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Effects of dental plaque antiseptic decontamination on bacterial colonization and nosocomial infections in critically ill patients

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Abstract *Objectives*: To document in intensive care unit (ICU) patients the effect of dental plaque antiseptic decontamination on the occurrence of plaque colonization by aerobic nosocomial pathogens and nosocomial infections.
Design: Single-blind randomized comparative study.
Setting: A 16-bed adult intensive care unit in a university hospital.
Patients: Patients consecutively admitted in the ICU with a medical condition suggesting an ICU stay of 5 days and requiring mechanical ventilation.
Interventions: After randomization, the treated group received dental plaque decontamination with 0.2 % chlorhexidine gel, three times a day during the ICU stay. The control group received standard oral care.
Specific measurements: Dental status was assessed by the Caries-Absent-Occluded index; the amount of dental plaque was assessed by a semi-quantitative plaque index. Bacterial sampling of dental plaque, nasal and tracheal aspirate, blood, and urine cultures were done on days 0, 5, 10, and every week.
Main results: Sixty patients were included; 30 in the treated group and 30 in the control one (mean age: 51 ± 16 years; mean Simplified Acute Physiological Score II: 35 ± 14 points). On admission, no significant differences were found between both groups for all clinical and dental data. Compared with the control group, the nosocomial infection rate and the incidence densities related to risk exposition were significantly lower in the treated group (18 vs 33‰ days in the ICU and 10.7 vs 32.3‰ days of mechanical ventilation; $P < 0.05$). These results were consistent with a significant preventive effect of the antiseptic decontamination (Odds Ratio: 0.27; 95 % CI: 0.09; 0.80) with a 53 % relative risk reduction. There was a trend to a reduction of mortality, length of stay, and duration of mechanical ventilation.
Conclusions: An antiseptic decontamination of dental plaque with a 0.2 % chlorhexidine gel decreases dental bacterial colonization, and may reduce the incidence of nosocomial infections in ICU patients submitted to mechanical ventilation.

Key words Critical care · Nosocomial pneumonia · Oropharyngeal colonization · Dental plaque · Antiseptic decontamination · Chlorhexidine

Introduction

The majority of nosocomial infections occurring in patients hospitalized in intensive care units (ICU) are of endogenous origin. They follow a sequence of previous colonization at the oropharyngeal and intestinal levels [1] with subsequent infection occurring either by occult inhalation in the tracheobronchial tree or after bacterial translocation in the blood stream [2, 3]. The oropharynx is usually considered the main reservoir of bacterial colonization in the upper airways [4]. Oropharyngeal colonization by aerobic pathogens occurs very rapidly in ICU patients, due to acquired changes in local antibacterial resistance, i.e., mucosal desiccation and epithelial injuries, decreased Ig-A salivary content, reduced salivary secretion, and mechanical injury induced by nasogastric and endotracheal tubes. Mucosal adhesion of aerobic bacilli is then facilitated, and allows a rapid bacterial growth on pharyngeal mucosa [5, 6]. Surprisingly, the hypothesis has been barely considered that dental plaque might be involved in the sequence of initial colonization and may represent an additional, although not specific, source of nosocomial colonization and infections in ICU patients.

Dental plaque is a specific and highly variable structural entity resulting from colonization and growth of micro-organisms on the surfaces of teeth, soft tissues, and dental prosthesis. It is a dynamic and complex system that associates micro-organisms embedded in an extra-cellular matrix. Plaque originates from the colonization of surfaces by bacteria due to selective adherence mechanisms. Plaque mass grows by cumulative addition of aerobic, anaerobic, and filamentous micro-organisms and without mechanical elimination it can cover the entire tooth surface. It predominates on the sub- and supra-gingival surfaces of the teeth. Bacteria constitute approximately 70–80 % of the solid material and 1 mm^3 of plaque contents more than 10^8 bacteria with more than 300 different aerobic and anaerobic species [5]. Aerobic bacteria predominate at the supragingival level and anaerobic bacteria at the sub-gingival one, but aerobic pathogens are not usually present in the plaque. Numerous factors are involved in making the plaque flora resistant to colonization by aerobic pathogens [6]. However poor oral hygiene and lack of mechanical elimination are the main factors leading to proliferation and accumulation of dental plaque and subsequent colonization.

