



Analysis of oral risk factors for ventilator-associated pneumonia in critically ill patients

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Abstract

Objective This a cross-sectional study to evaluate the association between oral health findings and ventilator-associated pneumonia (VAP) among critically ill patients in intensive care units (ICU).

Material and methods Data were collected from medical records, and a detailed oral physical examination was performed on 663 critically ill patients on mechanical ventilation. Data were statistically analysed using univariate and logistic regression models relating the development of VAP with the oral findings.

Results At oral physical examination, the most frequent findings were tooth loss (568–85.67%), coated tongue (422–63.65%) and oral bleeding (192–28.96%). Patients with a coated tongue or oral bleeding on the first day of ICU hospitalization developed more VAP than did patients without these conditions (20.14 vs 13.69%, $p = 0.02$; 23.44 vs 15.50%, $p = 0.01$, respectively). In the logistic regression, a coated tongue and oral bleeding were considered independent risk factors for VAP development (OR = 1.61 (1.03–2.51) and OR = 1.69 (1.08–2.66), respectively).

Conclusions The presence of a coated tongue and oral bleeding in ICU admission could be considered markers for the development of VAP.

Clinical relevance The results of this paper reinforce the importance of proper maintenance of oral hygiene before intubation, which may lead to a decrease in the incidence of VAP in the ICU.

Keywords Ventilator-associated pneumonia · Risk factor · Oral health · Coated tongue

Introduction

It is becoming increasingly accepted that the oral cavity can be the site of origin for the dissemination of pathogenic microorganisms to distant sites, mainly in immunocompromised

patients [1]. One of these important infections is pneumonia, in which initiation and progression could be influenced by oral biofilm through the relocation of oral bacteria into the lower respiratory tract [2]. Some studies have associated oral bacteria-associated conditions, such as wearing dentures while sleeping, with a high risk of pneumonia and its complications [3].

In patients under mechanical ventilation in intensive care units (ICU), the endotracheal tube may act as a conductor of the microorganisms from the oral cavity to the lower airway, inducing the development of pneumonia [4, 5]. This invasion of microorganisms to the lower respiratory tract may lead to the development of ventilator-associated pneumonia (VAP). VAP is defined as a pneumonia that occurs after 2 days (48 h) of intubation and is the most common type of nosocomial pneumonia [6, 7]. The predominant microorganisms responsible for infection in VAP are bacteria, mainly *Staphylococcus*

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aureus, *Pseudomonas aeruginosa*, and *Enterobacteriaceae* [8], which are also found in the oral cavity of hospitalised individuals [9]. VAP represents approximately 9 to 40% of all infections acquired by critically ill patients in ICU. The diagnosis of VAP represents an important cause of morbidity and mortality, as well as of extended hospital stays and higher hospital costs [10].

Therefore, this study was conducted to evaluate the possible association between oral health and VAP among critically ill patients in the ICU.

Methods

Patient selection

This is a cross-sectional study conducted at the University Hospital of Londrina in Brazil between February 2016 and April 2019. All critically ill patients on mechanical ventilation (MV) admitted to the adult ICU were included in the study. Patients who could not tolerate oral hygiene, e.g. patients with intracranial hypertension, were excluded. All participants and their legal guardians received oral and written information prior to participation. The legal guardian of unconscious patients or those with a decreased level of consciousness signed a consent form on the patient's behalf. The study protocol was reviewed and approved by the local Human Research Ethics Committee (CAAE 53864716.9.0000.523).

Clinicodemographic data, such as age, gender, reason for ICU admission, presence of comorbidities and VAP development, were obtained from medical records. The diagnosis of VAP was performed by the intensive care team. The simplified acute physiology score 3 (SAPS3), which consists of a severity scoring system to predict hospital mortality in critically ill patients, was calculated for each patient. The score includes variables that collect patients' characteristics before ICU admission (e.g. age, comorbidities), the circumstances of ICU admission (e.g. reason for ICU admission) and the presence and degree physiologic alterations at ICU admission (e.g. temperature, systolic blood pressure, laboratory test results) [11].

Oral physical examination

A dental team composed of residents and professors performed a detailed oral physical examination on the patient's first day of ICU hospitalization, including an examination of the patient's teeth and oral mucosa. A previous training of the team, including review of criteria and protocol, demonstrations and practice examination together with the responsible researcher, was carried out for calibration. In the oral examination, we analysed the following characteristics: tooth loss, presence of removable dental prosthesis, visible cavitation of

dental caries, dental mobility, oral/gingival bleeding, coated tongue, hairy tongue, depapillated tongue and any other mucosal lesion. After this oral physical examination, the same dental team performed a daily protocol of oral hygienization of teeth and oral mucosa with toothbrushes and gauze soaked in chlorhexidine digluconate 0.12%.

