Original Article

Impact of subglottic secretion drainage on microaspiration in critically ill patients: a prospective observational study

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Background: Microaspiration is a major factor in ventilator-associated pneumonia (VAP) pathophysiology. Subglottic secretion drainage (SSD) aims at reducing its incidence.

Methods: Single-center prospective observational study, performed in a French intensive care unit (ICU) from March 2012 to April 2013, including adult patients mechanically ventilated for at least 24 hours divided in two groups: patients in the SSD group intubated using tracheal tubes allowing SSD and patients in the control group intubated with standard tracheal tubes. Pepsin and salivary amylase concentrations were measured for 24 hours in all tracheal aspirates. Primary objective was to determine the impact of SSD on gastric or oropharyngeal microaspiration using pepsin or amylase concentration in tracheal aspirates.

Results: Fifty-five patients were included in the SSD group and 45 in the control group. No difference was found between groups regarding the incidence of microaspiration defined as at least one tracheal aspirate positive for either pepsin or amylase [49 (89%) *vs.* 37 (82%), P=0.469]. Percentage of patients with VAP [16 (29%) *vs.* 11 (24%), P=0.656], ventilator-associated tracheobronchitis (VAT) [7 (13%) *vs.* 4 (9%), P=0.750] or early airway colonization [15 (35%) *vs.* 8 (18%), P=0.219] were not significantly different in study groups.

Conclusions: SSD did not reduce the incidence of microaspiration, VAP, VAT or airway colonization in this observational study.

Keywords: Ventilator-associated pneumonia (VAP); subglottic secretion drainage (SSD); microaspiration

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Introduction

Ventilator-associated pneumonia (VAP) is a major concern in intensive care units (ICU). VAP is the most common ICU-acquired infection, representing 30% to 50% of these infections (1). VAP has been shown to worsen patient outcome, with a reported mortality of 20% (2) and an attributable mortality of 10% to 30% (3). It has also been shown to increase the length of mechanical ventilation (MV), length of stay (4), and cost (5).

For these reasons, prevention, diagnosis and adequate treatment of VAP are priority goals in ICU patients. Several prevention strategies are recommended in international (6) and national (7) guidelines, implemented as "bundles": favoring non-invasive ventilation whenever possible, reducing sedation and neuromuscular blockade levels using sedation scales, early enteral nutrition initiation, regular

monitoring of endotracheal tube cuff pressure, favoring orotracheal intubation whenever possible, and subglottic secretion drainage (SSD), at least every 8 hours, using adequate tracheal tubes.

Most of these prevention strategies aim to reduce airway colonization, a major mechanism in VAP pathophysiology. The presence of the tracheal tube allows two paths for bacterial airway colonization: endoluminal colonization, a consequence of the formation of a biofilm inside the endotracheal tube lumen about 60 hours after intubation; and extraluminal colonization, which is a consequence of the progression of contaminated secretions of oral and gastric origin accumulated above the endotracheal tube cuff. This latter path, called microaspiration (8), is believed to be the most frequently implied in VAP pathophysiology (9,10).

The effectiveness of SSD in mechanically ventilated patients in the ICU has been evaluated by several randomized controlled studies and meta-analyses (11-17), with most of them concluding to a reduction of VAP incidence. However, no study to date has evaluated the impact of SSD on microaspiration.

The main objective of the present study was to assess the effectiveness of SSD in reducing the incidence of microaspiration in critically-ill patients requiring invasive MV.

Methods

This single-center, prospective, observational study was conducted in the Medical ICU of the University Hospital Center of Lille from March 2012 to April 2013.

For this strictly observational study, no approval was required from the local ethics committee. Patients or patients' proxy were informed of the patients' participation in the study and could refuse participating or withdraw from the study at any point.

Patient population

Patients 18 years of age or older who were admitted to our ICU, intubated and mechanically ventilated for more than 24 hours with an anticipated length of MV of at least 24 hours were included.

Exclusion criteria were: history of intubation within the last 6 months, intubation with a low volume high pressure tracheal cuff, patients whose tracheal cuff was inflated with water (which is a common practice for patients receiving hyperbaric oxygen therapy), patients ventilated using a tracheostomy at admission.