Elderly institutionalized patients and ICU patients represent a population at risk of dental plaque colonization by nosocomial pathogens, due to difficulties in oral hygiene, changes in salivary properties, and reduction of anaerobic flora by antibiotherapy. Poor oral hygiene may then contribute to the development of pneumonia [7]. To our knowledge, only three studies have specifically addressed this issue. In the institutionalized elderly population, a recent controlled study documented that oral care lowered the risk of pneumonia, with a significant increase in the relative risk of developing pneumonia when patients had no active oral care [8]. In critically ill patients the first study was done by Scannapieco et al. [9]. They studied 34 ICU patients who were prospectively compared to 25 non-ICU patients treated in a school of dental medicine. On admission, dental plaque was found colonized by aerobic pathogens in 62 % of ICU patients compared with 16 % of control patients. The amount of plaque was significantly higher in ICU patients but did not correlate with bacterial colonization. Sequential changes in dental status and plaque colonization during the ICU stay and their link with the occurrence of nosocomial infections were not documented. In 1998, we gave confirmation of these results in a prospective study including 65 ICU patients [10]. We found that dental plaque colonization occurred in about 40 % of patients on admission, with a significant increase in the amount of dental plaque during the ICU stay. When their length of stay in the ICU exceeded 10 days, 46 % of our patients acquired a colonization of dental plaque by nosocomial pathogens. Dental plaque colonization was highly predictive of concurrent or subsequent nosocomial infection with the same bacteria. Additionally, in selected cases, dental plaque colonization by gram-negative bacteria seemed to be the first source of infection.

According to these data, specific dental hygienic measures must be considered with the primary goal of preventing plaque colonization by nosocomial pathogens. Our previous study has shown that despite repeated standard oral care, the amount of plaque and the frequency of colonization increased during the ICU stay. This was likely to be explained by the lack of specific dental care. Taking into account the potential role for tooth brushing to lead to occult bacteremia, our findings suggested that the use of an antiseptic dental paste having a sufficient duration of action might be the better way to reduce the bacterial inoculum and avoid the risk of bacterial blood translocation from the dental site.

We designed the present prospective controlled study to document in ICU-ventilated patients the effect of dental plaque antiseptic decontamination on the occurrence of plaque colonization and nosocomial infections.

Patients and methods

Study design

The study was approved by the institutional ethics board of our hospital and done from June 1997 to July 1998 in our 16-bed tertiary-care medico-surgical ICU located in our university hospital. During that period, all patients admitted in the ICU were eligible for the study when they or their relatives gave informed consent

and fulfilled the following criteria: age > 18 years; medical condition suggesting an ICU stay of 5 days and requiring mechanical ventilation by oro- or naso-tracheal intubation or tracheostomy. Edentulous patients were excluded.

On admission, the patients were randomized into two groups according to a computer-generated balanced randomization table. In the patients included in the treated group (group T), a specific dental gel containing chlorhexidine at 0.2 % (Elugel, Inava Odonto-Stomatologie, Pierre Fabre Santé, Boulogne, France) was applied three times a day (at 08 h, 14 h, and 22 h) during their ICU stay. The chlorhexidine gel was chosen for the following reasons: its presentation identical to a dental tooth-paste tube is practical and easy to use at the bedside; its high viscosity is known to increase its adhesiveness to dental surfaces and to reduce its ability to be wasted in the oral cavity; it has a long duration of action; its ability to decrease the growth of dental plaque has been documented in previously published studies [11]. Practically, after mouth rinsing and oropharyngeal aspiration, the gel was applied directly by nurses over the dental and gingival surfaces of the patient by a sterile glove-protected finger. The gel was left in place and the oral cavity was not rinsed after application. Patients were allowed to drink or eat freely according to their own ability and medical condition. Conversely, the patients included in the control group (group C) received standard oral care including mouth rinsing with bicarbonate isotonic serum followed by a gentle oropharyngeal sterile aspiration four times a day during their whole ICU stay.

At the time of the study, it was impossible to obtain a placebo gel having the same colour and taste as the chlorhexidine gel and the study could not be done in a double-blind fashion. We decided to blind the physicians in charge from the results of dental bacteriological sampling, and the bacteriologist from the treatment allocation code. Moreover, the evaluation of nosocomial infections was done by the hygienist nurse and a physician not aware of the treatment given. Lastly, the effect of the antiseptic decontamination was studied in intention-to-treat analysis.

Clinical assessment of patients

The patients' severity of condition was assessed by measurement of the Simplified Acute Physiological score (SAPS II) [12]. This score takes into account three chronic health diagnoses, age and type of admission, and 12 physiologic variables. All data are collected within 24 h after admission in the ICU. The Omega score was used as an assessment of the intensity in care loads [13]. This score is officially accepted in France to measure and compare care loads. It takes into account all the diagnostic and therapeutic procedures performed throughout the ICU stay, each one being given a definite number of points. The Omega-day score refers to the number of Omega points divided by the number of days in the ICU. For instance each day of mechanical ventilation is given a 10-points score. An Omega-day score of 7 points is considered the lowest value consistent with the care load of an ICU patient.

