=0.93, 95% CI=0.350–2.460), and

Table 1 Characteristics of the standard oral care and oral care with toothbrushing groups

	With toothbrushing (<i>n</i> =217)	Without toothbrushing (<i>n</i> =219)	<i>p</i> -value
Sex, female, <i>n</i> (%)	71 (32.7%)	74 (33.8%)	0.84
Age, mean years ± SD	61.0±15.6	60.4±16.6	0.71
Teeth, mean number ± SD	22.5±6.3	22.4±6.5	0.82
Diagnostic group, <i>n</i> (%)			0.57
Cardiac surgery	54 (24.9%)	48 (21.9%)	
Cardiology	43 (19.8%)	47 (21.5%)	
Respiratory	27 (12.4%)	32 (14.6%)	
Digestive	31 (14.3%)	39 (17.8%)	
Neurologic	30 (13.8%)	29 (13.2%)	
Trauma	20 (9.2%)	19 (8.7%)	
Intoxication	12 (5.5%)	5 (2.3%)	
APACHE II, mean score ± SD	17.88±8.84	19.16±9.88	0.15
ETT with SSD, <i>n</i> (%)	189 (87.1%)	194 (88.6%)	0.66
Antibiotics before VAP, <i>n</i> (%)	186 (85.7%)	191 (87.2%)	0.68
Antibiotic peri-intubation in coma, <i>n</i> (%)	43 (19.8%)	42 (19.2%)	0.90
Paralytic agents, <i>n</i> (%)	6 (2.8%)	8 (3.7%)	0.80
Reintubation, <i>n</i> (%)	11 (5.1%)	11 (5.0%)	0.99
Tracheotomy, <i>n</i> (%)	39 (18.0%)	44 (20.1%)	0.63
Enteral nutrition, <i>n</i> (%)	89 (41.0%)	88 (40.2%)	0.92
Duration of MV, mean days ± SD	9.18±14.13	9.93±15.39	0.59
ICU stay, mean days ± SD	12.07±15.55	13.04±17.27	0.54
ICU mortality, <i>n</i> (%)	62 (28.6%)	69 (31.5%)	0.53
VAP, <i>n</i> (%)	21 (9.7%)	24 (11.0%)	0.75
VAT, <i>n</i> (%)	4 (1.8%)	3 (1.4%)	0.73
VAP plus VAT, <i>n</i> (%)	25 (11.5%)	27 (12.4%)	0.88

ETT: endotracheal tubes; SSD: subglottic secretion drainage; VAP: ventilator-associated pneumonia; VAT: ventilator-associated tracheobronchitis

trauma patients (OR=0.72, 95% CI=0.053–7.430) (Table 3). We also found no significant differences in VAP incidence between patients with and without toothbrushing among patients with antibiotic exposure (OR=0.88, 95% CI=0.440–1.740) and without antibiotic exposure (OR=0.90, 95% CI=0.011–72.993) (Table 3). We have not found significant differences between survivor patients with (*n*=155) and without (*n*=150) toothbrushing in terms of antibiotic-free

days (7.43±14.84 vs. 8.39±16.83; *p*=0.59), mechanical ventilation-free days (4.03±3.22 vs. 4.42±3.93; *p*=0.34), and days of ICU stay (14.58±17.19 vs. 15.55±18.87; *p*=0.64).

We have not found significant differences in the PIRO score, SOFA score, chest X-ray quadrants, and PaO₂/FIO₂ between the VAP diagnosed in each group of patients (Table 4).

Table 2 Comparison of VAP proportions between groups among the overall study population and classified according to throat flora, onset, and microorganism responsible

	With toothbrushing (<i>n</i> =217)	Without toothbrushing (<i>n</i> =219)	<i>p</i> -value
VAP in whole study population, <i>n</i> (%)	21 (9.7%)	24 (11.0%)	0.75
Primary endogenous VAP, <i>n</i> (%)	4 (1.8%)	7 (3.2%)	0.54
Secondary endogenous VAP, <i>n</i> (%)	16 (7.4%)	17 (7.8%)	0.99
Endogenous VAP, <i>n</i> (%)	20 (9.2%)	24 (11.0%)	0.63
Exogenous VAP, <i>n</i> (%)	1 (0.5%)	0	0.50
Early-onset VAP, <i>n</i> (%)	8 (3.7%)	8 (3.7%)	0.99
Late-onset VAP, <i>n</i> (%)	13 (6.0%)	16 (7.3%)	0.70
VAP due to GPC, <i>n</i> (%)	5 (2.3%)	5 (2.3%)	0.99
VAP due to GNB, <i>n</i> (%)	16 (7.4%)	19 (8.7%)	0.72

