ORIGINAL ARTICLE

Effectiveness of a Dental Care Intervention in the Prevention of Lower Respiratory Tract Nosocomial Infections among Intensive Care Patients: A Randomized Clinical Trial

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OBJECTIVE. To evaluate whether dental treatment may enhance oral antisepsis, thus preventing more effectively lower respiratory tract infections (LRTIs) among critically ill patients.

DESIGN. Observer-blind randomized clinical trial.

SETTING. General intensive care unit (ICU) for adult patients.

PATIENTS. We analyzed data from 254 adult patients who stayed for at least 48 hours in the ICU.

INTERVENTION. Patients were randomized by means of rolling dice. The experimental group ($n = 127$) had access to dental care provided by a dental surgeon, 4–5 times a week. Besides routine oral hygiene, care also included teeth brushing, tongue scraping, removal of calculus, atraumatic restorative treatment of caries, and tooth extraction. The control group ($n = 127$) had access to routine oral hygiene only, which included the use of chlorhexidine as a mouth rinse, which was performed by the ICU nurse staff.

RESULTS. The primary study outcome was the LRTI incidence, which was 8.7% in the experimental group and 18.1% in the control group (adjusted relative risk [RR], 0.44 [95% confidence interval (CI), 0.20–0.96]; $P = .04$). Ventilator-associated pneumonia rates per 1,000 ventilator-days were 16.5 (95% CI, 9.8–29.5) in the control group and 7.6 (95% CI, 3.3–15.0) in the experimental group ($P < .05$). Mortality rates were similar between both study groups: 31.5% in the control group versus 29.1% in the experimental group (adjusted RR, 0.93 [95% CI, 0.52–1.65]; $P = .796$). No severe adverse events related to oral care were observed during the study.

CONCLUSION. Dental treatment was safe and effective in the prevention of LRTI among critically ill patients who were expected to stay at least 48 hours in the ICU.

TRIAL REGISTRATION. Brazilian Clinical Trials Registry, affiliated with the World Health Organization's International Clinical Trial Registry Platform: U1111-1152-2671.

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Nosocomial infections are considered a major public health threat worldwide, frequent among hospitals, from both high- and low-income countries.[1-5] Lower respiratory tract infections (LRTIs) are the most frequent nosocomial infections, particularly affecting patients admitted to intensive care units (ICUs). This fact leads them to stay longer in hospitals for 6.5–11 days and decreases their chances of surviving and getting discharged from the hospital. It has been observed that 34.5%–50% of patients affected by ventilator-associated pneumonia (VAP)—the most frequent LRTI—die. Also, there are estimates that VAP is directly responsible for the deaths of at least 13.0% of affected patients.[1,5-7] This scenario may become worse with the recent exponential escalation of antimicrobial resistance among gram-negative bacteria, which are the main etiologic agents of LRTI.[8]

It is well known that the pathophysiology of LRTI begins in the vast majority of cases with the migration of pathogenic bacteria from the oral cavity to the lower respiratory tract. In this sense, poor oral health and poor oral hygiene are considered relevant risk factors for nosocomial LRTI.[9,10]

Despite being supported by a strong rational logic, oral antisepsis as a preventive measure against LRTI has yielded

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conflicting results in previous studies.[11-16] We hypothesize that oral antiseptics may be effective only in the context of good oral health and hygiene and that the great microbial concentration on teeth biofilms and periodontal pockets may render them ultimately ineffective.

Thus, we aim to study whether a dental care program directly implemented by a dental surgeon—along with the usual oral antisepsis protocol—could help in preventing LRTI among intensive care patients.

METHODS

This study was a randomized observer-blind clinical trial. Inclusion started on January 1, 2011, and finished on August 8, 2013. All adult patients admitted to a single general ICU at the University Hospital of Ribeirão Preto Medical School, a tertiary care public facility, were eligible to participate in our study if they had a perspective of staying at least 2 consecutive days. Exclusion criteria were pregnancy and blood dyscrasia.

Study protocol was submitted and approved by institutional and national ethics review committees before being implemented. Written consent was obtained from all participating patients or from their relatives, in the case of unconscious patients.

Patients were randomized by the dental surgeon using dice. Patient blindness was unfeasible, but the hospital infection control team who was in charge of assessing all outcomes was blinded to the patient's allocation in the study.