Assessment of dental status

Assessment of dental status and bacterial plaque sampling were done by the same investigator. All patients were examined within 24 h after admission (day 0) and then between day 5 and 7, day 10 and 12, and every week when they were still in the ICU. Dental status was assessed by the Caries-Absent-Occluded dental index (CAO) described by Klein and Palmer [14]. This score is identical to the DMFT score, and is recommended by the World Health Organization and the International Dental Federation to measure dental status [15]. It is calculated as the sum of the Decayed (caried), Missing (absent), and Filled (occluded) teeth and could range from 0 (normal dental status) to 28 (all teeth absent or decayed). This score is different from the DMFS score which measures the presence of caries on all dental surfaces. In our study we chose the CAO (or DMFT) score, because the assessment of all dental surfaces was considered too difficult to be done in severely ill intubated patients. In our study a tooth was considered decayed when there was at least a decay in the superficial enamel (dental classification S1). The amount of dental plaque was assessed by a score modified from the semi-quantitative plaque index described by Silness and Loe [16]. The amount of plaque was scored from 0 to 3: the tooth surface was given 0 when it looked clean, 1 when it looked clean and supragingival plaque could be removed from its gingival third with a sharp explorer, and 3 when the tooth surface was covered by abundant deposits of plaque. Examination was done on the upper first premolars or when missing, on closest remaining teeth. Due to difficulties in oral examination, the assessment of dental plaque and periodontal disease could not be done on all teeth and a single score was given for each patient, representing the score of the tooth with the greatest amount of plaque. Changes in plaque score were assessed on the same teeth during the ICU stay.

Sampling of plaque for bacterial culture was done in the same teeth, on days 0, 5–7, 10–12, and every week. To avoid false negative results, the sampling was done at 0800 hours, just before application of the antiseptic decontamination in group T. The tooth surface was first carefully dried by a sterile gauze to avoid contamination by saliva. Samples of supragingival plaque were collected from the gingival third tooth surface by using sterile absorbent paper points (Mynol Block Professional Dental Products, Jersey City, N.J., USA). Each paper point was immersed in 1 ml of Ringer solution. The sample was immediately transported to the laboratory, vortexed for 3 min, and serially diluted in sterile saline. All dilutions were plated on blood-enriched agar with and without nalidixic acid, purple bromo-cresol, and heated blood with bacitracin, and then aerobically cultured at 37 °C during 72 h. All colonies were subcultured and identified by standard methods. Susceptibility tests were realized in semi-liquid medium (API ATB, bioMérieux, Marcy l'Etoile, France). Plaque culture was considered positive when concentration was 10^3 CFU/ml of Ringer solution. This bacteriologic protocol was aimed to specifically identify aerobic and facultative bacteria, and fungi. Dental plaque colonization by anaerobic bacteria was not assessed.

Assessment of colonization and nosocomial infections.

All patients were routinely submitted to nosocomial survey. Epidemiological data, risk factors, duration of exposition to risk factors, and bacteriological data were taken down by one hygienist nurse, independently from physicians in charge.

During the study, nasal and tracheal aspirate, and urinary samples were systematically drawn for bacterial cultures on admission and every fifth day. Colonization of venous and arterial catheters was documented by skin culture at the entry site (skin culture collection and transport system Culturette, Becton-Dickinson, Md., USA). When their skin culture were positive, catheters were systematically withdrawn and the catheter tip cultured according to the technique described by Brun-Buisson et al. [17]. Blood cultures and broncho-alveolar lavage (BAL) cultures were performed during the stay according to the clinical status. BAL was performed according to the technique of Chastre et al. [18]. Prophylactic and antibiotic policy in our ICU included written procedures of antibiotherapy and no selective digestive decontamination. Patients

were intubated either via the oral or nasal route according to the clinical status and the habits of physicians in charge. Anti-H2 medications were not used.

The following definitions were considered in the study: (1) colonization was defined as the isolation of micro-organisms from nasal swab, tracheal aspirate, urine, and catheter culture, without signs of clinical infection; (2) nosocomial infection was considered present on admission in the ICU when the patient had been admitted in the ICU after 24 h of stay at least in another ward (including the emergency ward) and when all criteria of infection were present on admission in the ICU or had developed within 2 days after admission; (3) nosocomial infection was considered acquired in the ICU if the clinical condition fulfilling the criteria developed after the patient was in the ICU for 2 days and until 5 days after discharge; (4) the diagnosis of nosocomial pneumonia was established with the following criteria: temperature above 38 °C or below 36 °C; presence of infiltrates on chest radiographs; leukocytosis ($> 10.10^3/mm^3$) or leukopenia ($< 3.10^3/mm^3$); positive culture from tracheal aspirate and/or positive culture of BAL. Tracheal aspirate cultures were considered positive at 10^6 CFU/ml, and BAL was considered positive at 10^4 CFU/ml; (5) the diagnosis of bacteremia was established with the following criteria: temperature above 38 °C or below 36 °C and one positive blood culture. Two positive blood cultures were required for coagulase-negative *Staphylococci*; (6) bacterial strains isolated from different sites were considered identical when the susceptibilities to all tested antimicrobial agents were similar.