VAP: ventilator-associated pneumonia; GPC: Gram-positive cocci; GNB: Gram-negative bacilli

Table 3 Effects of toothbrushing according to diagnostic group and antibiotics exposure

	With toothbrushing (<i>n</i> =217)	Without toothbrushing (<i>n</i> =219)	<i>p</i> -value
VAP incidence according to diagnostic group, <i>n</i> (%)			
Surgical	9/83 (10.8%)	10/80 (10.8%)	0.81
Medical	10/119 (8.5%)	11/122 (8.5%)	0.99
Trauma	2/15 (13.3%)	3/17 (13.3%)	0.99
VAP incidence in patients with antibiotics exposure, <i>n</i> (%)	20/186 (10.8%)	23/191 (12.0%)	0.75
VAP incidence in patients without antibiotics exposure, <i>n</i> (%)	1/31 (3.2%)	1/28 (3.6%)	0.99

VAP: ventilator-associated pneumonia

VAP was found in 21 patients during 1,993 days of mechanical ventilation in the toothbrush group and in 24 patients during 2,175 days of mechanical ventilation in the group without toothbrush use. Poisson regression analysis showed no difference in the VAP incidence density between patients with and without toothbrushing (10.54 vs. 11.03 VAPs/1,000 days of mechanical ventilation; OR=0.95, 95 CI=0.53–1.72; *p*=0.88). We have not found significant differences in regard to the patients free of VAP according to the Kaplan–Meier curve (Fig. 1).

Table 5 provides a description of the microorganism responsible for VAP and of the microorganism classifying VAP according to throat flora (primary endogenous, secondary endogenous, and exogenous) and according to onset (early- or late-onset).

Discussion

No significant differences in the incidence of VAP were found according to the use or non-use of toothbrushing in oral care. To our knowledge, this is the largest randomized trial studying this issue for the prevention of VAP.

Poor oral hygiene is one of the main factors leading to the proliferation and accumulation of dental plaque and subsequent

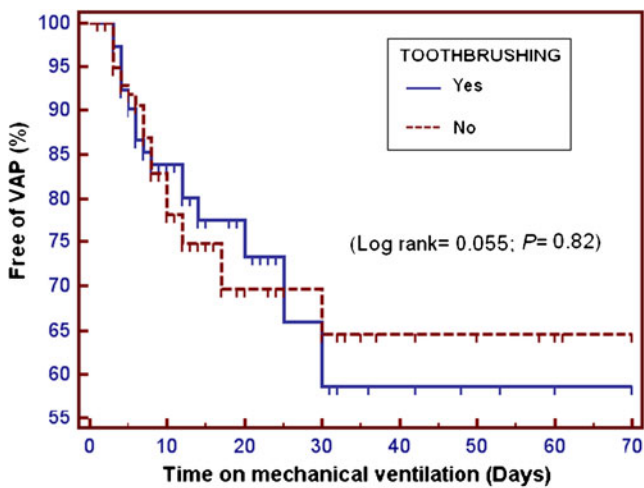
colonization by pathogens [31]. The number of positive dental plaque cultures in patients admitted to the ICU is high, being between 23 and 60% [32–34]. The amount of dental plaque and its positive culture by aerobic pathogens increases during ICU stay [32]. Most VAP is caused by microorganisms that are present in the oropharynx [35–39], and aspiration of pathogenic bacteria from the oropharynx is, therefore, the main pathophysiologic mechanism involved. According to some studies, respiratory pathogens isolated from the lung are often genetically indistinguishable from strains of the same species isolated from dental plaque [33, 40] and the tongue [41]. A systematic review found an association between periodontal disease and nosocomial infections [42]. Therefore, it seems logical that improved oral care may reduce the risk of nosocomial respiratory infection. In this regard, some authors have investigated the utility of oral decontamination by the application of antibiotic or antiseptic agents [8–13, 43, 44]. However, the role of toothbrushing has scarcely been studied [14–18].

With respect to oral decontamination with chlorhexidine in critically ill patients, some studies have reported a reduction in positive dental plaque cultures [43, 44], and some meta-analyses have found a reduction in VAP [8–13]. A meta-analysis published by Chan et al. in 2007, including 11 randomized trials and 3,242 patients, evaluated the effect of oral decontamination on the incidence of VAP [11]. In the subanalysis of four studies with 1,098 patients, the oral application of antibiotics (gentamicin, colistin, vancomycin, polymyxin B, or iseganan) did not result in a significantly reduced incidence of VAP (relative risk [RR]=0.69, 95% CI=0.41–1.18). In the subanalysis of seven studies with 2,144 patients, the oral application of antiseptics (chlorhexidine 0.12–2% or 10% povidone iodine) did significantly reduce the incidence of VAP (RR=0.56, 95% CI=0.39–0.81). A later meta-analysis published by Carvajal et al. in 2010, including ten randomized trials and 2,978 patients, focused on the efficacy of oral chlorhexidine in reducing the rate of VAP. A lower risk of VAP was found in the intervention group compared to controls (OR=0.56, 95% CI=0.44–0.73) [12]. However, no reduction was found in the mortality, duration of mechanical ventilation, or ICU stay

