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Effectiveness of supervised implementation of an oral health care protocol on ventilator-associated pneumonia patients in intensive care units: a double-blind multicenter randomized controlled trial

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SUMMARY

Background: The available scientific evidence suggests a significant association between oral bacteria and the incidence of ventilator-associated pneumonia (VAP).
Aims: The aim of this study was to determine the effectiveness of an oral health protocol in the prevention of ventilator-associated pneumonia.
Methods: In this multi-center RCT, conducted in the intensive care units of neurological patients in three general teaching hospitals of two provinces located in the west of the Iran, a consecutive sample of 200 intubated patients were initially recruited. Patients were randomly allocated to the intervention (received oral health care based on evidence-based oral health protocol) or control (routine oral health care) groups. Both groups received their prescribed treatment regimen for seven consecutive days. The percentage of VAP diagnoses as main outcome assessed using clinical pulmonary infection score (CPIS).
Findings: The rate of VAP in the intervention and control groups was 5% and 64%, respectively. The intervention reduced the risk of VAP by 97% and this difference was statistically significant ($P < 0.001$). The chance of VAP occurrence in patients with lower levels of consciousness in univariate and multivariate analysis was significantly higher (OR: 2.38; 95%CI: 1.11−5.26) $P < 0.05$).
Conclusion: The results of our study suggest that the use of a dynamic supervised oral health care guideline is more effective than the routinely used protocols in the intensive care units of hospitals.

Introduction

Pneumonia that occurs 48 hours after intubation (or tracheostomy) in a mechanically ventilated patient is defined as

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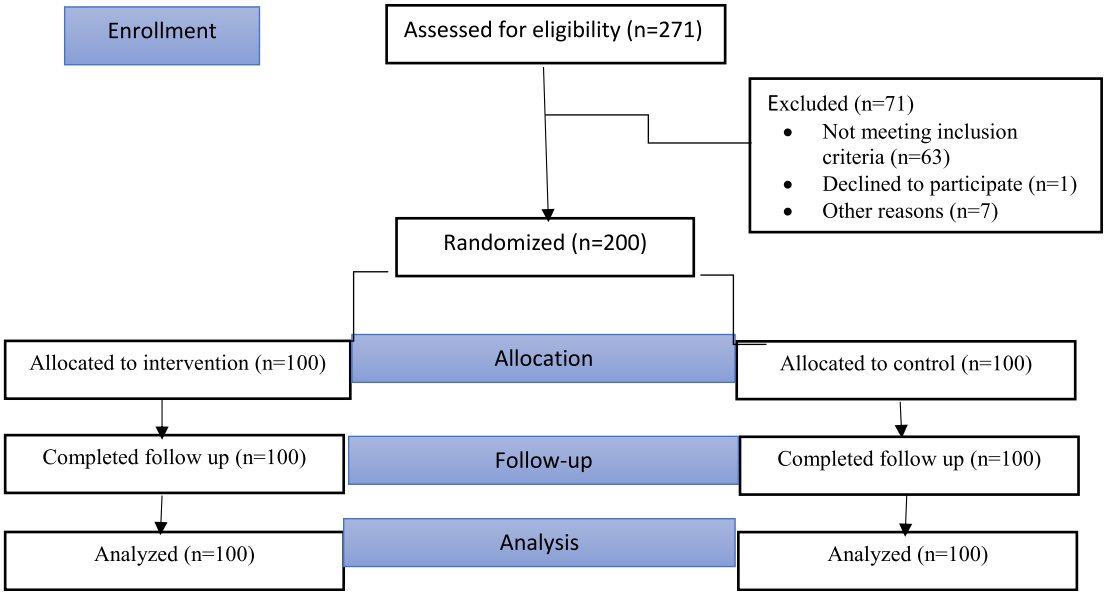

Figure 1. CONSORT flow diagram.

ventilator-associated pneumonia (VAP), if there is no evidence of pneumonia at the time of intubation. [1] Micro aspiration of bacterial-infected secretions from the oral-pharyngeal and gastric regions plays a role in the pathogenesis of the disease, in which the endotracheal tube plays a major role. VAP is one of the most common causes of death from mechanical ventilation as well as a common infection in the intensive care unit (ICU). [2] The most common organisms involved in VAP are *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Other important pathogens are enteric Gram-negative bacteria including Enterobacter species, *Escherichia coli*, *Klebsiella pneumoniae*, Proteus species, *Serratia marcescens*, and Acinetobacter species. [3].

