https://doi.org/10.15360/1813-9779-2024-4-2384

The Main Effects of the Original Oral Care Protocol Implementation in Patients on Invasive Mechanical Ventilation

Ilya N. Leyderman[1]*, Alexander O. Marichev[1], Igor U. Kasherininov[1], Natalia A. Lesteva[1], Alyona D. Ponomareva[1], Alexey O. Sivcov[2], Daria V. Ryabova[3], Mikhail M. Nosenko[4], Georgi A. Ablesimov[1]

[1] V. A. Almazov National Medical Research Center, Ministry of Health of Russia, 2 Akkuratova Str., 197341 Saint Petersburg, Russia
[2] Medical and Sanitary Unit «Neftyanik», 8 Yuri Semovskikh Str., Bldg. 1, 625000 Tyumen, Russia
[3] B. V. Petrovsky Russian Research Center for Surgery, 2 Abrikosov Lane, 119435 Moscow, Russia
[4] City Clinical Hospital № 17, Moscow City Health Department, 7 Volynskaya Str., 119620 Moscow, Russia

For citation: *Ilya N. Leyderman, Alexander O. Marichev, Igor U. Kasherininov, Natalia A. Lesteva, Alyona D. Ponomareva, Alexey O. Sivcov, Daria V. Ryabova, Mikhail M.Nosenko, Georgi A. Ablesimov.* The Main Effects of the Original Oral Care Protocol Implementation in Patients on Invasive Mechanical Ventilation. *Obshchaya Reanimatologiya = General Reanimatology. 2024;* 20 (4): 39–47. https://doi.org/10.15360/1813-9779-2024-4-2384 [In Russ. and Engl.]

***Correspondence to:** Ilya N. Leyderman, Leyderman_IN@almazovcentre.ru

Summary

Respiratory infection is the most common nosocomial infection found in intensive care units (ICUs). Dental plaques and oral mucosa can be colonized by respiratory pathogens within a few days after tracheal intubation. Oral care plays an important role in reducing the incidence of ventilator-associated infections.

Aim of the study. To evaluate clinical effectiveness of the original oral care protocol in ICU patients on invasive mechanical ventilation (IMV).

Materials and Methods. A multicenter, open-label, randomized, prospective, controlled study was conducted in 55 surgical ICU patients on long-term mechanical ventilation. Oral care for patients in the study group (group 1, *N*=30) included brushing with disposable toothbrushes and rinsing with an aqueous solution of 0.05% chlorhexidine digluconate three times daily. In the control group (group 2, *N*=25), patients' oral care was performed twice a day using sterile cotton swabs soaked in 0.05% aqueous chlorhexidine digluconate solution. The results were statistically processed using IBM SPSS Statistics 21. The relative risk (RR) of events was calculated with a 95% confidence interval (95% CI). The 95% CIs for event density parameters such as incidence rate (IR) and incidence rate ratio (IRR) were calculated using the exact Poisson test.

Results. The incidence of ventilator-associated pneumonia (VAP) was 13.6 cases [95% CI: 4.4; 31.7] per 1,000 ventilation days in group 1 and 23.6 cases [95% CI: 7.7; 55] per 1,000 ventilation days in group 2. The incidence of VAP was 1.74 times lower [95% CI: 0.4, 7.54] in group 1 vs. group 2 (*P*=0.398). The identity of oral and tracheal flora on day 7 was 20% in group 1 and 50% in group 2, RR=0.4, 95% CI: 0.165–0.973, *P*=0.037. Serum C-reactive protein levels were significantly lower in group 1 on day 7 of ventilation compared to group 2 (*P*=0.04).

Conclusion. The original oral care protocol, based on toothbrushing 3 times daily with a set of disposable toothbrushes and 0.05% aqueous solution of chlorhexidine digluconate, is associated with a tendency to lower VAP incidence per 1000 days of ventilation, significantly lower similarity between oral and tracheal flora, and lower serum C-reactive protein levels on day 7 of IMV. Further research on various aspects of oral care in ICU patients is needed, especially in the absence of complete clinical guidelines and clearly effective strategies for the prevention of ventilator-associated infections.

Keywords: oral care; mechanical ventilation; infectious complications; ventilator-associated pneumonia; disposable toothbrushes; cotton swabs

Conflict of interest. The authors declare that the study was supported by the Intersurgical Company, which provided oral care supplies and conducted a series of educational seminars for nurses to train them in oral care techniques for mechanically ventilated patients prior to initiation of the study.

Introduction

Respiratory infections are the most common nosocomial infections in intensive care units [1]. Approximately 60–65% of ICU patients require mechanical ventilation as a result of acute or decompensated chronic respiratory failure [2]. In some cases, ventilatory support is used not only to increase blood oxygenation and normalize lung ventilation, but also to keep the airway open and prevent aspiration. Ventilator-associated pneumonia (VAP) is one of the most common nosocomial infections, accounting for at least 25% of all nosocomial infections in the ICU, depending on the unit profile [3, 4].

Maintaining the upper airway with an endotracheal tube compromises the protective function of the airway mucosa, allowing various microorganisms to enter the lower airway directly or via silent aspiration [5]. Pathogenic microorganisms

such as *Pseudomonas* and *Escherichia coli* can enter the lower respiratory tract directly through the endotracheal tube (ET) or its leaky cuff, resulting in tracheobronchitis and pneumonia due to compromised natural immune defenses caused by critical illness. As a result, the overall risk of VAP associated with endotracheal intubation is highest during the first week of a patient's ICU stay [6]. Mucus accumulation in the supra-cuff space, mouth opening and dryness of the oral mucosa, impaired cough reflex, difficulties in removing secretions through the mouth and larynx, and poor oral hygiene can all contribute to the development of VAP [7]. Aspiration of microorganisms from the gastrointestinal tract is another important mechanism for oropharyngeal colonization during mechanical ventilation, which becomes an important source of opportunistic bacteria in the hypoxia associated with critical illness [8].