Group attribution

Patients were separated in two groups depending on the type of tracheal tube:

- The SSD group, consisting of patients with no tracheal tube at ICU admission, but later requiring tracheal intubation for MV. These patients were intubated using tracheal tubes allowing SSD, commonly used in our ICU (TaperGuard Evac®, Mallinckrodt). Those tracheal tubes include a tapered polyvinyl chloride (PVC) cuff. Inner diameters were 7.5 mm for adult females and 8 mm for adult males. Intermittent SSD was performed by nurses every three hours using a syringe;
- The control group was composed of patients already intubated at ICU admission with a tracheal tube that did not allow SSD. All tracheal tubes in this group had a cylindrical PVC cuff.

Standard preventive measures for VAP were performed as usual in our ICU, including semi-recumbent position between 30° and 45°, oral care, assessment of cuff pressure every 8 hours using a manometer to maintain a cuff pressure (Pcuff) as close to 25 cmH_2O as possible, minimal positive end-expiratory pressure (PEEP) of 5 cmH_2O whenever possible, hand hygiene, isolation precautions for patients colonized or infected with multidrug-resistant bacteria, and written antimicrobial therapy protocols.

Data collection

Laboratory tests

During the 24 hours following patient inclusion, all tracheal aspirates were collected in both groups, and conserved at temperature of –20 ℃. Quantitative measurement of pepsin and the salivary isoenzyme of amylase were achieved using ELISA technique (18). Concentrations above 200 µg/L for pepsin and 1,685 IU/L for amylase were used to define positive samples (19). Laboratory technicians performing the measurements were blinded for patients' group.

Bacteriological examination of tracheal aspirate was performed twice a week, with a quantitative analysis performed with a threshold of 10^3 CFU/mL to allow for detection of tracheobronchial tract bacterial colonization.

Demographic data

All demographic data were prospectively collected. The following data were collected at ICU admission: gender, age, simplified acute physiology score II (SAPS II) (20),

McCabe (21) and logistic organ dysfunction (LOD) (22) score, medical history (diabetes mellitus, chronic obstructive pulmonary disorder (COPD), chronic heart failure, cirrhosis with a class B or C Child-Pugh score, end-stage chronic kidney disease requiring chronic hemodialysis, gastroesophageal reflux disease (GERD), chronic respiratory failure due to restrictive lung disease), patient location before ICU admission (home, hospital, another ICU), active infection at admission, recent antimicrobial treatment (during the last 3 months), main diagnosis at admission.

The following data were collected at patient inclusion: LOD score, tracheal tube characteristics (type, size, orotracheal or nasotracheal intubation).

Follow-up data

The following data were collected during the 24 hours following patient inclusion: enteral feeding volume, gastric residual volume, vomiting, use of gastroprokinetic agents, stress ulcer prophylaxis type (sucralfate or proton pump inhibitors), mean tracheal cuff pressure (Pcuff), Pcuff <20 cmH_2O, sedation, use of neuromuscular blocking drugs, Glasgow coma scale (GCS), Ramsay sedation scale, elevation of the head-of-bed, out-of-ICU patient transport, prone positioning, mean PEEP, MV mode [assist-control ventilation (ACV), bilevel positive airway pressure (BiPAP), pressure-support ventilation (PSV)]. The number of tracheal aspirates and subglottic secretion suctioning were also collected.

The following data were collected during the whole ICU stay: mortality, length of stay, VAP, VAT.