The experimental group was submitted to dental care provided by a dental surgeon (plus the usual oral antisepsis protocol), 4–5 times a week, starting at admission and ending at ICU discharge. Dental care included vigorous teeth brushing with a child toothbrush, tongue scraping, removal of calculus, atraumatic restorative treatment of caries,[17] teeth extraction, and oral topical application of chlorhexidine. Although chlorhexidine 2.0% gel was preferable and used by unconscious patients, its inherent bitter taste precluded it to be used by fully conscious patients, who used chlorhexidine 0.12% solution. Both products were manufactured in our institution by hospital pharmacists.

The control group was submitted only to the routine oral hygiene protocol, which was provided by the ICU nurse staff 3 times a day and consisted of mechanical cleansing of the oral cavity with a spatula wrapped in gauze, followed by

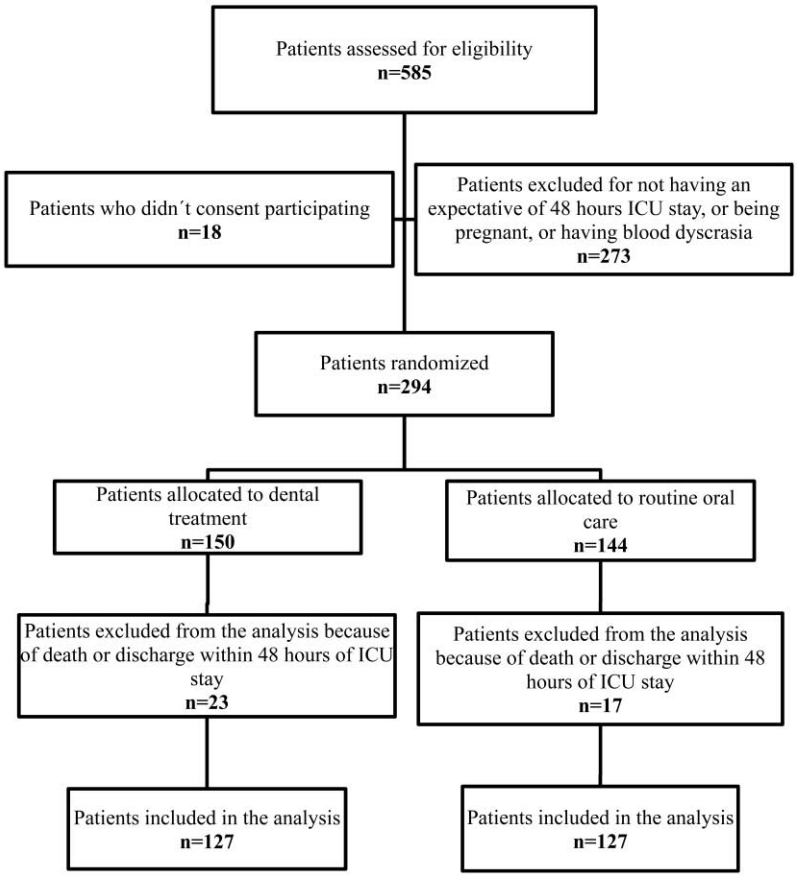

FIGURE 1. Flowchart of inclusion process in the study. ICU, intensive care unit.

TABLE 1. Baseline Clinical and Demographic Characteristics of Patients Submitted to Routine Oral Care or Dental Treatment at Intensive Care Unit (ICU) Admission

Baseline characteristic	Routine oral care (n = 127)	Dental treatment (n = 127)
Demographic		
Sex, male	66 (52.0)	67 (52.8)
Age, mean ± SD, years	60.1 ± 17.5	53.4 ± 18.3
Clinical		
LOS prior to ICU admission, mean ± SD, days	11.7 ± 13.3	13.2 ± 17.5
Diabetes mellitus	33 (26.0)	42 (33.0)
Hypertension	68 (53.5)	57 (45.0)
Renal failure	67 (52.8)	53 (41.7)
Hepatic failure	15 (11.8)	15 (11.8)
Heart failure	20 (15.7)	21 (16.5)
Cerebral vascular disease	14 (11.0)	14 (11.0)
Pulmonary thromboembolism	6 (4.7)	5 (3.9)
Respiratory infections	38 (29.9)	46 (36.2)
HIV/AIDS	5 (3.9)	3 (2.4)
Malignancy	44 (34.6)	38 (29.9)
Coronary disease	15 (11.8)	10 (7.9)
COPD	20 (15.7)	20 (15.7)
Autoimmune disease	19 (15.0)	18 (14.2)
Neuromuscular disease	1 (0.8)	6 (4.7)
Obesity	36 (28.3)	90 (70.9)
Malnutrition	26 (20.5)	15 (11.8)
APACHE II score, mean ± SD	23.3 ± 7.7	21.7 ± 8.0
Estimated risk of death, mean ± SD	47.3 ± 26.1	44.4 ± 26.1
Reason for ICU admission		
Respiratory failure	91 (71.6)	101 (79.5)
Shock	72 (56.7)	66 (51.2)
Compromised mental status	44 (34.6)	37 (29.1)
Major surgery, postoperative	26 (20.5)	23 (18.1)