The use of systemic or inhaled antimicrobial chemotherapy alone may not be the most effective way to reduce VAP. N.Beloborodova et al. conducted a pilot study in 2021 that demonstrated the safety and comparable clinical efficacy of inhaled phagotherapy in neurological intensive care patients with recurrent nosocomial pneumonia [9].

Tracheal intubation is known to cause mechanical trauma to the oral mucosa, xerostomia and changes in plaque and oral flora, all of which increase the risk of respiratory infections [10, 11]. Potential respiratory pathogens can colonize dental plaque and oral mucosa within days of tracheal intubation. During this time, the spectrum of oral microorganisms gradually shifts from gram-positive to gram-negative species and yeasts, mainly due to a decrease in fibropectin, which regulates the activity of phagocyte-binding streptococci [12, 13]. Genetically identical pathogens have been isolated from plaque samples and bronchoscopic specimens from long-term ventilated patients suffering from various types of nosocomial respiratory infections, including tracheobronchitis and pneumonia [14, 15]. The mechanisms underlying this «microbial shift» are unclear, but could be attributed to both the physical presence of ET and other invasive procedures, as well as medication side effects. Plaque composition is known to be diverse and dynamic, with many microbial strains adapting to their environment [16]. Any change in saliva production or composition may affect the microbial composition of plaque. The presence of ET in critically ill patients with compromised immune status on antibiotics and other drugs causes significant changes in the salivary proteome [17].

Over the past decade, various mechanical and pharmacological methods have been used in clinics to reduce the «microbial load» of the oral mucosa and dental plaque. For example, a study conducted by Russian scientists found that combined multispectral decontamination of the upper respiratory tract, including the subligamentous space, with octenidine antiseptic and bacteriophage can reduce the risk of VAP and influence the respiratory tract microbiome [18].

Numerous randomized trials have shown that regular (at least every 12 hours) oral treatment with 0.2% aqueous chlorhexidine solution can reduce the risk of VAP [19, 20]. However, practical application of these recommendations has shown that the recommended concentration of chlorhexidine causes significant damage to the patient's oral mucosa.

Observational studies on the efficacy of toothbrushing in patients on prolonged mechanical ventilation show a decrease in the titer of microorganisms in the oral mucosa and dental plaque, but data on the incidence of VAP are somewhat contradictory [21]. Recently, there has been an increase in the use of various dental treatment modalities in ICU patients, which could be attributed to the development of new technological solutions to improve the quality of oral care. However, prospective randomized controlled trials have produced conflicting results regarding the effect of toothbrushing procedures in patients undergoing prolonged ventilation on the incidence of nosocomial respiratory infections [22, 23].

In the nursing literature, recommendations of low level of evidence for tooth brushing in adult patients with intubated trachea can be found. In contrast, current clinical and national guidelines for the prevention of VAP do not mention tooth brushing [24–26]. Surveys of nurses indicate that tooth brushing is time consuming and that nurses would like to receive specific training in this technique because it is «not as easy as it seems at first glance» [27, 28].

It should be recognized that current approaches to oral care and tooth brushing in ICU patients on prolonged mechanical ventilation are diverse and often defined by traditional approaches, which seems to be due to the lack of a clearly better technique or technology. Therefore, the issue of clinical efficacy and safety of new methods for prevention of nosocomial respiratory infections in patients undergoing prolonged mechanical ventilation requires further investigation.

Aim of the study was to evaluate the clinical efficacy of the original oral cavity treatment protocol based on the use of a set of disposable toothbrushes and chlorhexidine digluconate 0.05% aqueous solution in mechanically ventilated intensive care patients.

Materials and Methods

We conducted a multicenter, prospective, open-label, controlled study in patients in the surgical intensive care units of the Almazov National Medical

Research Center of the Ministry of Health of Russia (St. Petersburg, Russia), the Petrovsky Russian Scientific Center of Surgery (St. Petersburg, Russia), and the City Clinical Hospital No. 17 (Moscow, Russia).

The study was approved by the local ethics committee of the Almazov National Medical Research Center of the Ministry of Health of the Russian Federation, protocol No. 11–21 dated November 03, 2021.

Surgical intensive care unit patients on mechanical ventilation in the early postoperative period were randomized to one of two groups to evaluate the clinical efficacy of the original oral treatment protocol.

Randomization. The principal investigator generated the randomization table using the resource www.randomizer.org.

According to the table, all patients were randomized into two groups: main (*N*=30, group 1) and control (*N*=25, group 2).

Inclusion criteria for the study (all criteria were mandatory):

1. Patients of both sexes between 18 and 80 years of age.
2. Mechanical ventilation for more than 24 hours
3. Orotracheal intubation
4. Expected duration of mechanical ventilation of at least 72 hours
5. Informed consent of the patient to participate in this study, signed prior to surgery.

Study exclusion criteria (at least one criterion):

1. Prehospital aspiration
2. Antimicrobial therapy 14 days prior to surgery
3. Community-acquired pneumonia on admission
4. Chronic obstructive pulmonary disease (COPD)
5. Thoracic trauma
6. Missing teeth
7. Fat embolism
8. Decompensated chronic renal failure
9. Decompensated chronic liver failure
10. Pregnancy or lactation
11. Use of corticosteroids
12. Chemotherapy less than 6 months prior to study entry
13. Any other condition that the investigator deemed inappropriate for participation in the study.