Other definitions

Gastric microaspiration was defined by the presence of pepsin at significant concentration (200 µg/L) in at least one tracheal aspirate. Oropharyngeal microaspiration was defined by the presence of salivary amylase at significant concentration (>1,685 IU/L) in at least one tracheal aspirate. Microaspiration, regardless of origin, was defined by the presence of pepsin or salivary amylase at significant concentrations in at least one tracheal aspirate. Tracheobronchial colonization was defined as a positive tracheal aspirate $\geq 10^3$ CFU/mL. Pneumonia was defined according to ATS/IDSA guidelines (6) as a new or progressing radiological infiltrate associated with two of the following criteria: temperature >38.5 or <36 ℃, white blood cell count >10 or <1.5 G/L, purulent tracheal aspirates. Bacteriological confirmation was required, with a threshold of 10^6 CFU/mL in tracheal aspirate or 10^4 CFU/mL in BAL. VAP was defined as a pneumonia diagnosed 48 hours or more after intubation, with early VAP defined as a VAP occurring 2 to 5 days after intubation and late VAP defined as a VAP occurring ≥5 days after intubation. Ventilator-associated tracheobronchitis (VAT) was defined as the association of (I) a temperature >38 ℃ without other explanation, (II) purulent tracheal aspirates, (III) positive ETA with a threshold of 10^6 CFU/mL and (IV) no radiological criteria for pneumonia. ICU-acquired infections other than VAP and VAT were defined using modified CDC criteria (23).

Outcomes

The primary outcome of this study was the percentage of patients with microaspiration.

The secondary outcomes were percentage of patients with microaspiration of gastric contents, microaspiration of oropharyngeal secretions, VAP, VAT, and tracheobronchial colonization.

Statistical analysis

Qualitative variables were compared using chi-squared test or Fisher's exact test. The distribution of quantitative variables was tested for normality using Kolmogorov-Smirnov test. Quantitative variables following normal distribution were compared using Student's *t*-test and are expressed using mean value and standard deviation. Quantitative variables not following a normal distribution were analyzed using Mann-Whitney U test and are expressed using median value and 25th–75th percentiles. Observed differences were considered statistically significant if P values were inferior to 0.05. In order to adjust for significant differences between the two groups, a multivariate analysis was performed with microaspiration of gastric or oropharyngeal secretions as dependent variable. Statistical tests were performed using version 15.0 of SPSS software.

Results

From February 2012 to January 2013, 100 patients were included in the study: 55 patients in the SSD group and 45 patients in the control group.

Patient characteristics

Baseline characteristics are presented in *Table 1*. Patients included in the SSD group were significantly less likely to

Table 1 Patient characteristics at ICU admission

Characteristics	SSD group (n=55)	Control group (n=45)	P†
Age, median (IQR)	65 (58.0–75.0)	61 (50–73.5)	0.107
Male, n [%]	40 [73]	31 [69]	0.825
Location before ICU admission, n [%]			
Home	20 [36]	13 [29]	0.523
Ward	35 [64]	22 [49]	0.159
ICU	0 [0]	10 [22]	<0.001
Admission diagnosis, n [%]			
Acute exacerbation of COPD	11 [20]	5 [11]	0.280
Acute respiratory distress syndrome	8 [15]	7 [16]	1
Septic shock	14 [25]	16 [36]	0.284
Community-acquired pneumonia	16 [29]	13 [29]	1
Hospital-acquired pneumonia	11 [20]	11 [24]	0.634
VAP	0 [0]	1 [2]	0.450
Healthcare-associated pneumonia	15 [27]	3 [7]	0.009
Neuromuscular disorder	2 [4]	6 [13]	0.135
Acute poisoning	2 [4]	3 [7]	0.655
Recent surgery	2 [4]	7 [16]	0.074
Healthcare context, n [%]			
Regular care in preceding 30 days	18 [33]	5 [11]	0.016
Nursing home	0 [0]	1 [2]	0.450
Hospital admission <3 months	19 [35]	3 [7]	0.001
Chronic disease, n [%]			
Diabetes mellitus	11 [20]	13 [29]	0.351
COPD	17 [31]	15 [33]	0.832
Chronic respiratory failure	8 [15]	7 [16]	1
Chronic heart failure	10 [18]	4 [9]	0.250
Cirrhosis	2 [4]	6 [13]	0.135
Chronic kidney disease	2 [4]	0 [0]	0.500
SAPS II, median (IQR)	46 (36.0–60.0)	51 (39–69.5)	0.172‡
LOD score, median (IQR)	6 (3.0–9.0)	8 (4.0–10.0)	0.820‡
McCabe score >1, n [%]	26 [47]	23 [51]	0.961§
GERD, n [%]	1 [2]	2 [4]	0.587
Orotracheal intubation, n [%]	46 [84]	45 [100]	0.004
Prior antibiotic treatment <3 months, n [%]	35 [64]	26 [58]	0.681
Infection, n [%]	43 [78]	39 [87]	0.307

†, P value calculated using Fisher's exact test unless specified otherwise; ‡, P value calculated using Mann-Whitney U test; §, Linear regression *t*-test. SSD, subglottic secretion drainage; IQR, interquartile range; COPD, chronic obstructive pulmonary disease; SAPS II, simplified acute physiology score II; LOD, logistic organ dysfunction; ICU, intensive care unit.