NOTE. Data are no. (%) of patients, unless otherwise indicated. AIDS, acquired immunodeficiency syndrome; APACHE II, acute physiology and chronic health disease classification system II; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; LOS, length of stay; SD, standard deviation.

topical application of chlorhexidine 0.12% or 2.0%, according to the level of consciousness, as described above.

All data were collected prospectively, on the basis of the patients' medical records and physical examination of patients. To compare our study populations, we collected baseline clinical and demographic characteristics—including oral health status and frequency of exposure to classical risk factors for LRTI—during ICU stay. Oral hygiene status was evaluated using the simplified oral hygiene index, according to the World Health Organization recommendation.[18]

Primary outcome was the incidence of LRTI during ICU stay. Secondary outcomes included LRTI-free survival, use of antimicrobial drugs, crude mortality and mortality attributable to LRTI, duration of mechanical ventilation, and length of stay in the ICU. Nosocomial LRTIs were diagnosed after 48 hours of ICU admission and until 48 hours after ICU discharge, by the hospital infection control team, following the Centers for Disease Control and Prevention criteria, current at the beginning of the study.[19] We acknowledge that this definition was changed during study implementation in January 2013, but we have decided to keep using the former definition so that each patient included in the study would be evaluated by the same criteria.[20]

Data were analyzed with the Stata program (ver. 9.0) using a Pearson corrected χ^2 test, 2-tailed Fisher exact test, Wilcoxon test, and a logistic regression model. Sample size was calculated on the basis of the previous LRTI incidence at the study site (20.0%), having an α of 5% and a study power $(1 - \beta)$ of 80%. For a 60% reduction in the baseline LRTI incidence, we estimated that 147 patients were needed in each arm of the study.

RESULTS

Figure 1 shows a flowchart of the inclusion process. From 585 patients potentially eligible to our study, we were able to include 294 patients, with 150 in the experimental group and 144 in the control group. Those who died or were discharged

TABLE 2. Oral Health Status of Patients Submitted to Routine Oral Care Protocol or Dental Treatment at Intensive Care Unit Admission

Characteristic	Routine oral care (n = 127)	Dental treatment (n = 127)
Edentulism	57 (44.9)	40 (31.5)
Caries	38 (29.9)	36 (28.3)
Residual tooth roots	25 (19.7)	18 (14.2)
Gingival inflammation	65 (51.2)	74 (58.3)
Periodontal pockets	44 (34.6)	30 (23.6)
Intraoral abscess	2 (1.6)	0 (0)
Mucositis	8 (6.3)	8 (6.3)
Intraoral candidiasis	3 (2.4)	1 (0.8)
OHI-S, mean ± SD	2.33 ± 0.9	1.96 ± 0.8

NOTE. Data are no. (%) of patients, unless otherwise indicated. OHI-S, simplified oral hygiene index; SD, standard deviation.

within the first 48 hours of ICU stay were excluded from the analysis because, from the infection diagnosis criteria, if they had any healthcare-associated infection at this point, this would be attributable to the original ward and not to the ICU.

Except for age and frequency of obesity, both study groups displayed similar baseline clinical features (Table 1). While age was slightly superior in the control group compared with the experimental group (mean, 60.1 vs 53.4 years), obesity was more frequent among experimental patients (70.9% vs 28.3%). Despite that, Table 1 also shows that, at baseline, both study populations were equally and severely ill, with a mean acute physiology and chronic health evaluation II (APACHE II) score of 23.3 and 21.7 for the control and experimental groups, respectively.[21]

Analyzing oral health status at admission (Table 2), we found that study populations were also similar, regarding most of the characteristics evaluated (exception of the frequency of periodontal pockets and edentulism, both more frequent in the control group). While the first one is a potential risk factor for LRTI, edentulism may be protective against LRTI because of the absence of teeth biofilm.

Table 3 describes the occurrence of classical risk factors for LRTI among our study population during ICU stay. Once again, we observed a quite similar distribution of those risk factors between the control and experimental groups of the study.