Other exclusion criteria:

1. Mechanical ventilation for less than 72 hours
2. Development of pulmonary embolism
3. Hemothorax
4. Pneumothorax
5. Acute gastrointestinal bleeding
6. Failure to monitor clinical and laboratory parameters
7. Tracheostomy during the first 5 days of treatment
8. Erroneous inclusion in the study
9. Patient refusal to participate in the study
10. On investigator's decision in order to ensure patient safety
11. Violation of the protocol that may affect the outcome of the study and/or increase the risk to the patient.

Oral cavity treatment methods. From day 1 (the moment of tracheal intubation) to day 10 of ventilation, oral cavity treatment and teeth cleaning of patients were performed by nurses who had received prior in-person training. Patients in group 1 (main group) had their oral cavity cleaned three times a day with a set of disposable toothbrushes «OroCare-Q8» and chlorhexidine digluconate 0.05% aqueous solution. Patients in group 2 (control) had their oral cavity treated twice a day with a sterile cotton swab moistened with chlorhexidine bigluconate 0.05% aqueous solution.

In both groups, standard methods for prevention of nosocomial respiratory infections were used, such as closed suction systems, regular pressure control in the cuff of the endotracheal tube, elevation of the head end of the bed by 30 degrees and more, regular cleaning of the supra-cuff space, as well as timely transition to other modes of ventilation and minimization of sedation [29].

Patients' oral status was assessed daily using the Beck Oral Assessment Scale (BOAS). This scale, which is most appropriate for assessing oral mucosa and plaque, included five criteria, including inspection and assessment of the lips, gums and oral mucosa, tongue, teeth, and saliva. Each criterion was scored from 1 to 4, for a total score of 5 to 20. No changes were scored as 5 points, mild changes were scored as 6–10 points, moderate changes were scored as 11–15 points, and severe changes were scored as 16–20 points [30, 31].

Each patient underwent chest radiography, registration of sex and age, assessment with the Acute Physiology and Chronic Health Evaluation (APACHE) II and SOFA (Sequential Organ Failure Assessment) scales, measurement of body temperature, white blood cell count, blood C-reactive protein, procalcitonin levels, PaO_2/FiO_2, routine biochemical parameters, assessment of duration of mechanical ventilation and ICU stay. 28-day mortality was also evaluated. Ventilator-associated infectious events (VAP, VAT, asymptomatic airway colonization) were recorded by microbiological monitoring and serial assessment using the Clinical Pulmonary Infection Score (CPIS) [32]. VAP was diagnosed when the CPIS score exceeded 6 points.

Microbiological examination of tracheobronchial tree and oral cavity secretions was performed on days 3, 7, and 10 from the time of tracheal intubation. Samples were collected early in the morning before the next antiseptic and tracheal hygiene treatment. A colony forming unit (CFU)

titer $\geqslant 10^5$ was considered diagnostically significant and a titer $\geqslant 10^3$ was considered colonization [33].

The primary endpoint of the study was the incidence of VAP at day 10 of mechanical ventilation. Secondary endpoints were the incidence of pulmonary infiltrates, identity of oral and tracheal flora, oral cavity status as assessed by the BOAS scale, and laboratory parameters of systemic inflammatory response on day 7 of ventilation.

Statistical analysis. Statistical analysis was performed with IBM SPSS Statistics 21. Normality of distribution was tested using the Shapiro–Wilk criterion. In the case of normal distribution, data were presented as *M*±*SD* (95% CI) (*M* — arithmetic mean, *SD* — standard deviation, 95% CI — confidence interval), and in the case of non-normal distribution, as median with interquantile range of 25 and 75 percentiles. Pearson's χ^2 and Fisher's exact test were used to compare qualitative variables. Student's *t*-test was used to analyze normally distributed quantitative variables. In case of non-normal distribution, the Mann–Whitney test was used. The critical level of significance was considered to be *P*=0.05. We also calculated the relative risk (RR) of the event with 95% confidence intervals (CI 95%) and the number needed to treat (NNT) values. The 95% confidence intervals (95% CI) for incidence rate (IR) and incidence rate ratio (IRR) were estimated using the exact Poisson method [34]. The exact two-sided test with mid-P correction was used to test the null hypothesis of equality of incidence rates in the two groups [35].

Results and Discussion

From December 2021 to June 2023, 55 patients on mechanical ventilation in surgical intensive care units were evaluated. 8 patients were excluded for the following reasons: erroneous inclusion — 5 patients, protocol violation that could affect the results of the study — 3 patients. Initially, the groups did not differ in age, sex, APACHE II, SOFA, body and blood temperature (Swan–Ganz catheter thermosensor), blood biochemistry, white blood cell count, and blood C-reactive protein concentration. No significant differences in SOFA, CPIS and BOAS scores, body temperature, blood leukocyte count and serum procalcitonin (PCT) levels were found between the compared groups during the 10-day follow-up period. However, the level of serum C-reactive protein was significantly lower (*P*=0.04) in the main group on day 7 from the time of patient enrollment. There were no significant differences in parameters such as duration of mechanical ventilation and ICU length of stay between the groups (Table 1).

There was a trend toward a decreased incidence of pulmonary infiltrates in the main group on day 7 of the study (36% of cases in the main group and 59.1% in the control group) (Table 2).

The frequency of oral and tracheal flora identity on day 3 of ventilation did not differ between groups (*P*>0.05) (Fig. 1), on day 7 it was 20% in the main group and 50% in the control group (RR=0.4; 95% CI, 0.165–0.973; *P*=0.037) (Fig. 1, Table 3).