Table 2 Patient characteristics in the 24 hours following inclusion

Characteristics	SSD group (n=55)	Control group (n=45)	P[†]
Enteral nutrition volume (mL), mean ± SD	613±453	365±462	0.003[‡]
Gastric residual volume (mL), mean ± SD	57±164	105±179	0.027[‡]
Prokinetic drugs, n [%]	2 [4]	1 [2]	>0.999
Proton pump inhibitors, n [%]	30 [55]	23 [51]	0.841
Sucralfate, n [%]	20 [36]	18 [40]	0.836
Vomiting, n [%]	1 [2]	4 [9]	0.171
Mean cuff pressure (cmH_2O), median (IQR)	23 (21.0–30.0)	29 (22.5–30)	0.015[‡]
Cuff pressure <20 cmH_2O, n [%]	20 [36]	11 [24]	0.277
Sedation, n [%]	27 [49]	25 [56]	0.522
Neuromuscular blocking agents, n [%]	2 [4]	8 [18]	0.040
Mean bed head elevation, median (IQR)	35 (30.0–40.0)	32.5 (30–39.5)	0.239[‡]
Out-of-ICU transport, n [%]	2 [4]	1 [2]	>0.999
Prone positioning, n [%]	0 [0]	3 [7]	0.088
Ventilation modes[§], n [%]			
Assist-control	24 [44]	27 [60]	0.113
Pressure support	40 [73]	26 [58]	0.140
Biphasic positive airway pressure	0 [0]	1 [2]	0.450
Mean positive end-expiratory pressure (cmH_2O), median (IQR)	6 (5.0–8.0)	8 (5.0–10.0)	0.116[‡]

[†], P value calculated using Fisher's exact test unless specified otherwise; [‡], P value calculated using Mann-Whitney U test; [§], each patient could receive multiple ventilation modes. SSD, subglottic secretion drainage; SD, standard deviation; IQR, interquartile range; ICU, intensive care unit.

be admitted from another ICU, but were significantly more likely to be admitted for healthcare-associated pneumonia, to have received antibiotics or wound care, or to have stayed at a hospital for at least 48 hours in the preceding 3 months. Nasotracheal intubation was only observed in the SSD group (9 patients, 16%, P=0.004). There was no difference regarding tracheal tube sizes between groups, with the most frequently used size being 7.5 [25 of 55 (45%) *vs.* 25 of 45 (56%), in SSD and control group, respectively; P=0.990].

Although enteral nutrition volume was significantly higher, residual gastric volume and mean cuff pressure were significantly lower in SSD as compared with control group (*Table 2*). No significant difference was found in other patient characteristics in the 24h following inclusion.

Primary and secondary outcomes

During the 24 hours following inclusion, no significant difference was found in the number of tracheal aspirates performed for pepsin and salivary amylase analyses [4 (2 to 5) in the SSD group *vs.* 3 (1.5 to 5.5) in the control group, P=0.642].

No significant difference was found in percentage of patients with microaspiration between the two groups (*Table 3*). After adjustment for significant differences between the two groups, the rate of patients with microaspiration was still not significantly different between the two groups (P=0.586). Similarly, no significant difference was found regarding the proportion of tracheal aspirates positive for pepsin or amylase [mean ± SD (81.4±31.4% *vs.* 75.6±36.6%), P=0.584], for pepsin [0 (0–50%) *vs.* 0 (0–17.8%), P=0.152] or for amylase [88 (58.5–100%) *vs.* 100 (33–100%), P=0.859], in SSD and control groups; respectively.