Statistical analysis

Results are given in mean ± SD. The incidence of nosocomial infection was calculated as the number of nosocomial infections divided by the number of patients in each group. It is given in % of patients. The incidence density was calculated as the number of nosocomial infections divided by the number of days of risk exposition (length of stay and days of mechanical ventilation). It is given in ‰ days. Intergroup comparisons were made by ANOVA and Student's t-test. Comparisons of frequency, incidence, and density incidence were done by using contingency tables and the chi-squared test. Differences existing in baseline (Day 0) items between the two groups were analyzed by logistic regression with nosocomial infections as output. The efficacy of the decontamination protocol on dental plaque colonization and nosocomial infections was assessed by intention-to-treat analysis. The numbers of days free of nosocomial infections were compared between both groups by the Kaplan-Meier method, and differences were assessed by the log-rank test. The concordance between bacteria isolated from dental plaque and bacteria isolated during the nosocomial episodes was tested by the Kappa test. Statistical significance was considered at $P < 0.05$.

Results

Prior to our study we verified whether the chlorhexidine gel exhibited an antiseptic bactericidal activity on aerobic nosocomial pathogens in vitro. Five strains were studied: methicillin resistant *Staphylococcus aureus, Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa,* and *Candida albicans*. Each strain was cultured during 4 h in Müller-Hinton broth (4 ml), then submitted to a sequential 1/10 and 1/50 dilution. Control tubes containing 40 ml of the diluted bacterial culture and 40 ml Müller-Hinton were compared with tubes containing 40 ml of bacterial culture and 40 ml of chlorhexidine gel at 0.2 %. The quantitative bacterial growth was measured in control and chlorhexidine tubes just after dilution, after 1 h, 3 h, 6 h, and 24 h. Compared to control tubes where mean bacterial concentration increased from 1.10^5 to 2.10^9 in 24 h, no bacterial growth could be detected in chlorhexidine tubes at any time, giving confirmation of the strong bactericidal activity of the gel.

Table 1 Demographic characteristics compared between the treated *(T)* and the control *(C)* groups

Data	Group T ($n = 30$)	Group C ($n = 30$)	Statistical significance
Age (years)	51.2 ± 15.2	50.4 ± 15.5	NS
Secondary admission (n; %)	24 (80 %)	17 (53 %)	NS
Sex ratio (M/F)	19/11	19/11	NS
SAPS II (points)	37 ± 15	33 ± 13	NS
Omega score (points)	355 ± 359	424 ± 525	NS
Omega/day score	18 ± 6	18 ± 6	NS

Patients included

Sixty patients entered the study: mean age: 51 ± 16 years (range: 18–75); sex ratio: 63 % males / 37 % females; mean length of stay in the ICU: 21 ± 18 days (range: 18–85); mean SAPS II: 35 ± 14 points (range: 12–76); mean Omega score: 424 ± 451 points (range: 15–2462). Thirty patients were included in the control group and 30 in the treated group. On admission no significant differences were found between both groups for all demographic characteristics, SAPS II, Omega score, and Omega/day scores (Table 1). In the treated group, there was a trend to a higher number of patients admitted after hospitalization in another ward (secondary admissions) but no significant difference in mean age, SAPS II, CAO score, and dental plaque score could be found on admission between patients directly admitted and patients secondarily admitted to the ICU.

Assessment of dental status

All patients were examined on admission (day 0). Due to discharge from the ICU or death, the number of patients progressively decreased over the study period. In group C, 27 patients were still present in the ICU on day 5, 20 on day 10, 12 on day 17, and eight on day 24.