The incidence rate (IR) of infectious events per 1000 ventilation days was 13.6 cases of VAP [95% CI, 4.4–31.7] in the main group and 23.6 cases of VAP [95% CI, 7.7–55] in the control group. There was a trend toward a lower incidence of VAP in group 1, which was 1.74 times lower than in group 2 [95% CI, 0.4–7.54; *P*=0.39].

Poor oral hygiene in ICU patients undergoing prolonged mechanical ventilation is one of the main factors leading to plaque accumulation and subsequent excessive colonization by pathogens. According to various authors, the percentage of positive plaque cultures in ICU patients ranges from 23 to 60% [36, 37].

Respiratory pathogens isolated from the lungs are often genetically identical to strains of the same species isolated from dental plaque and the patient's tongue [38]. Therefore, it seems logical that improved oral hygiene could reduce the risk of ventilator-associated infections.

In this regard, many authors have investigated the feasibility of oral decontamination with antibacterial or antiseptic agents [38, 39]. Regarding oral decontamination with chlorhexidine solution in critically ill patients, some studies have reported a decrease in the frequency of positive bacterial cultures from plaque samples, and a number of meta-analyses have found a decrease in the incidence of VAP with its use [40, 41].

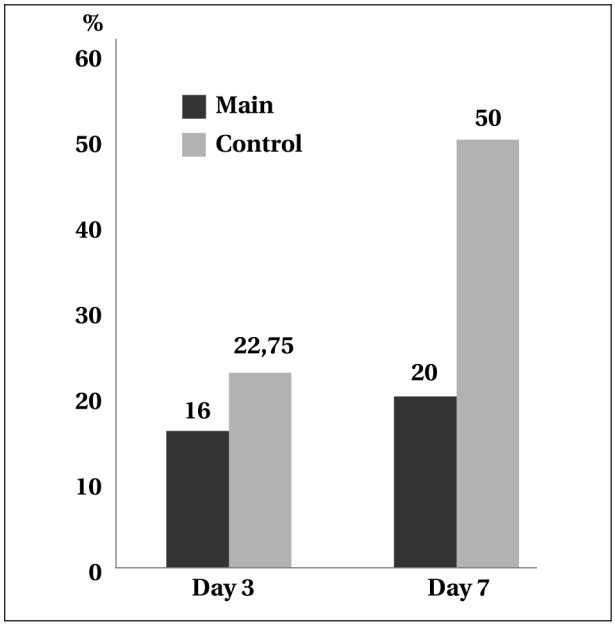

Fig. Frequency of oral and tracheal flora identity on days 3 and 7 of lung ventilation.

Table 1. Changes in clinical, laboratory, and paraclinical parameters in the groups during the study.

Parameter	Values in groups		*P*–value
	Group 1, *N*=25	Group 2, *N*=22	
Age, years	65 (53.5; 72)	70 (65; 74)	0.66**
APACHE II, points	13.05 (9.6–16.4)	13.1 (8.6–17.5)	0.98*
SOFA, points	8.33 (6.10–10.56)	7.64 (5.6–9.6)	0.65*
	Day 0		
Blood temperature, °C	37.4 (37.1; 37.8)	37.4 (37; 38)	0.78**
Body temperature, °C	36.85 (36.5; 37.3)	37.05 (36.7; 37.5)	0.5**
White blood cells, thousands per mm³	13.37 (11.3–15.4)	13.76 (11–16.5)	0.81*
CRP, mg/L	129.5 (90–169.1)	167.83 (100.3–235.3)	0.27*
BOAS , points	6 (5; 9)	8 (6; 11)	0.47**
CPIS , points	4.2 (3.1–5.4)	4.28 (2.9–6)	1.0*
	Day 1		
SOFA, points	7.5 (5; 13)	8.5 (5; 11)	0.95**
Blood temperature, °C	37.5 (37.2–37.8)	37.63 (37.2–38)	0.73*
Body temperature, °C	36.6 (36.5; 37.5)	37 (36.7; 37.6)	0.53**
White blood cells, thousands per mm³	13.5 (11.2–15.8)	13.55 (11.01–16.08)	0.99
CRP, mg/L	135 (105.5; 235.6)	195.4 (119; 273.4)	0.3**
BOAS , points	7.28 (6.05–8.5)	8.35 (6.5–10.2)	0.3*
CPIS , points	4.21 (3.3–5.08)	4.57 (3.2–5.8)	0.61*
	Day 3		
SOFA, points	8 (6–10.03)	7.2 (5–9.4)	0.6*
Blood temperature, °C	37.45 (37; 37.8)	37.4 (37.2; 37.6)	0.8**
Body temperature, °C	37 (36.7; 37.1)	37 (36.7; 37.3)	0.52**
White blood cells, thousands per mm³	12.2 (10.02–14.4)	12 (10.1–13.6)	0.83*
CRP, mg/L	129,6 (90,5–149,6)	147.67 (94.7–200.6)	0.3*
PCT, pg/L	0.7 (0; 10)	0.4 (0; 5.1)	0.88**
BOAS, points	7 (5; 8)	7 (5; 9)	0.74**
CPIS, points	5 (2; 6)	5 (3; 6)	0.66**
Pulmonary infiltrates, number and percentage of patients	7 (28.0 %)	7 (31.8%)	0.5***
	Day 5		
SOFA, points	8.4 (5.5–11.2)	6.8 (4.5–9.2)	0.36*
White blood cells, thousands per mm³	12.7 (10.1–15.3)	10.8 (9.6–12.1)	0.17*
CRP, mg/L	119.3 (81.6–157.04)	125.6 (81.06–170.2)	0.81*
BOAS, points	6.8 (5.1–8.6)	7.6 (6.6–8.7)	0.43*
CPIS, points	4.8 (3.4–6.2)	4.7 (3.3–6.2)	0.95*
	Day 7		
SOFA, points	7.4 (5.0–9.8)	6.4 (3.2–6.5)	0.56*
Blood temperature, °C	37.2 (37.1; 37.4)	37.5 (37.2; 37.8)	0.3**
Body temperature, °C	37 (36.8; 37.8)	37.05 (36.5; 37.2)	0.44**
White blood cells, thousands per mm³	12 (8.5; 14.4)	12.1 (9.7; 14)	0.8**
CRP, mg/L	75 (45; 184)	130.6 (33; 155.2)	0.04*
PCT, pg/L	1.4 (0; 14.2)	2.6 (0; 16.6)	0.3**
BOAS, points	7 (5.2–8,7)	8.1 (6.8–9.4)	0.36*
CPIS, points	5.05 (3.6–6.4)	4.5 (3.3–5.6)	0.55*
Duration of lung ventilation, days	15.5 (6; 20)	10 (4; 12)	0.2**
Length of stay in the ICU, days	19.6 (15.5–25.8)	14.9 (9.8–16.2)	0.65*