Although placing the patient in a semi-recumbent position during mechanical ventilation is one of the most cost-effective ways to prevent VAP, it is important to pay attention to dental hygiene. Based on the available scientific evidence, the association between oral microbial flora and VAP is undeniable. [4] Because dental plaque can act as a reservoir for microorganisms that cause VAP, adherence to oral hygiene protocols can reduce the acquisition of this type of pneumonia. [5].

Two methods of mechanical interventions (including brushing and rinsing the oral cavity) and pharmacological interventions (including the use of antimicrobial agents) are used to remove dental plaque and microbes in the mouth. It should be noted that the application of routine oral health care guidelines might be difficult or impossible for a critically ill patient or their caregiver. Due to these limitations, plaque removal and its main components and microbial flora may be insufficient. [6,7].

Based on a review of existing scientific literature, there is little scientific evidence on the effects of oral health interventions on patients under mechanical ventilation. [8] In recent years, the development and implementation of evidence-based protocols for the oral health of critically ill patients with intubated hospitalization in the ICU has been considered. [9,10] The present study was conducted to evaluate the use of a supervised oral health care protocol to reduce the risk of VAP in two teaching hospitals in western Iran.

Methods

Subjects, study design and setting

This was a double-blinded multicenter randomized controlled trial that was conducted on 200 intubated patients in ICUs of three teaching hospitals of two provinces, Kurdistan and Kermanshah, west of Iran. Two teaching hospitals in Kermanshah province, Imam Reza and Taleghani, and a teaching hospital in Kurdistan province, Besat, were the centers of our trial. All steps of this trial were done based on Consolidated Standards of Reporting Trials (CONSORT) (Figure 1).

Inclusion and exclusion criteria

Age 18 years and older, no trauma to the mouth, no fracture of the face, intubation during the first 24 hours of arrival, intubation period of at least one and maximum 12 weeks, no hospitalization during the last 48 hours in any other hospital, [11] were the inclusion criteria. Critically ill patients (with the possibility of death within 48 hours), facial fractures and cases with possibility of endotracheal tube removal in less than 48 hours were among the exclusion criteria.

Randomization and blinding

The design of the present study was double blind. Patients and outcome assessors were unaware of patients' random allocation and type of intervention received.

Intervention

The control group received all standard oral care (rinsing the mouth with normal saline and mouth and lung suctioning, cleaning the tongue and teeth with gauze, rinsing with chlorhexidine 0.2%, and suctioning the rinsing solution). For the intervention group, in addition to all standard oral care, a

Table I
The clinical pulmonary infection score (CPIS)

Assessed parameter	Result	Score
Temperature (°Celsius)	36.5—38.4 °C	0
	38.5—38.9 °C	1
	≤ 36 or ≥ 39 °C	2
Leukocytes in blood (cells/mm3)	4,000—11,000/mm3	0
	< 4,000 or > 11,000/mm3	1
	≥ 500 Band cells	2
Tracheal secretions (subjective visual scale)	None	0
	Mild/non-purulent	1
	Purulent	2
Radiographic findings (on chest radiography, excluding CHF and ARDS)[a]	No infiltrate	0
	Diff use/patchy infiltrate	1
	Localized infiltrate	2
Culture results (endotracheal aspirate)	No or mild growth	0
	Moderate or florid growth	1
	Moderate or florid growth AND pathogen consistent with Gram stain	2
Oxygenation status (defined by PaO2:FiO2)	> 240 or ARDS	0
	≤ 240 and absence of ARDS	2

[a] CHF: congestive heart failure; ARDS: acute respiratory distress syndrome.

supervised implementation of oral health guideline including seven items was considered as follows.