Table 4 presents the study primary outcome, which was the LRTI incidence, showing that dental treatment was superior to the routine oral care protocol in the prevention of VAP and all LRTI taken together (on univariate analysis) and only for the prevention of all LRTI (on multivariate analysis). This last one was performed using a logistic regression model, as predicted in the original protocol, including age and sex as independent variables and APACHE II score and length of stay prior to ICU admission as baseline severity markers. VAP rates per 1,000 ventilator-days were 16.5 (95% confidence interval [CI], 9.8–29.5) in the control group and 7.6 (95% CI, 3.3–15.0) in the experimental group ($P < .05$). We also calculated the number needed to treat in the prevention of 1 LRTI, which was 10.6. Table 4 also exhibits secondary outcomes, revealing that we could not find any statistical significant difference between the study groups.

Most of the episodes of LRTI (86.5%; 32/37) were microbiologically confirmed. Table 5 describes the distribution of etiologic agents isolated from patients with LRTI and their source, according to the allocation in our study groups. Nonfermentative gram-negative bacteria accounted for most of the episodes in both groups, which had a similar distribution of reported etiologic agents. No statistically significant difference was demonstrated.

The most common adverse events related to oral care were mucosal irritation and minor intraoral bleeding, which were more frequently observed among patients submitted to dental treatment (13.4% vs 6.3%; $P = .058$). No severe adverse event related to oral care was detected during the study period.

TABLE 3. Distribution of Risk Factors for Lower Respiratory Tract Infections among Patients Submitted to Routine Oral Care Protocol or Dental Treatment during Intensive Care Unit Stay

Risk factors	Routine oral care (n = 127)	Dental treatment (n = 127)
Mechanical ventilation	96 (75.6)	98 (77.2)
Tracheostomy	48 (37.8)	44 (34.6)
Nasogastric tube	109 (85.8)	107 (84.2)
Use of corticosteroids	76 (59.8)	71 (55.9)
Use of other immunosuppressive drugs	13 (10.2)	17 (13.4)
Vomiting	28 (22.0)	40 (31.5)
Thoracic or abdominal surgery	45 (35.4)	45 (35.4)
Use of a proton pump inhibitor	119 (93.7)	116 (91.3)
Nonrespiratory nosocomial infections	24 (18.9)	28 (22.0)
Use of antimicrobial drugs	110 (86.6)	113 (89.0)

NOTE. Data are no. (%) of patients.

TABLE 4. Primary and Secondary Outcomes of Patients Submitted to Routine Oral Care Protocol or Dental Treatment during Intensive Care Unit (ICU) Stay

Outcome	Routine oral care (n = 127)	Dental treatment (n = 127)	Crude RR (95% CI)	P[a]	Adjusted RR (95% CI)	Adjusted P[b]
LRTI						
Tracheobronchitis	5 (3.9)	5 (3.9)	1.00 (0.28–3.54)	1.000	0.98 (0.27–3.62)	.979
Pneumonia in nonventilated patients	1 (0.8)	0 (0)	…	1.000	…	1.000
Ventilator-associated pneumonia	18 (18.7)	8 (8.2)	0.38 (0.16–0.93)	.030	0.42 (0.17–1.04)	.062
All LRTIs	23 (18.1)	11 (8.7)	0.43 (0.20–0.92)	.027	0.44 (0.20–0.96)	.040
Temporal data, mean ± SD, days						
LRTI-free survival	9.0 ± 6.7	9.0 ± 8.2	…	.460	…	…
Mechanical ventilation	11.3 ± 9.0	10.7 ± 10.6	…	.225	…	…
Antimicrobial use	8.7 ± 8.0	8.2 ± 8.5	…	.442	…	…
Length of stay in ICU	10.9 ± 8.7	10.4 ± 9.8	…	.318	…	…
Mortality						
Discharge	87 (68.5)	90 (70.9)	1.11 (0.65–1.91)	.682	0.93 (0.52–1.65)	.796
Death related to LRTI infection	8 (6.3)	5 (3.9)	0.61 (0.19–1.92)	.393	0.75 (0.23–2.42)	.633
Death not related to LRTI infection	32 (25.2)	32 (25.2)	1.00 (0.57–1.76)	1.000	1.17 (0.64–2.15)	.603

NOTE. Data are no. (%) of patients, unless otherwise indicated. CI, confidence interval; LRTI, lower respiratory tract infection; RR, relative risk; SD, standard deviation.

[a] Pearson corrected χ^2 or 2-tailed Fisher exact test, as appropriate, for categorical variables; Wilcoxon test for unpaired samples for continuous variables.

[b] Logistic regression adjusted for sex, age, acute physiology and chronic health evaluation II score, and length of stay prior to ICU admission.