Note. Data are reported as *M* (95% CI) or as *Me (Q1; Q3)*. * — Student's *t*-test; ** — Mann–Whitney test; *** — Fisher's exact test; **** — Pearson's χ^2 test.

Table 2. Frequency of pulmonary infiltrates in groups on day 7 of lung ventilation.

Group	Patients, *N* (%)		Relative risk (RR)	95% CI	*P*-value	NTT
	Without infiltrates	With infiltrates				
1, *N*=25	16 (64)	9 (36)	0.61	0.325–1.141	0.113*	4.33
2, *N*=22	9 (40.9)	13.0 (59.1)				

Table 3. Frequency of oral and tracheal flora identity in the groups on day 7 of lung ventilation.

Group	Patients, *N* (%)		Relative risk (RR)	95% CI	*P*-value	NTT
	With non-identical flora	With identical flora				
1, *N*=25	20 (80)	5 (20)	0.4	0.165–0.973	0.037*	3.33
2, *N*=22	11 (50)	11 (50)				

Note. * — Fisher's exact test.

There is now strong evidence that oral care with chlorhexidine reduces the risk of VAP. However, there is no evidence that brushing has an additional beneficial effect.

Cohort studies conducted between 2006 and 2009 [42, 43] found that oral care with antiseptics and toothbrushing reduced the incidence of VAP compared with no care. Important limitations of these studies were the comparison of historical and prospective cohorts, which made it impossible to isolate the effect of toothbrushing on the incidence of infectious complications.

Analyzing the effect of oral care with and without a toothbrush, L. Lorente et al. [21] demonstrated that the clinical effects of using a chlorhexidine-impregnated gauze swab and a soft toothbrush with chlorhexidine were not significantly different. In this study, care was provided every 8 hours and, in addition to the above measures, patients' oral mucosa was irrigated with 10 ml of 0.12% aqueous chlorhexidine solution.

C. F. De Lacerda Vidal et al. [44] found a higher incidence of VAP in the group of patients using chlorhexidine-impregnated swabs than in the group using a brush impregnated with chlorhexidine gel. There was also a significant reduction in the duration of mechanical ventilation and ICU length of stay when the toothbrush was used.

In mechanically ventilated patients, we compared the use of two oral care protocols (traditional and original) that did not differ in the type and duration of antiseptic use (0.05% aqueous chlorhexidine solution) on the incidence of ventilator-associated infections.

We observed a 1.7-fold reduction in the incidence of VAP with triple brushing using disposable brushes with an aspiration system in combination with oral cavity treatment with 0.05% aqueous chlorhexidine solution. There was also a trend toward a decreased incidence of pulmonary infiltrates on day 7 of the study.

In a systematic review, L. de Camargo et al. showed that the addition of toothbrushes to the patient care program had no significant effect on reducing the incidence of VAP. However, L. de Camargo et al. analyzed studies in which tooth brushing was part of the oral care program and did not consider the similarities or differences in other interventions that affect the likelihood of developing ventilator-associated infections. They also compared the effectiveness of mechanical interventions and did not mention brushing frequency [45].

A study by J. Ory et al. [46] found a higher incidence of VAP with chlorhexidine-impregnated swabs compared to toothbrushes and chlorhexidine treatment. However, this study also did not examine the frequency of brushing during the day.

In our study, three treatments with disposable aspiration brushes combined with oral mucosal irrigation with 0.05% aqueous chlorhexidine solution resulted in a significant reduction in the incidence of identical oral and tracheal flora in the main group on day 7 of the study.

Limitations. The study had several limitations. First, the presence of caries and periodontal disease was not preassessed. We also did not compare the incidence of complications of the treatment procedure itself in the groups, such as wounds and bleeding of the oral mucosa, or the incidence of accidental removal of the endotracheal tube. The technique for diagnosing VAP was non-invasive, using only tracheal aspirate samples rather than culture of bronchoalveolar lavage fluid. Limitations also include both the open nature of the study, due to the obviousness of the manipulations, and the lack of a priori calculation of sample size.

Conclusion

The use of the original oral care protocol based on triple brushing with a set of disposable toothbrushes and 0.05% chlorhexidine digluconate aqueous solution is associated with significantly lower oral and tracheal mucosal flora identity and serum C-reactive protein on day 7 of invasive ventilation.

Further research on various aspects of oral care, especially in the absence of comprehensive clinical guidelines, and the development of effective methods to prevent ventilator-associated infections are needed.