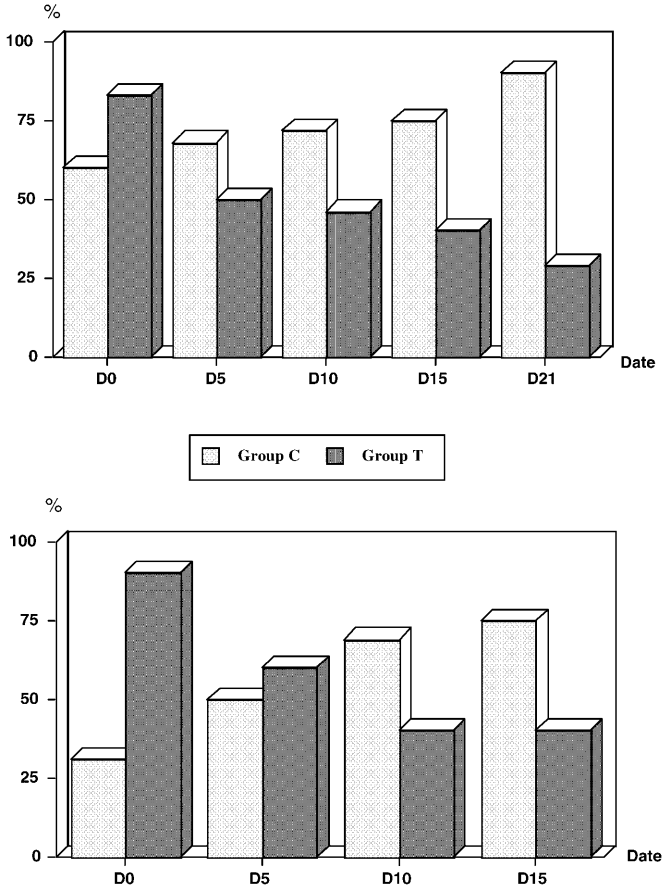

Fig. 1 Sequential changes in plaque scoring during the ICU stay. Percentages refer to the proportion of patients having a score > 1 in each group. *Top panel* all included patients ($n = 60$); *bottom panel* results in patients still present on day 15 ($n = 26$)

In group T, 23 patients were still present on day 5, 15 on day 10, 11 on day 17, and seven on day 24.

On admission mean value of the CAO score was 18 ± 8 in group C vs 16 ± 7 in group T (NS). The CAO score remained unchanged in both groups during the ICU stay.

Sequential changes in plaque scoring are shown in Fig. 1. On admission, mean plaque score was 1.7 ± 0.7 in group C vs 2.1 ± 0.7 in group T (NS). The plaque score was not different between patients directly admitted in the ICU and patients admitted after a previous hospital course (1.9 ± 0.8 vs 1.9 ± 0.6, respectively). Serial study of patients remaining in the ICU during 2 weeks or more showed that plaque score significantly increased in group C, with 75 % of patients having a score of 2 on day 17, contrasting with only 40 % in group T. Significant higher levels of plaque scores were found in group C on day 10, 17, and 24.

Table 2 Frequency of dental plaque colonization with aerobic nosocomial bacteria and *C. albicans*

Day	0	5–7	10–12	15–17	24	30
Control group	10/30 27 %	13/27 48 %	11/20 55 %	7/12 58 %	4/8 50 %	4/6
Bacterial species						
S. aureus	2	2	–	–	–	–
SCN	1	2	2	1	1	1
E. coli	2	2	–	–	–	–
E. aerogenes	1	2	2	–	1	–
P. mirabilis	–	1	1	–	–	–
P. aeruginosa	–	1	1	3	1	1
S. maltophilia	–	–	1	1	–	1
C. jeikii	–	–	1	–	–	–
A. baumannii	2	1	1	–	–	–
C. albicans	2	2	2	2	1	1
Treated group	4/30 13 %	7/23 30 %	7/15 46 %	4/11 36 %	2/7 28 %	2/5
Bacterial species						
S. aureus	1	–	–	–	–	–
SCN	1	2	2	–	1	1
E. coli	1	1	1	–	–	–
K. oxytoca	–	1	–	–	–	–
P. aeruginosa	–	–	–	1	–	–
S. marcescens	–	–	1	1	1	1
C. freundii	–	–	1	–	–	–
A. baumannii	–	2	2	2	–	–
C. albicans	1	1	–	–	–	–
Difference between groups	NS	$P < 0.05$	NS	NS	NS	ND

Colonization of dental plaque

On admission, 38 % (23/60) of dental plaque samples were found colonized by aerobic strains: 50 % (15/30) in group C; 26 % (8/30) in group T (NS). When plaque colonization was restricted to aerobic bacteria (excluding non-identified yeasts and aerobic bacteria considered saprophytic as for example non-hemolytic *Streptococcus*), 27 % of patients were found colonized in group C, and 13 % in group T (NS).

Frequency of dental plaque colonization and results of bacteriological sampling of dental plaque are given in Table 2. On day 5–7, there was a higher frequency of positive plaque samples in the control group than in the treated one. No significant differences could be found between both groups after day 10.