Statistical analysis

Data were analysed using the Stata/SE 13.0 (StataCorp LP, TX, USA). Comparisons between subgroups of categorical variables with VAP were calculated using Fisher's exact test and Student's *t* test. The Shapiro-Wilk test was used to perform normality test. Logistic regression was performed to identify independent predictors for VAP and control for possible confounders, such as age, comorbidities and reason for ICU admission, which are included in the SAPS3. A *p* value of < 0.05 was considered significant.

Results

The study sample consisted of 663 critically ill patients under mechanical ventilation, most of them with orotracheal tube (633–95.48%). Most subjects were male (413–62.29%), while 250 (37.71%) were female. The mean age of the patients was 57.02 years, with patient age ranging from 18 to 96 years. The most common reason for ICU admission was cardiovascular diseases, corresponding to 152 patients (22.93%), followed by trauma (112–16.89%), respiratory system diseases (79–11.92%), sepsis (77–11.61%), gastrointestinal disorders (60–9.05%), malignant neoplasms (21–3.17%), orthopaedic problems (19–2.87%) and kidney disease (17–2.56%). For the SAPS3, the mean was 67.91, and the range was from 17 to 114.

At the oral physical examination, we observed that most patients had some dental loss (568–85.67%), 309 (46.61%) of whom were totally edentulous. Eleven patients (1.66%) were intubated without removing removable prosthesis. Visible cavitation of dental caries were found in 155 patients (23.38%) and dental mobility in 28 (4.22%). When examining the patient's oral mucosa, 422 patients (63.65%) presented coated tongue, 12 (1.81%) had depapillated tongue, and 12 (1.81%) had hairy tongue. Some patients presented other oral mucosal lesions, most of which were oral ulcers (113–17.04%). In addition, 192 patients (28.96%) presented oral/gingival bleeding during the physical examination.

During the period of ICU hospitalization, 118 (17.80%) of the 663 patients developed VAP. Of those 174 patients, 43 (36.44%) were women and 75 (63.56%) were men, and the mean age of the patients was 53.47 years. For most of them, trauma (32–27.12%) or cardiovascular diseases (26–22.03%) were the reason for hospitalization, and the mean SAPS3 was

64.97. Patients with PAV had higher mean of SAPS3 comparing with patients who did not develop VAP according to the *t* test (64.97 vs 68.55; *p* = 0.02).

Fisher’s exact test revealed that patients with coated tongue or oral/gingival bleeding on the first day of ICU hospitalization developed more VAP than patients without these conditions (20.14 vs 13.69%, *p* = 0.02; 23.44 vs 15.50%, *p* = 0.01, respectively). The results from the association between all variables with VAP development are summarised in Table 1. In the logistic regression, these two variables, together with the SAPS3, sex, age and edentulism, were included in the analysis to control for possible confounders. The presence of edentulism was added in this analysis due to the large number of patients with this characteristic in our group, which could influence the risk. Coated tongue and oral bleeding were

considered independent risk factors for VAP development (coated tongue OR = 1.61 (95% CI 1.03–2.51), *p* = 0.03; oral bleeding OR = 1.69 (95% CI 1.08–2.66) *p* = 0.02) (Table 2).

Discussion

Pneumonia is an important cause of morbidity and mortality in the older population. Aspiration is an important pathogenic mechanism for pneumonia in the elderly, and poor oral health and hygiene are increasingly recognised as a major risk factor [12]. VAP remains one of the most common nosocomial infections in the ICU, affecting approximately 10 to 40% of the patients on mechanical ventilation, with an overall mortality of approximately 13% [13, 14]. Patients with VAP need longer periods of ventilatory assistance and hospital stays, in addition to an increased level of care and the need for additional procedures and treatments [10, 15]. The diagnosis of VAP represents approximately US\$40,000 of additional hospital costs per patient [10, 15]. Patients who develop VAP seem to have twice the risk of death compared with similar patients without VAP [16]. The percentage of patients on mechanical ventilation who developed VAP in our study (18.69%) was similar to the findings in the literature.