Authors' contributions. All authors were equally involved in the design of the article, acquisition and analysis of the evidence, drafting and editing of the manuscript, and review and approval of the text.

References

1. *Fernando S.M., Tran A., Cheng W., Klompas M., Kyeremanteng K., Mehta S., English S.W., et al.* Diagnosis of ventilator-associated pneumonia in critically ill adult patients — a systematic review and meta-analysis. *Intensive Care Med.* 2020; 46 (6): 1170–1179. DOI: 10.1007/s00134-020-06036-z. PMID: 32306086.
2. *Zhao T., Wu X., Zhang Q., Li C., Worthington H.V., Hua F.* Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database Syst Rev.* 2020: 12 (12): CD008367. DOI: 10. 1002/ 14651858. CD008367.pub4. PMID: 33368159.
3. *Klompas M., Branson R., Cawcutt K., Crist M., Eichenwald E.C., Greene L.R., Lee G., et al.* Strategies to prevent ventilator-associated pneumonia, ventilator-associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 Update. *Infect Control Hosp Epidemiol.* 2022; 43 (6): 687–713. DOI: 10.1017/ice.2022.88. PMID: 35589091.
4. *Бычинин М.В., Антонов И.О., Клыпа Т.В., Мандель И.А., Минец А.И., Колышкина Н.А., Голобокова Я.Б.* Нозокомиальная инфекция у пациентов с тяжелым и крайне тяжелым течением COVID-19. *Общая реаниматология.* 2022; 18 (1): 4–10. *Bychinin M.V., Antonov I.O., Klypa T.V., Mandel I.A., Minets A.I., Kolyshkina N.A., Golobokova Ya.B.* Nosocomial infection in patients with severe and critical COVID-19. *General Reanimatology=Obshchaya Reanimatologya.* 2022; 18 (1): 4–10. (in Russ.&Eng.). DOI; 10.15360/1813-9779-2022-1-4-10.
5. *Wu D., Wu C., Zhang S., Zhong Y.* Risk factors of ventilator associated pneumonia in critically III patients. *Front Pharmacol.* 2019; 10: 482. DOI: 10. 3389/fphar. 2019.00482. PMID: 31143118.
6. *Edwardson S., Cairns* C. Nosocomial infections in the ICU. *Anaesth Intensive Care Med.* 2019; 20 (1): 14–18. DOI: 10. 1016/j.mpaic.2018.11.004.
7. *Yekefallah L., Shafaei M., Dehghankar L.* Strategies for the prevention of ventilator-associated pneumonia in the intensive care units: a review. *J Qazvin Univ Med Sci.* 2019; 23 (4): 352–363. DOI: 10.32598/ JQUMS.23.4.352.
8. *Ибадов Р.А., Сабиров Д.М., Эшонходжаев О.Д., Ибрагимов С.Х., Азизова Г.М., Угарова Т.Б.* Факторы риска развития и тяжелого течения вентилятор-ассоциированного трахеобронхита у пациентов на пролонгированной искусственной вентиляции легких. *Общая реаниматология.* 2023; 19 (5): 46–52. *Ibadov R.A., Sabirov D.M., Eshonkhodjaev O.D., Ibragimov S.Kh., Azizova G.M., Ugarova T.B.* Risk factors for the development and severe course of ventilator-associated tracheobronchitis in patients with prolonged mechanical ventilation. *General Reanimatology=Obshchaya Reanimatologya.* 2023; 19 (5): 46–52. (in Russ.&Eng). DOI: 10.15360/1813-9779-2023-5-2320.
9. *Белобородова Н.В., Гречко А.В., Гуркова М.М., Зурабов А.Ю., Зурабов Ф.М., Кузовлев А.Н., Меглей А.Ю., с соавт.* Адаптивная фаготерапия пациентов с рецидивирующими пневмониями (пилотное исследование). *Общая реаниматология.* 2021; 17 (6): 4–14. *Beloborodova N.V., Grechko A.V., Gurkova M.M., Zurabov A.Yu., Zurabov F.M., Kuzovlev A.N., Megley A.Yu., et al.* Adaptive phage therapy in the treatment of patients with recurrent pneumonia (pilot study). *General Reanimatology=Obshchaya Reanimatologya.* 2021; 17 (6): 4–14. (in Russ.&Eng.). DOI: 10.15360/1813-9779-2021-6-4-14.
10. *Munro C.L., Grap M.J.* Oral health and care in the intensive care unit: state of the science. *Am J Crit Care.* 2004; 13 (1): 25–33. PMID: 14735645.
11. *Stonecypher K.* Ventilator-associated pneumonia: the importance of oral care in intubated adults. *Crit Care Nurs Q.* 2010; 33 (4): 339–347. DOI: 10.1097/CNQ.0b013e3181f649a6. PMID: 20827066.
12. *Prendergast V., Hallberg I.R., Jahnke H., Kleiman C., Hagell P.* Oral health, ventilator-associated pneumonia, and intracranial pressure in intubated patients in a neuroscience intensive care unit. *Am J Crit Care.* 2009; 18 (4): 368–376. DOI: 10.4037/ajcc20096 21.PMID: 19556415.
13. *Munro C.L., Grap M.J., Elswick R.K. Jr, McKinney J., Sessler C.N., Hummel 3rd R.S.* Oral health status and development of ventilator-associated pneumonia: a descriptive study. *Am J Crit Care.* 2006; 15 (5): 453–460. PMID: 16926366.
14. *El-Solh A.A., Pietrantoni C., Bhat A., Okada M., Zambon J., Aquilina A., Berbary E.* Colonization of dental plaques: a reservoir of respiratory pathogens for hospital-acquired pneumonia in institutionalized elders. *Chest* 2004; 126 (5): 1575–1582. DOI: 10.1378/chest.126.5.1575. PMID: 15539730.
15. *Heo S.-M., Haase E.M., Lesse A.J., Gill S.R., Scannapieco F.A.* Genetic relationships between respiratory pathogens isolated from dental plaque and bronchoalveolar lavage fluid from patients in the intensive care unit undergoing mechanical ventilation. *Clin Infect Dis.* 2008; 47 (12): 1562–1570.DOI: 10.1086/ 593193. PMID: 18991508.
16. *Hojo K., Nagaoka S., Ohshima T., Maeda N.* Bacterial interactions in dental biofilm development. *J Dent Res.* 2009; 88 (11): 982–990. DOI: 10.1177/0022034 509346811. PMID: 19828884.
17. *Колесов С.А., Коркоташвили Л. В.* Протеом слюны и его диагностические возможности. *Клиническая лабораторная диагностика.* 2015; 60 (5): 54–58. *Kolesov S.A., Korkotashvili L.V.* The proteome of saliva and its diagnostic capabilities. *Clinical Laboratory Diagnostics=Klinicheskaya Laboratornaya Diagnostika.* 2015; 60 (5): 54–58. (in Russ.). URL: https: //cyberleninka.ru/article/n/proteom-slyuny-i-ego-diagnosticheskie-vozmozhnosti.
18. *Лапин К.С., Фот Е.В., Кузьков В.В., Киров М.Ю.* Влияние мультизональной деконтаминации верхних дыхательных путей на частоту вентилятор-ассоциированной пневмонии: многоцентровое рандомизированное пилотное исследование. *Вестник интенсивной терапии им. А. И. Салтанова.* 2023, 3: 66–81. *Lapin K.S., Fot E.V., Kuzkov V.V., Kirov M.Yu.* Impact of multizonal decontamination of upper respiratory tract on incidence of ventilator-associated pneumonia: multicenter randomized pilot study. *Ann Crit Care=Vestnik Intensivnoy Terapii im AI Saltanova.* 2023, 3: 66–81. (in Russ.). DOI: 10.21320/18-474 X-2023-3-66-81.
19. *Khan M., Mohamed Z., Ali S., Saddki N., Masudi S. M., Sukminingrum N.* Oral care effect on intubated patient with 0.2% chlorhexidine gluconate and tooth brushing in intensive care unit. *Journal of Advanced*