Effect of the antiseptic decontamination on nosocomial infections

On admission, there was no significant difference in the frequency of colonization of the nasal and tracheal sites between both groups: 58 % of nasal samples were found colonized by aerobic bacteria in group C vs 42 % in

Table 3 Results of plaque sampling and strains isolated in nosocomial infections acquired in the ICU

Group	Plaque pathogen	Days sampling	N.I.1	N.I 1 pathogen	Date N.I. 1	Strain identity	N.I. 2	N.I. 2 pathogen	Date N.I. 2	Strain identity
C	*S. aureus*	0–5–7	PN	*S. aureus*	7	Yes				
C	*S. coag neg*	10–15	PN	*S. aureus*	12	No				
C	*E. aerogenes*	0–5–10	BAC	*E. aerogenes*	10	Yes				
C	*Str. malto*	30	BAC	*S. aureus*	11	No	PN	*Str. malto.*	35	Yes
C	*A .bauman.*	0–5–10	PN	*A. bauman.*	10	Yes				
C	*S. aureus*	5	PN	*S. aureus*	12	Yes				
C	*C. albicans*	0 to 30	PN	*C. albicans.*	12	Yes				
C	*Str. malto.*	10–15	PN	*Str. malto.*	13	Yes				
C	*S. coag neg*	0–5–10	SIN	*S. coag neg*	10	Yes				
C	*P. aerugin.*	15	PN	*P. aerugin.*	16	Yes				
C	*A. bauman.*	0	PN	*A. bauman.*	11	Yes	PN	ND	25	?
C	*C. albicans*	0 to 15	PN	*C. albicans*	9	Yes	PN	*P. aerugin.*	33	No
C	*P. mirabilis*	5–10	PRT	*E. faecalis*	4	No	PN	*P. mirabilis*	9	Yes
C	*S. coag negE. aerogenes*	524	BAC	*S. coag neg*	17	Yes	PN	*E. aerogenes*	27	Yes
C	*S. aureus*	0	PN	*ND*	17	No	PN	*P. aerugin.*	29	No
C	*E. aerogenes*	5–10	PN	*E. aerogenes*	7	Yes	BAC	*B. fragilis*	10	No
C	*P. aerugin.*	5 to 30	BRC	*K. pneum.*	11	No	PN	*P. aerugin.*	25	Yes
T	*S. aureus*	0	BRC	*P. mirabilis*	5	No				
T	*A. bauman.*	10–15	PN	*A. bauman.*	10	Yes				
T	*C. freundii*	10	PN	*C. freundii*	12	Yes				
T	*A. bauman*	5 to 15	PN	*A. bauman.*	8	Yes				
T	*S. marscesc*	10 to 30	PN	*S. marsces.*	15	Yes	BAC	*S. marsces.*	22	Yes
T	*A. bauman.*	5 to 15	BAC	*A. bauman.*	5	Yes				
T	*Negative*	–	BAC	*C. perfring.*	19	No				
T	*P. aerugin.*	15	BAC	*S. coag neg*	10	No	PN	*P. aerugin.*	26	Yes

NI nosocomial infection, *PN* pneumonia, *SIN* sinusitis, *BAC* bacteremia, *BRC* purulent bronchitis, *PRT* peritonitis, *ND* not documented, *N. I 1* First nosocomial infection, *N. I 2* second infection

group T; 45 % of tracheal aspirate samples were found colonized in group C vs 28 % in group T. The logistic regression model taking into account the frequency of colonization of nasal samples, tracheal aspirate, and dental plaque did not show any significant influence of these variables in the occurrence of nosocomial infections (adjusted Odds Ratio: 1.15; 95 % CI: –4.9; 6.35; $P = 0.626$).

Three patients had already acquired a nosocomial infection prior to their admission in the ICU (two pneumonias in group C, one bacteremia in group T).

Seventeen patients (56.6 %) in group C acquired 25 nosocomial infections: 18 pneumonias, four bacteremias, one bronchitis, one peritonitis, and one sinusitis. Eight patients acquired two episodes of nosocomial infection. In group T, eight patients (26.6 %) acquired ten nosocomial infections: five pneumonias, four bacteremias, one bronchitis. Two patients had two episodes of nosocomial infection.

According to their susceptibility to antimicrobials, most strains isolated from dental plaque samples and during the nosocomial infection episode were found identical: 67 % in group C and 70 % in group T (Kappa test of the overall concordance: 0.30). Whatever the group, the concordance rate was higher in gram-negative than in gram-positive infections (68 % vs 50 %, respectively). Compared timing and results between plaque sampling and strains isolated in nosocomial infection are shown in Table 3.