1) Healthcare worker to wash hands and wear gloves.
2) Open the mouth and divide it into four quarters so that the oral examination can be done more easily from the upper right quarter to the lower right quarter. Report any abnormal findings such as white or red lesions, abnormal lumps, and halitosis on a form. (If such lesions are observed, nystatin should be prescribed according to the instructions: ten vials of 150,000 units/ml for two weeks/four times a day/two full droppers each time that should stay in the mouth for two minutes).
3) Increase the cuff pressure of the endotracheal tube to more than 20 mmHg while the patient's body is raised to 25 degrees, and then suction the subglottic area.
4) Turn the patient's head laterally and start brushing teeth and tongue, hard palate and gums in toothless patients with a baby toothbrush and toothpaste containing fluoride (not antibacterial). Brushing should be repeated every 8—12 hours for at least five minutes in each time.
5) Use normal saline solution to rinse your mouth after brushing and then suction (can spray normal saline on the teeth using a syringe)..
6) Use chlorhexidine gluconate 0.2% to rinse the patient's mouth, throat thoroughly, and suction after one to two minutes.
7) Every four hours, apply a moisturizing gel on all the tissues inside the mouth and then apply Vaseline on the lips with a finger.

Outcome and measures

Baseline data including demographic (age and sex) and clinical characteristics (hospitalization cause, Glasgow coma scale (GCS), the decayed, missing, and filled teeth (DMFT) index, having red lesions) were gathered for all studied patients before randomization. The main outcome of this study was VAP; there is no globally accepted gold standard for its diagnosis. Clinical criteria, the clinical pulmonary infection score (CPIS), initially described by Johanson *et al*. and suggested by Centers for Disease Control and Prevention (CDC), was used to assess for VAP. This tool consists of clinical, microbiological, physiological and radiological evidence and provides a numerical value to predict the presence/absence of VAP (Table I). Scores can range between 0 and 12 and a score of ≥ 6 indicates the presence of VAP. [12,13].

Blinding

This was a double-blind trial so that patients and outcome assessors were blinded to the intervention allocation of study subjects.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from a member of family (guardian) of each patient. Proposal of this study was assessed and approved by ethic committee in Kurdistan University of Medical Sciences (Ethic code: IR.MUK.REC.1395.59). The trial protocol was also registered in Iranian Registry of Clinical Trials (IRCT) with trial ID: IRCT20220215054026N1.

Statistical analysis

The SPSS 22 software package was used to analyze the data. Continuous variables were summarized using mean and standard deviation and compared using Student's t-test for between the two groups. The distribution of qualitative/categorized data were summarized using frequency and percentage and compared in intervention and control groups using Chi-2 test.

Table II
Baseline demographic and clinical characteristics of study participants

Variable	Intervention (%), n=100	Control (%), n=100	*P*-value
Age (Y), mean± SD	39.6±13.9)	37.8±13.8)	0.67
Female sex, n (%)	45 (45)	55 (55)	0.16
GCS, mean± SD	6.46 ±1.2	6.45±1.2	0.95
DMFT, mean± SD	17.15±4.97	15.92±4.54	0.07
Red or white lesions, n (%)	25 (25)	17 (17)	0.16
Hospitalization cause			
CVA, n (%)	52 (53.6)	46 (46.94)	0.39
TBI, n (%)	18 (41.86)	25 (58.14)	0.23
Brain tumor, n (%)	15 (53.57)	13 (46.43)	0.68
Car accident, n (%)	15 (48.39)	16 (51.63)	0.85

GCS: Glasgow Coma Scale; **DMFT:** Decayed, Missing and Filled Teeth; **CVA:** Cerebrovascular accident; **TBI:** Traumatic Brain Injury.

Since the outcome variable (VAP occurrence) was dichotomous, and to control potential confounders, we assessed the impact of oral health care on VAP occurrence through logistic regression modeling. Statistical significance was considered at a *P* value of 0.05 or less for all comparisons.