Oral Research. 2017; 8 (1): 1–8. DOI: 10.1177/2377960819850975.
20. *Zuckerman L. M.* Oral chlorhexidine use to prevent ventilator-associated pneumonia in adults: review of the current literature. *Dimens Crit Care Nurs*. 2016; 35 (1): 25–36. DOI: 10.1097/DCC.0000000000000154. PMID: 26627070.
21. *Lorente L., Lecuona M., Jimernez A., Palmero S., Pastor E., Lafuente N., Ramos M.J., et al.* Ventilator-associated pneumonia with or without toothbrushing: a randomized controlled trial. *Eur J Clin Microbiol Infect Dis*. 2012; 31 (10): 2621–2629. DOI: 10.1007/s10096-012-1605-y. PMID: 22422274.
22. *Hua F., Xie H; , Worthington H.V., Furness S., Zhang Q., Li C.* Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database Syst Rev*. 2016; 10 (10): CD008367. DOI: 10.1002/14651858.CD008367.pub3. PMID: 27778318.
23. *Dikmen Y.., Filiz Y.N.* A recent view and evidence-based approach to oral care of intensive care patient. *International Journal of Caring Sciences*. 2016; 9, 1177–1185. DOI: 10.1177/2377960819850975.
24. *Khasanah I.H., Sae-Sia W., Damkliang J.* The effectiveness of oral care guideline implementation on oral health status in critically ill patients. *SAGE Open Nurs*. 2019; 5: 23. DOI: 10.1177/2377960819850975. PMID: 33415244.
25. *American Association of Critical Care Nurses.* Oral care for acutely and critically ill patients. *Critical Care Nurse*. 2017; 37 (3): 19–21. DOI: 10.4037/ccn2017179. PMID: 28572113
26. *Yao L.-Y., Chang C.-K., Maa S.-H., Wang C., Chen C. C.-H.* Brushing teeth with purified water to reduce ventilator-associated pneumonia. *J Nurs Res*. 2011; 19 (4): 289–297 DOI: 10.1097/JNR.0b013e318236d05f. PMID: 22089654.
27. *Binkley C., Furr L.A., Carrico R., McCuren C.* Survey of oral care practices in US intensive care units. *Am J Infect Control*. 2004; 32 (3): 161–169. DOI: 10.1016/j.ajic.2003.05.001. PMID: 15153928.
28. *Jones H., Newton J.T., Bower E.J.* A survey of the oral care practices of intensive care nurses. *Intensive Crit Care Nurs*. 2004; 20 (2): 69–76. DOI: 10.1016/j.iccn.2004.01.004. PMID: 15072774.
29. *Klompas M., Branson R., Cawcutt K., Crist M., Eichenwald E.C., Greene L.R., Lee G., et al.* Strategies to prevent ventilator-associated pneumonia, ventilator-associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 Update. *Infect Control Hosp Epidemiol*. 2022; 43 (6): 687–713. DOI: 10.1017/ice.2022.88. PMID: 35589091.
30. *Beck S.* Impact of a systematic oral care protocol on stomatitis after chemotherapy. *Cancer Nurs*. 1979; 2 (3): 185–199. PMID: 255358.
31. *Collins T., Plowright C., Gibson V., Stayt L. Clarke S., Caisley J., Watkins C.H., et al.* British Association of Critical Care Nurses: evidence-based consensus paper for oral care within adult critical care units. *Nurs Crit Care*. 2021; 26 (4): 224–233. DOI: 10.1111/nicc.12570. PMID: 33124119.
32. *Gaudet A., Martin-Loeches I., Povoa P., Rodriguez A., Salluh J., Duhamel A., Nseir S.* Accuracy of the clinical pulmonary infection score to differentiate ventilator-associated tracheobronchitis from ventilator-associated pneumonia. *Ann Intensive Care*. 2020; 10 (1): 101. DOI: 10.1186/s13613-020-00721-4. PMID: 32748025.
33. *Sahai H., Khurshid A.* Statistics in epidemiology: methods, techniques, and applications. CRC-Press; 1st edition; 1996: 172-174. ISBN: 0-8493-9444-9.
34. *Gerald van Belle, Lloyd D. Fisher, Patrick J. Heagerty, and Thomas S. Lumley.* Biostatistics: a methodology for the health sciences. Second Edition; 2004. ISBN 0-471-03185-2.