Overall, the rate of nosocomial infection acquired in the ICU was significantly higher in the control group ($\chi^2 = 5.54$; $P = 0.018$). Compared with the control group, the nosocomial infections incidence density related to risk exposition (number of nosocomial infections for 1000 days in the ICU, and number of ventilator-associated pneumonias (VAP) for 1000 days of mechanical ventilation) was significantly lower in the treated group (18 vs 33‰ days and 10.7 vs 32.3‰ days, respectively, $P < 0.05$). These results were consistent with a significant preventive effect of the antiseptic decontamination on subsequent occurrence of nosocomial infections (Odds Ratio: 0.27; 95 % CI: 0.09; 0.80) with a 53 % relative risk reduction. The cumulative curves of stay in the ICU without acquired nosocomial infection estimated by the Kaplan-Meier analysis and results of the log-rank test are shown in Fig. 2. Compared with the control group, the treated group had a shorter length of stay in the ICU, a shorter duration of mechanical ventilation and a lower mortality rate (24 ± 19 vs 18 ± 16 days; 18 ± 20 vs 13 ± 12 days; and 23 vs 10 %, respectively) but these differences did not reach the statistical significance.

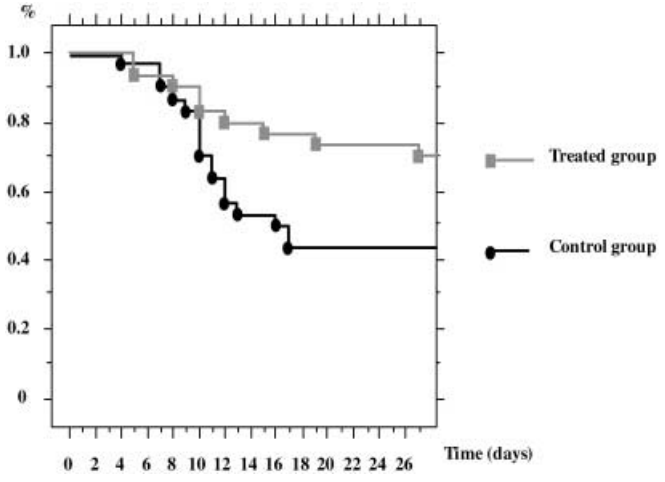

Fig. 2 Cumulative curves of stay in the ICU free of nosocomial infection compared between group T and group C (Kaplan-Meier analysis; log-rank test: $P < 0.05$)

Discussion

The results of our study give confirmation that dental plaque might play an important role as a reservoir of nosocomial colonization and support the hypothesis that antiseptic dental plaque decontamination might decrease the rate of acquired nosocomial infection in ICU patients.

The study was designed to compare a control group of patients submitted to standard oral care and a treated group who received specific dental care with application of a 2% chlorhexidine gel. Inclusion criteria were chosen to include a specific population of ICU patients more able to obtain benefit from the antiseptic decontamination, i.e., having a sufficient length of stay in the ICU to give time for the decontamination to be efficient. All patients had a general medical status requiring mechanical ventilation, with a high level of severity and care loads scores. Their mean SAPS II score reached 35 ± 14, indicating a 20% probability of death [12].

On admission no difference in demographics and general characteristics could be found between both groups and according to clinical criteria the randomization was considered well balanced. As in our previously published study [10], the included patients had a mean CAO score of 17 ± 8, indicating a general dental status identical to a control population at the same mean age. No significant difference could be found in the dental plaque score between both groups. The mean dental plaque score value reached 1.9 ± 0.7, indicating a poor dental hygiene status on admission.

The antiseptic decontamination had a significant effect on dental plaque growth. In the control group, the dental plaque score worsened throughout the ICU stay. When their stay exceeded 15 days, 90% of control patients had a score reaching 2 or 3, indicating a rapid growth of dental plaque despite standard oral care. On the contrary, the plaque score progressively decreased in treated patients with 70% of patients having a score of 0 or 1 on day 15. These results suggest that the antiseptic chlorhexidine gel has a powerful effect on dental plaque growth, even without mechanical elimination by tooth brushing [11].

The study gives confirmation of the high rate of dental plaque colonization in ICU patients. On admission the dental site was colonized by aerobic bacteria and yeasts in 38% of our patients and by aerobic pathogens in 20%. Ten days after admission, more than 50% of patients were colonized by aerobic pathogens at the dental site. Bacteriological study revealed that on admission some patients were colonized by highly resistant nosocomial pathogens with high concentrations of methicillin resistant *Staphylococcus aureus*, *Enterobacter aerogenes*, and *Acinetobacter baumannii*. These results demonstrate that the standard of oral care currently accepted in critical care units is insufficient to control plaque formation and oral infection by nosocomial pathogens.