The oral cavity is an important source of bacteria that may cause lung infections, and several studies have associated the presence of oral biofilm with the development of VAP. Dental plaque, which is a complex biofilm relatively resistant to chemical control [17], accumulates rapidly in the oral cavity of critically ill patients [4]. Dental plaque in hospitalized patients with chronic lung diseases may serve as a reservoir of bacteria known to cause nosocomial pneumonia in susceptible individuals [18]. The oral cavity of patients on mechanical ventilation contains high amounts of respiratory pathogens such as methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa* and gram-negative bacilli [9]. These same pathogens were identified in the lungs of patients on mechanical ventilation who developed VAP [19, 20]. In a prospective study evaluating oral health and VAP development among 162 critically ill patients, Saenson et al. [21] found a strong association between poor oral health and increased risk for early-onset VAP. Munro et al. [5] reported that more dental plaque and lower salivary volume are correlated with a high rate of pneumonia. Azarpazhooh and Leake [22] also found that poor oral health significantly increases the risk of pneumonia, up to 9.6-fold. Nakajima et al. found that bacterial pneumonia, poor oral hygiene and severe dry mouth were significantly associated with oral candidiasis [23]. We found a high incidence of dental-related problems among our patients; however, only coated tongue and oral bleeding were considered independent risk factors for the development of VAP. Oral bleeding may be a sign of biofilm-induced gingivitis or be secondary to traumatic ulcers. In addition, the

Table 1 Presence of the main oral findings in the 663 patients according to the development of ventilator-associated pneumonia

Oral characteristics	Without VAP	With VAP	<i>p</i> *	Total
Coated tongue				
No	208 (86.31%)	33 (13.69%)	0.02	241 (100%)
Yes	337 (79.86%)	85 (20.14%)		422 (100%)
Oral/gingival bleeding				
No	398 (84.50%)	73 (15.50%)	0.01	471 (100%)
Yes	147 (76.56%)	45 (23.44%)		192 (100%)
Tooth loss				
No	76 (80%)	19 (20%)	0.31	95 (100%)
Yes	469 (82.57%)	99 (17.43%)		568 (100%)
Edentulism				
No	289 (81.64%)	65 (18.36%)	0.76	354 (100%)
Yes	256 (82.85%)	53 (17.15%)		309 (100%)
Caries				
No	417 (82.09%)	91 (19.91%)	0.49	508 (100%)
Yes	128 (82.58%)	27 (17.42%)		155 (100%)
Tooth mobility				
No	525 (82.68%)	110 (17.32%)	0.10	635 (100%)
Yes	20 (71.43%)	8 (28.57%)		28 (100%)
Intubated using removable prosthesis				
No	535 (82.06%)	117 (17.94%)	0.39	652 (100%)
Yes	10 (90.91%)	1 (9.09%)		11 (100%)
Hairy tongue				
No	534 (82.03%)	117 (17.97%)	0.34	651 (100%)
Yes	11 (91.67%)	1 (8.33%)		12 (100%)
Depapillated tongue				
No	535 (82.18%)	116 (17.82%)	0.63	651 (100%)
Yes	10 (83.33%)	2 (16.67%)		12 (100%)
Oral ulcers				
No	456 (82.91%)	94 (17.09%)	0.17	550 (100%)
Yes	89 (78.76%)	24 (21.24%)		113 (100%)

Data are presented as *n* (%). *p* values were calculated by the Fisher’s exact test (*p* < 0.05)

VAP ventilator-associated pneumonia

Table 2 Analysis of independent risk factors for ventilator-associated pneumonia

Oral findings/VAP	Odds ratio	Std. err.	<i>z</i>	<i>p</i> > <i>z</i>	95% conf. interval
Oral bleeding	1.69	.388	2.32	0.02	1.085–2.661
Coated tongue	1.61	.365	2.11	0.03	1.035–2.514
Edentulism	1.60	.447	1.71	0.08	0.9328–2.7739
Sex	0.97	.213	−0.10	0.91	0.6379–1.4997
Age	0.98	0.007	−1.73	0.08	0.9719–1.0017
SAPS3	0.98	0.007	−1.40	0.16	0.9748–1.004

Calculated by logistic regression ($p < 0.05$). The SAPS3 (simplified acute physiology score 3) is a severity scoring system to predict hospital mortality in critically ill patients

presence of blood clots in the oral cavity in patients with oral bleeding may favour bacterial proliferation and increase the risk of VAP.