Table 4 Characteristics of the VAP patients with and without toothbrushing

	With toothbrushing (<i>n</i> =217)	Without toothbrushing (<i>n</i> =219)	<i>p</i> -value
PIRO score for VAP	1.52±0.75	1.33±0.76	0.40
SOFA score	7.57±2.54	7.17±3.05	0.63
Chest X-ray quadrants	2.14±1.01	1.96±1.08	0.56
PaO ₂ /FIO ₂	238±96	237±110	0.97

VAP: ventilator-associated pneumonia; PIRO: Predisposition, Insult, Response and Organ dysfunction; SOFA: Sepsis-related Organ Failure Assessment; PaO₂/FIO₂: pressure of arterial oxygen/fraction inspired oxygen



TOOTHBRUSHING	Number of patients at risk							
	217	47	17	8	5	3	1	0
Yes	217	47	17	8	5	3	1	0
No	219	49	21	12	6	4	2	0

Fig. 1 Cumulative proportion of patients remaining free of ventilator-associated pneumonia (VAP) with and without toothbrushing

with the oral application of chlorhexidine. In addition, there was a lack of uniformity in the concentration (0.12–2%) and application interval (2–4 times/day) of chlorhexidine

With respect to toothbrushing, its use has been found to reduce the risk of caries and periodontal disease in the general population [45–47]. Controversy exists about the efficacy of toothbrushing to reduce dental plaque in mechanically ventilated patients. One randomized study with 46 patients found lower dental plaque in the toothbrushing group [48]; however, in another randomized study with 146

patients, there were no significant differences in the dental plaque associated with toothbrush use or not [49].

Some cohort studies [14–16] have found that oral care using an antiseptic agent and toothbrushing reduced the incidence of VAP compared with no oral care. The limitations of these studies are that a historical cohort was compared with a prospective cohort, and that it is not possible to discriminate the influence of toothbrushing alone, since oral care in the intervention group involved the simultaneous use of both an antiseptic agent and toothbrushing.

In the randomized study published by Pobo et al. in 2009, which included a total of 147 patients receiving oral care with 0.12% chlorhexidine every 8 h, the patients were assigned to receive toothbrushing or not [17]. The authors found no significant differences between groups regarding the incidence of VAP (20.3% vs. 24.7%, $p=0.55$), microbiologically documented VAP (RR=0.84, 95% CI=0.41–1.73), mortality, days without antibiotics, duration of mechanical ventilation, or length of hospital or ICU stay. However, this study was stopped after enrolling only 37% of the expected number of patients (the sample size calculated was 400 patients), because the estimated time to recruit the number of patients needed to achieve a statistically significant difference was too long for a single-center study.

In the randomized study published by Munro et al. in 2009, including 471 patients mechanically ventilated for more than 24 h assigned into four groups (119 patients received chlorhexidine oral care, 113 patients toothbrushing, 116 patients toothbrushing and chlorhexidine oral care, and 123 patients usual care only), toothbrush use did not reduce the incidence of VAP [18]. In this study, we analyzed VAP at days 3, 5, and 7, and the authors found that chlorhexidine,

Table 5 Microorganism responsible for VAP and classifying VAP according to throat flora (first set of parentheses) and onset (second set of parentheses) of VAP