35. *Fourrier F., Duvivier B., Boutigny H., Roussel-Delvallez M., Chopin C.* Colonization of dental plaque: a source of nosocomial infections in intensive care unit patients. *Crit Care Med*.1998; 26 (2): 301–308. DOI: 10.1097/00003246-199802000-00032. PMID: 9468169.
36. *Shi Y., Huang Y., Zhang T.-T., Cao B., Wang H., Zhuo C., Ye F., et al.* Chinese guidelines for the diagnosis and treatment of hospital-acquired pneumonia and ventilator-associated pneumonia in adults (2018 edition). *J Thorac Dis*. 2019; 11 (6): 2581–2616. DOI: 10.21037/jtd.2019.06.09. PMID: 31372297.
37. *El-Solh A.A., Pietrantoni C., Bhat A., Okada M., Zambon J., Aquilina A., Berbary E.* Colonization of dental plaques: a reservoir of respiratory pathogens for hospital-acquired pneumonia in institutionalized elders. *Chest*. 2004; 126 (5): 1575–1582. DOI: 10.1378/chest.126.5.1575. PMID: 15539730.
38. *Bahrani-Mougeot F.K., Paster B.J., Coleman S., Barbuto S., Brennan M.T., Noll J., Kennedy T., et al.* Molecular analysis of oral and respiratory bacterial species associated with ventilator-associated pneumonia. *J Clin Microbiol*. 2007; 45 (5): 1588–1593. DOI: 10.1128/JCM.01963-06. PMID: 17301280.
39. *Fourrier F., Dubois D., Pronnier P., Herbecq P., Leroy O., Desmettre T., Pottier-Cau E., et al*; PIRAD Study Group. Effect of gingival and dental plaque antiseptic decontamination on nosocomial infections acquired in the intensive care unit: a double-blind placebo controlled multicenter study. *Crit Care Med*. 2005; 33 (8): 1728–1735. DOI: 10.1097/01.ccm.0000171537.03493.b0. PMID: 16096449.
40. *Carvajal C., Pobo A., Díaz E., Lisboa T., Llauradó M., Rello J.* Oral hygiene with chlorhexidine on the prevention of ventilator-associated pneumonia in intubated patients: a systematic review of randomized clinical trials. *Med Clin (Barc)*. 2010; 135 (11): 491–497. DOI: 10.1016/j.medcli.2010.02.039. PMID: 20557902.
41. *Labeau S.O., Van de Vyver K., Brusselaers N., Vogelaers D., Blot S.I.* Prevention of ventilator-associated pneumonia with oral antiseptics: a systematic review and meta-analysis. *Lancet Infect Dis*. 2011; 11 (11): 845–854. DOI: 10.1016/S1473-3099 (11)70127-X. PMID: 21798809.
42. *Mori H., Hirasawa H., Oda S., Shiga H., Matsuda K., Nakamura M.* Oral care reduces incidence of ventilator-associated pneumonia in ICU populations. *Intensive Care Med*. 2006; 32 (2): 230–236. DOI: 10.1007/s00134-005-0014-4. PMID: 16435104.
43. *Hutchins K., Karras G., Erwin J., Sullivan K.L.* Ventilator-associated pneumonia and oral care: a successful quality improvement project. *Am J Infect Control*. 2009; 37 (7): 590–597. DOI: 10.1016/j.ajic.2008.12.007.PMID: 19716460.
44. *de Lacerda Vidal C.F., de Lacerda Vidal A.K., de Moura Monteiro J.G., Cavalcanti A., da Costa Henriques*

A.P., Oliveira M., Godoy M., et al. Impact of oral hygiene involving toothbrushing versus chlorhexidine in the prevention of ventilator-associated pneumonia: a randomized study. *BMC Infect Dis.* 2017; 17 (1): 112. DOI: 10.1186/s12879-017-2188-0. PMID: 28143414.

45. *de Camargo L., da Silva S.N., Chambrone L.* Efficacy of toothbrushing procedures performed in intensive care units in reducing the risk of ventilator-associated pneumonia: a systematic review. *J Periodontal Res.* 2019; 54 (6): 601–611. DOI: 10.1111/jre.12668. PMID: 31206663.
46. *Ory J., Raybaud E., Chabanne R., Cosserant B., Faure J.S., Guérin R., Calvet L., et al.* Comparative study of 2 oral care protocols in intensive care units. *Am J Infect Control.* 2017; 45 (3): 245–250. DOI: 10.1016/j.ajic.2016.09.006. PMID: 28341071.

Received 02.11.2023
Accepted 31.05.2024