The coated tongue forms on the dorsal surface and includes keratin, food residue and bacteria attached to the tongue papillae [24]. The surface of the tongue dorsum is filled with papillae, which increases the area available for bacterial colonization and facilitates the accumulation of desquamated epithelium and food debris [25]. It represents an important reservoir for bacteria, including periodontopathic bacteria [26]. Patients with a coated tongue present a higher number of salivary bacteria than patients without this alteration, and several reports have indicated that tongue cleaning reduced the total number of these microorganisms [27]. In a study involving 71 edentulous elderly adults in nursing homes, those with a coated tongue demonstrated significantly higher salivary bacterial counts than those without it, suggesting that a coated tongue could be a risk factor for aspiration pneumonia [28]. Kageyama et al. [29] also reported that tongue microbiota is related to the risk of and death via aspiration pneumonia among elderly patients living in nursing homes. Dry mouth has been associated with a coated tongue and VAP [30, 31]. In our study, we found a high incidence of coated tongue, representing 63.80% of all patients. It was also considered an independent risk factor for VAP development. These results reinforce the importance of adequate oral hygiene, including teeth and oral mucosa, especially the tongue. We know that in cases of illness, oral hygiene can be neglected.

Some studies have related tooth loss and denture use with the development of respiratory infections, possibly associated with aspiration of oral microorganisms from the mouth or prosthetic appliances [3, 32]. Suma et al. [33] found in their study that a large number of teeth lost may indicate an increased risk of mortality from pneumonia. Inai et al. [34] performed a study to determine the risk factors to postoperative complications after surgery under general anaesthesia according to respiratory function test results and oral conditions. They found that the most important risk factor for pneumonia was edentulism, and a possible explanation for this would be that dentures are usually taken off during intubation for

surgery, and their dentures are still off in the night following surgery, which might affect deglutition and may lead to microaspiration. In our study, a high proportion of patients were edentulous, which were independently at higher risk of VAP (OR 1.6 in multivariate model). Although this association was not statistically significant at the 5% significance level, which may be due to a lack of power, our results suggest a trend ($p = 0.08$) which needs to be further investigated in future studies with a larger sample size.

Given that the microbiota of the oral cavity plays an important role in the development of VAP, some studies have indicated that the initiation of the topical application of antiseptic agents, such as chlorhexidine, before intubation reduces nosocomial infections [19, 20]. The value of chlorhexidine oral care has been studied extensively. A meta-analysis including 12 randomized studies encompassing 2341 patients reported a significant overall risk reduction in VAP in patients with chlorhexidine hygienisation [35]. Besides, the oral hygiene with chlorhexidine has proven to reduce the incidence of *Staphylococcus aureus* colonisation in dental plaque of patients under mechanical ventilation [36]. Oral hygiene with chlorhexidine has been proposed as one of the five components of a core set of interventions in the ventilator bundle defined by the Institute for Healthcare Improvement. In our patients, daily oral hygienization with chlorhexidine was performed but only after ICU admission, and most patients were intubated beforehand.

Some limitations of our study should be mentioned. First, the oral physical examination was difficult in some cases, mainly due to the tube and their securement devices. Second, the caries diagnosis is much more complex than just a visual physical examination, involving detection of active white-spot lesions and sometimes with the help of interproximal radiographs. So, in our study, only visible cavitation was considered, not taking into account which and how many teeth involved.

Besides, a cross-sectional study has some limitation, once the investigator measures the outcome and the exposures in the study participants at the same time. However, this methodology can be used to calculate the odds ratio as a measure

of association, and it has been used to evaluate risk factors for pneumonia, including VAP [34, 37, 38].

According to our results and within the limits of the study, we may conclude that the presence of a coated tongue and oral bleeding in the ICU admission could be considered markers of VAP development in critically ill patients. Proper maintenance of oral hygiene, especially the tongue, before intubation may lead to a decrease in the incidence of VAP in the ICU.

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Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Ademar Takahama Junior, Vitoria Iaros de Sousa, Elisa Emi Tanaka, Evelise Ono, Fernanda Akemi Nakanishi Ito, Priscila Paganini Costa, Maria Beatriz Bergonse Pedrialli, Heliton Gustavo de Lima, Marco Aurélio Fornazieri, Lucienne Tibery Queiroz Cardoso and Claudia Maria Dantas de Maio Carrilho. Data collection was also performed by Leticia Sasaki Correia. The statistical analysis was performed by Ademar Takahama Jr. and Marco Aurélio Fornazieri. The first draft of the manuscript was written by Ademar Takahama Jr. and Vitoria Iaros de Sousa, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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