No significant difference was observed in the average pepsin level [median 114 (IQR 62–266) *vs.* 99 (IQR 52–185) µg/L, P=0.389] or amylase [10,675 (IQR 2,293–79,705) *vs.* 4,279

Table 3 Impact of SSD on outcomes

Outcomes	SSD group (n=55)	Control group (n=45)	P‡
Primary outcome			
Microaspiration, n [%]	49 [89]	37 [82]	0.469
Secondary outcomes			
Microaspiration of gastric contents, n [%]	23 [42]	13 [29]	0.185
Microaspiration of oropharyngeal secretions, n [%]	47 [85]	36 [80]	0.666
VAP, n [%]	16 [29]	11 [24]	0.656
VAT, n [%]	7 [13]	4 [9]	0.750
Tracheobronchial colonization, n [%]	15 [35]	8 [18]	0.219
Other outcomes			
ICU mortality, n [%]	27 [49]	24 [53]	0.693
ICU length of stay (days), median (IQR)	14 (10.0–26.0)	15 (9.0–34.0)	0.914§
MV duration (days), median (IQR)	10 (5.0–18.0)	11 (7.0–28.0)	0.158§
Duration of antibiotic treatment (days), median (IQR)	12 (8.0–19.0)	10 (7.0–22.0)	0.617§

‡, P value calculated using Fisher's exact test, unless otherwise specified; §, P value calculated using Mann-Whitney U test. No statistically significant difference was observed. SSD, subglottic secretion drainage; ICU, intensive care unit; IQR, interquartile range; MV, mechanical ventilation, GCS, Glasgow coma scale.

(IQR 1,564–55,572) IU/L, P=0.357] between SSD and control groups, respectively.

No significant difference was found regarding the percentage of patients with VAP, VAT or tracheobronchial colonization between the two groups. Similarly, no significant difference was found in other outcomes, including duration of MV, ICU length of stay or ICU mortality between the two groups (*Table 3*).

Discussion

Our results suggest that SSD is not associated with reduced microaspiration in intubated critically ill patients. No significant difference was found in microaspiration of gastric contents, or oropharyngeal secretions. Furthermore, the percentage of patients with VAT, VAP, or tracheobronchial colonization was not significantly different between patients who received SSD and those who did not.

To our knowledge, our study is the first to evaluate the impact of SSD on microaspiration in critically-ill patients. The strengths of this study include exhaustive epidemiological and potential confounding factor collection, its prospective design, and the combined use of salivary amylase and pepsin for microaspiration assessment.

Some limitations must be outlined. First, the number of included patients was relatively small. Therefore, different results could have been obtained had the number of patients been higher. Second, the observational design resulted in some differences between the two groups. However, after adjustment for significant differences between the two groups, similar results were found regarding the impact of SSD on microaspiration. Third, there was a major difference in tracheal tube cuff design between groups, namely that patients in the SSD group were intubated with tapered cuff tracheal tubes, while patients in the control group were intubated with standard (cylindrical) cuff tracheal tubes. Recent studies showed that tapered cuffed tracheal tubes were associated with significantly higher variations in cuff pressure (24), compared with standard-cuff tracheal tubes. This finding is consistent with the mean cuff pressure observed in our study being significantly lower in the SSD group, compared with control group [23 (21.0–30.0) *vs.* 29 (22.5–30), P=0.015] and the higher number of patients showing cuff pressure <20 cmH_2O. Finally, our study was performed in a single center, and its result might not be generalizable to other ICU patients.

Several previous randomized controlled studies reported significant reduction in VAP rates when SSD is used, compared with routine care. Mao *et al.* recently performed a meta-analysis of 20 randomized controlled trials, including

3,544 patients (25). SSD decreased VAP incidence and duration of MV and delayed VAP onset. However, this measure did not reduce mortality and length of ICU stay. SSD is recommended for preventing VAP by recent statements of the Intensive Care Society given consistent data on VAP rate reduction in three meta-analyses (12,14,15,26).

Conclusions

In conclusion, the use of SSD was not associated with a reduction of microaspiration or VAP incidence in our study. Further, large multicenter studies are required to evaluate the impact of SSD on microaspiration in intubated critically-ill patients.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: For this strictly observational study, no approval was required from the local ethics committee and patients and patients' proxy received written information about participation to this study and could refuse participating or withdraw at any point.

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