DISCUSSION

As we stated before, several studies addressing oral antisepsis as a preventive measure against LRTI have yielded conflicting results. Some of them revealed a protective effect associated with this procedure, while others revealed no clinical impact.[11-16] Complementarily, it is well known that organic burden may inactivate many antiseptic products, including chlorhexidine, and that teeth biofilms and periodontal pockets are reservoirs of both organic bioburden and large microbial concentrations. In this sense, if a good oral hygiene may not be accomplished in critical patients, the application of any oral antiseptic may be of no value at all.[22-24]

In most ICUs worldwide, oral care is performed by nurse staff, but they do not have enough training or legal permission to treat caries, remove calculus, drain intraoral abscesses, or perform tooth extractions, as critical patients may need.[25-27] In Brazil, many of these procedures are frequently needed because of the poor oral health of the general population, with a mean decayed/missing/filled/teeth index of 27.53 in the age range of 65–74 years.[28]

Our data support the hypothesis that a dental surgeon may make a difference in this scenario, thus enhancing the effect of oral antiseptics and preventing around 56.0% of LRTI episodes. Although other authors have reported having a dental surgeon within their ICU team,[29,30] to the best of our knowledge, this is the first study to address the impact of that on a relevant clinical outcome, such as the LRTI incidence. The number needed to treat of 10.5 suggests that intervention may be cost effective, if we consider that 1 VAP episode may produce an extra cost of US$10,019–US$25,072.[31,32]

We did not find a statistically significant difference in mortality rates between study groups, but it must be pointed out that 83.1% (64/77) of the patients included in the study who had death as outcome died of causes not directly related to LRTI. If we look at the other side, the advent of death related to LRTI infection was 38.1% less in the experimental group than in the control group (3.9% vs 6.3%). The fact that these differences have not reached statistical significance may be related to an insufficient sample size, since the power of the study was calculated taking into account the primary outcome. Thus, it is possible that larger studies may demonstrate such differences as well as regarding the other outcomes evaluated. Also, the mortality rates attributable to LRTI observed in this study were lower than those reported in other studies (13.0% on average), which may also have influenced our results.[7]

Adverse events were more common in the group assigned to dental treatment, but they were all mild or moderate and did not motivate any exclusion of the study. Prior to the initiation of the study, we were concerned about the possibility of major intraoral bleeding during sessions of dental treatment, which, fortunately, did not occur but could happen in patients with blood dyscrasia.

Our study is subjected to at least 3 limitations. First, our findings may not be generalized to all critical patients because of the fact that our inclusion criteria excluded both the less severe and the highly severe patients, whose expectations of ICU stay were fewer than 48 hours. Beyond that, the intervention may not produce the same clinical impact observed here in ICU populations with better baseline oral health status.

Second, this was not a double-blind study because patient

TABLE 5. Distribution of Etiologic Agents Isolated from Patients with Lower Respiratory Tract Infection and Their Source, according to Allocation to Routine Oral Care Protocol or Dental Treatment during Intensive Care Unit Stay

Microbiological data	Routine oral care (n = 23)	Dental treatment (n = 11)	P[a]
Etiologic agent classification			
Gram-positive cocci	3 (13.0)	3 (27.3)	.363
Nonfermentative gram-negative bacilli	15 (65.2)	10 (90.9)	.214
Enterobacteriaceae	1 (4.3)	0 (0)	1.000
Yeasts	1 (4.3)	0 (0)	1.000
All cultures negative	4 (17.4)	1 (9.1)	1.000
Source of positive cultures			
Blood culture	1 (4.3)	2 (18.2)	.239
Bronchoalveolar lavage	1 (4.3)	0 (0)	1.000
Tracheal aspirate	17 (73.9)	10 (90.9)	.384
Lung biopsy	1 (4.3)	0 (0)	1.000

NOTE. Data are no. (%) of patients. Some patients had more than 1 bacteria isolated, and some patients had bacteria isolated from different sources.

[a] Two-tailed Fisher exact test.

blindness was unfeasible due to the nature of the intervention. But considering that most of the patients were on natural or medicated unconsciousness during protocol implementation, and considering that most of the diagnostic criteria were based on clinical signs and radiological or laboratory findings rather than on clinical symptoms, we do not believe that this could represent a significant source of bias.

Finally, since various dental procedures were performed according to the patients' needs, we were not able to discriminate which of them were the most relevant and truly influenced the primary outcome.

CONCLUSIONS

Dental treatment was considered to be safe and effective for the prevention of LRTI among critically ill patients expecting to stay more than 48 hours in the ICU setting.

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