The effect of the antiseptic decontamination protocol on plaque aerobic colonization must be discussed. On day 0 we did not find any clinical difference between both groups, but the number of included patients was low and there was a trend to a higher rate of dental, nasal, and tracheal colonization in control patients. However, these differences were not statistically significant and the logistic regression analysis did not show any significant influence of these variables on the rate of nosocomial infections. On day 5–7, treated patients had a lower rate of colonization and the overall evaluation of the decontamination protocol showed a trend to a higher rate of success in the treated group. After day 10, differences between both groups were no longer significant. This finding may have several explanations: (1) Even if nurses were asked to notify on a daily basis the number of decontamination procedures, we did not check the quality of the application at the bedside. Thus it is possible that patients having a prolonged length of stay may not have properly received the antiseptic gel; (2) An acquired resistance of nosocomial pathogens to the chlorhexidine gel might also account for this lack of long lasting effect. This possibility could not be documented in our study but seems unlikely since serial bacteriological sampling was more consistent with a non-eradication of the aerobic bacteria than with a secondary acquisition of resistance with a re-growth phenomenon; (3) The lack of bacterial eradication in some patients might be due to the constitution of a dental biofilm, embedding bacteria in the plaque matrix and rending them inaccessible to the antiseptic gel. This hypothesis is supported by the fact that in Scannapieco's study [9], as in ours [10], there was no correlation be-

tween plaque score and the rate of plaque colonization. In such a situation, dental plaque sampling might remain positive even though the decontamination procedure could protect gingival surfaces and oropharynx from bacterial growth and diffusion. Nevertheless, this hypothesis deserves further studies to document the constitution of such a dental biofilm in ICU patients. In such a case, mechanical elimination of dental plaque by tooth brushing may render the patients at risk of bacterial translocation from the dental site to the blood stream.

The decontamination procedure was associated with a decreased rate of nosocomial infections acquired in the ICU. The numbers of ICU days free of nosocomial infection were strikingly different between both groups, with a 53% relative risk reduction. The antiseptic decontamination seems to merely alter the rate of nosocomial pneumonias, since the incidence density of VAP was significantly different between both groups, with a three-fold reduction in the treated one. This result is consistent with the primary effect of the decontamination procedure which could reduce the amount of nosocomial bacteria in the oral reservoir and then decrease the consequences of occult inhalations in the trachea.

We cannot compare our results with any other study, since to our knowledge, this is the first study specifically designed to document the effect of a dental plaque decontamination procedure in ICU patients. Comparatively, DeRiso et al. [19] documented in a double-blind placebo-controlled study that a twice daily 0.12% chlorhexidine oral rinse significantly decreased the incidence of total nosocomial respiratory infection and systemic antibiotic use in patients undergoing open heart surgery. Their study included 180 patients in the control group and 173 in the treated one. In the latter the overall nosocomial infection rate decreased by 65% (13% vs 4%, respectively), the rate of gram-negative infections was significantly less and, as in our study, there was a trend to a reduced mortality rate. In that study the decontamination procedure included the rigorous application of the 0.12% chlorhexidine oral rinse on pharyngeal, tongue, gingival, and tooth surfaces. The possibility must then be considered that the procedure might have acted in part by dental plaque decontamination. Conversely in our study, we used a 0.2% chlorhexidine gel, whose chemical characteristics allow a low diffusion and a high adherence to dental surfaces. But due to its high permanence, a progressive diffusion of the antiseptic might occur in the oral cavity and then the decontamination procedure might partly act by decreasing salivary and pharyngeal colonization. Indeed, in our previous observational study, there was a high bacterial concordance between dental and salivary colonization, so that it was impossible to determine the primary site of colonization. These findings give confirmation that the oropharynx must be regarded as a global 'communicating' bacterial reservoir. However, the need for a specific dental decontamination procedure must be taken into account, considering the high bacterial concentrations and adherence of aerobic bacteria on dental surfaces. Moreover, the procedure of antiseptic decontamination does not share the risk of antibiotic resistance induced by classic selective digestive decontamination. Its cost is low, around 5 Euros per patient, and it is easier to apply even in intubated patients. Dual application of the antiseptic in the oropharynx and at the dental site might also enhance its efficacy.

We conclude from our results that an antiseptic decontamination of dental plaque with a 0.2% chlorhexidine gel is an easy to apply and well-tolerated procedure that decreases the growth of dental plaque and might reduce the incidence of nosocomial infection in ICU patients submitted to mechanical ventilation. These results need confirmation in a double-blind placebo-controlled study.

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