Results

Of the 200 patients included in this study, 146 patients were from Kermanshah province (Imam Reza and Taleghani hospitals) and 64 patients were from Kurdistan province (Kowsar hospital). All patients (100 individuals in the intervention group and 100 individuals in the control group) remained until the end of the study based on primary randomization and entered into the analysis. Table II shows the demographic and clinical characteristics of the two groups. Based on the results of baseline data comparison, the intervention and control groups were comparable in terms of almost all potentially confounding variables and there was no statistically significant difference between the two groups in terms of age, sex, GCS and reason for admission to the ICU (Table II).

The results showed that the rate of VAP in the intervention and control groups was 5% and 64%, respectively. In other words, the intervention reduced the risk of VAP by 97% and this difference was statistically significant (P <0.001). Table III shows the occurrence of VAP in both intervention and control groups as well as in terms of different variables. The chance of VAP occurrence in patients who had received the supervised oral health care protocol was 33.3 (14.28—97.08) times lower than the control group. As shown in Table III, apart from the difference in the occurrence of VAP in the intervention and control groups, the only variable that had a significant effect on the incidence of VAP was patient GCS, so that the chance of VAP occurrence in patients with lower levels of consciousness in univariate and multivariate analysis was significantly higher (P <0.05). The chance of VAP occurrence in patients with lower levels of consciousness in univariate and multivariate analysis was significantly higher (OR: 2.38; 95%CI: 1.11—5.26). Although the risk of VAP in women was slightly higher than men, this difference was not statistically significant (P-value = 0.102). The risk of VAP in patients under 35 years was slightly higher than patients 35 years and older, but this difference was not statistically significant (P-value = 0.839).

Discussion

Pneumonia resulting from ventilation is one of the most important and frequent hospital-acquired infections in intubated patients. Because of higher mortality, morbidity, and costs of VAP, there is a need to solicit further research to find more effective preventive strategies. VAP has been suggested as a quality-of-care indicator in hospitals.

The aim of this study was to evaluate the effect of an oral health care protocol on the risk of VAP in intubated patients admitted to ICU of hospitals. The findings show that the proposed oral health protocol used for intubated patients significantly reduced the rate of VAP. Strict implementation of this protocol is economical and cost-effective, as well as important for the survival of patients.

In general, many studies have revealed the role of oral health cares in reducing VAP. For example, Wip *et al*. suggested that the oral health care protocol is an effective way to reduce the rate of pneumonia in patients admitted to intensive care units, but that the protocol should be updated on an evidence-based basis. [14] The protocol used in our study was designed based on existing scientific evidence. Some details of other similar interventions were added to our protocol, including hand washing, cuff pressure above 25 mm of water, brushing with baby toothbrush and toothpaste, moisturizing lips, change in patient position according to patient's condition, using chlorhexidine 0.2% mouthwash, and subglottic suctioning. [14].

Similar to our findings, a two-year study by Hutchins *et al.*,showed that using oral care every four hours reduced the percentage of VAP by 89.7%. The protocol used included brushing the teeth with cetylpyridinium chloride (changed to 0.12% chlorhexidine gluconate in 2007) using a suction toothbrush, cleansing the oral cavity with suction swabs treated with hydrogen peroxide every four hours, deeply oropharyngeal suctioning, replacement of oral suction catheter every 24 hours, brushing teeth twice a day without toothpaste, and moisturizing lips and oral mucosa [15].

Consistent to our study, Mori *et al*. compared 1,252 patients who received oral health care with 414 patients who did not receive the oral care protocol between 1997 and 2002. Their results indicated a significant reduction in the incidence of VAP in the intervention group. Their proposed protocol includes increasing tracheal cuff pressure, suctioning the secretions behind the cuff, placing the patient in a lateral position, examining the mouth, rinsing with diluted betadine, brushing and then rinsing the mouth with weakly acidic water, oral cavity suctioning and finally reducing Cuff pressure to the point. Nurses performed this care on a regular schedule during each working shift. [16] In another study, Panchabhai *et al*. evaluated the effect of using oropharyngeal cleansing with 0.2% chlorhexidine in comparison 0.01% potassium permanganate solution on reducing nosocomial pneumonia during ICU stay in patients admitted to the ICU. Their results showed that although the frequency of this type of pneumonia in two treatment groups was not significantly different, a significant reduction in the rate of pneumonia was observed in both groups compared to before the study. [17] In general, good oral health care is a main preventive measure to decrease the risk of death in intubated