Microorganisms	With toothbrushing	Without toothbrushing
Total GPC	5 (2 PE, 3 SE) (1 EO, 4 LO)	5 (1 PE, 4 SE) (1 EO, 4 LO)
MSSA	2 (2 PE) (2 LO)	1 (1 PE) (1 LO)
MRSA	2 (2 SE) (2 LO)	3 (3 SE) (1 EO, 2 LO)
<i>Enterococcus faecalis</i>	1 (1 SE) (1 EO)	1 (1 SE) (1 LO)
Total GNB	16 (2 PE, 13 SE, 1 EXO) (7 EO, 9 LO)	19 (6 PE, 13 SE) (7 EO, 12 LO)
<i>Pseudomonas aeruginosa</i>	5 (4 SE, 1 EXO) (3 EO, 2 LO)	5 (5 SE) (5 LO)
<i>Stenotrophomonas maltophilia</i>	1 (1 SE) (1 LO)	1 (1 SE) (1 LO)
<i>Acinetobacter</i> spp.	1 (1 SE) (1 LO)	0
<i>Escherichia coli</i>	2 (2 SE) (1 EO, 1 LO)	3 (1 PE, 2 SE) (1 EO, 2 LO)
<i>Klebsiella</i> spp.	0	3 (2 PE, 1 SE) (1 EO, 2 LO)
<i>Enterobacter</i> spp.	2 (2 SE) (1 EO, 1 LO)	3 (1 EP, 2 SE) (2 EO, 1 LO)
<i>Serratia marcescens</i>	2 (2 SE) (1 EO, 1 LO)	0
<i>Proteus mirabilis</i>	1 (1 SE) (1 LO)	1 (1 PE) (1 LO)
<i>Haemophilus influenzae</i>	2 (2 PE) (1 EO, 1 LO)	1 (1 PE) (1 EO)
<i>Morganella morganii</i>	0	2 (2 SE) (2 EO)
Total	21 (4 PE, 16 SE, 1 EXO) (8 EO, 13 LO)	24 (7 PE, 17 SE) (8 EO, 16 LO)

VAP: ventilator-associated pneumonia; PE: primary endogenous; SE: secondary endogenous; EXO: exogenous; EO: early-onset pneumonia; LO: late-onset pneumonia; GPC: Gram-positive cocci; MSSA: methicillin-sensitive *Staphylococcus aureus*; MRSA: methicillin-resistant *Staphylococcus aureus*; GNB: Gram-negative bacilli

but not toothbrushing, reduced early VAP. However, in this study, data on VAP incidence beyond 7 days of mechanical ventilation were not reported.

The results of our study are consistent with those reported by Pobo et al. [17] and Munro et al. [18], since neither found significant differences in the incidence of VAP according to toothbrush use or not. Our study differed from that by Pobo et al. in that they used an electric toothbrush and we used a manual toothbrush; in the study by Munro et al., the toothbrush used was not described. In addition, our study involved a greater sample size (436 patients) to compare the efficacy of adding toothbrushing to chlorhexidine oral care in the VAP incidence reduction, compared with 147 patients in the study by Pobo et al. [17] and 235 patients in the study by Munro et al. [18].

The process of toothbrushing can give rise to certain complications, such as the appearance of oral bleeding in patients with severe coagulopathy due to the application of greater force than when applied by the patient. In addition, the action of toothbrushing could facilitate the accidental removal of the endotracheal tube, with the need for reintubation, and this fact has been associated with VAP in some studies [50–52].

These observations suggest that the oral cavity may be an important reservoir of pathogens that could cause VAP and that oral care could reduce the risk of VAP. For the moment, there is evidence that oral care with chlorhexidine reduces VAP; however, there is no evidence that toothbrushing provides an additional benefit.

Currently, there is insufficient evidence in the literature on oral hygiene to be able to recommend what measures should be performed in critically ill patients. Possible lines of research could include the chemical and mechanical aspects of oral care. With respect to the chemical agent, we could explore the type of agent used, the concentration, and the frequency of application. In relation to mechanical care, the use of a toothbrush and dental floss could be studied. And with respect to the brush, we could explore the effect of the brush type (manual or electric) and the frequency of application.

Our study has certain limitations. First, we did not perform an assessment of dental plaque, caries, and periodontal state. Another limitation is that we did not compare the incidence of complications, such as oral wounds and bleeding, and the rate of accidental removal of the endotracheal tube. Another point is that the study was performed within a single ICU, and the results may, therefore, not be applicable elsewhere. A further limitation is that the VAP diagnostic procedure was not invasive and we used only tracheal aspirate samples; however, a recent randomized clinical trial found no significant differences in clinical outcomes and the administration of antibiotics using a diagnostic strategy for VAP based on the quantitative culture of bronchoalveolar

lavage fluid and the non-quantitative culture of endotracheal aspirate [53]. Another limitation was the blinding process; since toothbrushing or not is visually apparent, the study could not be blinded for the attending nurses and physicians; however, the kind of oral care was blinded for the expert panel who established the diagnosis of VAP. Another limitation is that we have not checked compliance with the VAP prevention measures and oral care; the problem of deficiency in the adherence to the proposed measures has been demonstrated in previous studies [54–56]. Finally, in our study, we found an absolute difference in the VAP rate between groups of 1.3% and a 10% reduction in VAP incidence, and the statistical power was 12%. According to these previous results, we needed to include 13,576 patients in our study so as to reach an 80% statistical power.

Conclusion

Adding manual toothbrushing to chlorhexidine oral care does not help to prevent ventilator-associated pneumonia (VAP) among critical care patients on mechanical ventilation.

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