Table III
Comparison of VAP occurrence between the two study groups

Variable	Percentage (95%CI) of VAP occurrence	*P*-value[a]	Crude OR (95%CI)	*P*-value[a]	Adjusted OR (95%CI)	*P*-value[b]
Treatment group						
Control	0.64 (0.55–0.73)	<0.0001	Ref.		Ref.	
Intervention	0.05 (0.007–0.09)		0.03 (0.01–0.07)	<0.001	0.03 (0.011–0.07)	<0.001
Gender						
Female	0.40 (0.31–0.49)	0.1	Ref.			
Male	0.29 (0.21–0.38)		0.61 (0.34–1.10)	0.110		
Age group						
Less than 35	0.35 (0.25–0.45)	0.8	Ref.	0.801		
35 and more	0.34 (0.25–0.42)		0.94 (0.52–1.69)			
GCS						
6 and less	0.41 (0.32–0.50)	0.035	Ref.		Ref.	
7 and over	0.14 (0.17–0.36)		0.53 (0.29–0.96)	0.036	0.42 (0.19–0.90)	0.026
DMF						
14 and less	0.32 (0.21–0.43)	0.620	Ref.	0.611		
15 and more	0.35 (0.27–0.44)		1.17 (0.63–2.18)			
Red lesion						
No	0.35 (0.27–0.42)	0.621	Ref.			
Yes	0.31 (0.17–0.45)		0.83 (0.39–0.74)	0.621		
Hospitalization cause						
CVA	0.29 (0.21–0.39)	0.370	Ref.			
Brain tumor	0.32 (0.16–0.52)		1.12 (0.45–2.78)	0.795		
Car accident	0.39 (0.22–0.58)		1.50 (0.65–3.49)	0.344		
TBI	0.44 (0.29–0.60)		1.88 (0.89–3.95)	0.094		

[a] Univariate analysis.
[b] Multivariate analysis.

patients. Mohamed El-Rabbany *et al*. published a systematic review of 28 trials, indicating that prophylactic oral health care could be associated with a reduction in the risk of hospital-acquired pneumonia and VAP in high-risk patients. [18].

Based on the data modeling of this study, in addition to the supervised implementation of oral health care, the level of patient's consciousness also played a major role in the occurrence of VAP. In a study by Munro *et al.*, The entry of oral-pharyngeal secretions into the lungs was identified as a major cause of VAP. [19] In a clinical trial conducted by Bergmans *et al.*, pharyngeal oral colonization was introduced as a key predictor for development of VAP among patients in the intensive care unit. [20].

Conclusion

Using different strategies for VAP prevention is a continuously evolving field. The results of our study suggest that the use of a dynamic supervised oral health care guideline is more effective than the routinely used protocols in the ICU of hospitals. In fact, all components of our developed protocol are evidence-based. Since these components together have been able to significantly reduce VAP, understanding the role of each of these components in VAP reduction requires further studies.

Ethics approval and consent for publication

This study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from a member of family (guardian) of each patient. Proposal of this study was assessed and approved by ethic committee in Kurdistan University of Medical Sciences (Ethic code: IR.MUK.REC.1395.59). The trial protocol was also registered in Iranian Registry of Clinical Trials (IRCT) with trial ID: IRCT20220215054026N1.

Authorship statement

Sharare Karimi: Conceptualization, Validation, Writing, Reviewing and Editing.

Khaled Rahmani: Writing, Original draft, Methodology, Data analysis, Supervision.

Ensi Koliaei: Data Collection, investigation, reviewing final manuscript.

Pooya Karimi: Data collection, investigation, reviewing final manuscript.

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Author contributions

SK and KR designed the study.
EK and PK involved in the data collection.
SK and EK and KR conducted all the study and analyzed the data.
KR drafted the manuscript.
All authors read and approved of the final manuscript.

Conflict of interest statement

The author(s) declared no potential conflicts of interest concerning this article's research, authorship, and publication.

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