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DOI: 10.4103/ejop.ejop_62_18

# Does subglottic secretion drainage prevent ventilator-associated pneumonia?

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**Abstract:**

**AIM:** To compare the incidence of ventilator-associated pneumonia (VAP) in patients who were admitted to the intensive care unit (ICU) for reasons other than pneumonia and followed up under mechanical ventilation either with standard endotracheal tubes or endotracheal tubes with subglottic secretion drainage (SSD).

**MATERIALS AND METHODS:** Patients who were admitted to the ICU between April 2012 and January 2013 were prospectively and sequentially randomized to standard endotracheal and SSD intubation groups. Patients with pulmonary infection at ICU admission were excluded. Pulmonary imaging, blood, and sputum cultures were routinely screened, and pleural fluid and bronchial lavage examinations were done on demand.

**RESULTS:** Mean age, gender distribution, APACHE II scores, duration of mechanical ventilation, and follow-up of patients with standard ($n$ = 30) and SSD ($n$ = 12) intubation tubes were similar; 71 ± 10.4 versus 64.4 ± 13.9 years ($P$ > 0.05), male/female 18/12 versus 9/3 ($P$ > 0.05), APACHE II scores 20.2 ± 3.8 versus 17.0 ± 3.8 ($P$ = 0.02), 15.9 ± 11.5 versus 11.0 ± 8.1 days ($P$ > 0.05), and 18.0 ± 12.4 versus 15.5 ± 12.2 days ($P$ > 0.05), respectively. The incidence of VAP was similar in both groups (36.7% vs. 33.3%, $P$ > 0.05, in standard vs. SSD groups, respectively). The mortality rate was higher in the standard intubation group, but the difference was not statistically significant (70% vs. 41%, $P$ > 0.05).

**CONCLUSION:** Compared to standard endotracheal intubation, intubation with SSD tubes was not associated with an improvement in the duration of mechanical ventilation, length of stay in the ICU, incidence of VAP, and mortality rate. Due to the limited number of patients included in this study, the results have to be confirmed in larger studies on more patients.

**Keywords:**

Endotracheal intubation, subglottic secretion drainage, ventilator-associated pneumonia

## Introduction

The most common nosocomial infection in patients admitted to the intensive care unit (ICU) is ventilator-associated pneumonia (VAP), which is associated with an increase in mortality, extended length of stay in the hospital, and higher healthcare costs. VAP occurs in 20% of patients who are mechanically ventilated for longer than 48 h.[1] Risk of pneumonia increases by 6–21-fold in intubated patients and increases by 1%–3% for each intubation day.[2,3] Mortality associated with VAP varies between 33% and 71%.[4,5] Particularly in case of VAP caused by *Pseudomonas* and *Acinetobacter* species that is associated with bacteremia, the reported infection-related mortality rate tends to be much higher.[6]

Impaired defense mechanism, colonization with pathogens, and presence of highly virulent microorganisms play an important role in the disease pathogenesis. Other

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**Received:** 02-11-2017
**Revised:** 29-01-2018
**Accepted:** 06-02-2018

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**How to cite this article:** Erinc A, Ozcelik HK, Yigitbas BA, Yurt S, Kosar F. Does subglottic secretion drainage prevent ventilator-associated pneumonia? Eurasian J Pulmonol 2018;20:122-7.



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important factors include oropharyngeal colonization by Gram-negative bacilli, reduced upper airway reflex as a result of intubation, reduced gastric acidity secondary to the use of H2-receptor blockers, aspiration of gastric content, and equipment used for mechanical ventilation, which may expose the patient to VAP-causing agents (ventilator, ventilator circuits, etc.).[7,8] It is, therefore, important to use various methods to prevent VAP and measures guided by modern practices are taken both during and after the intubation procedure at any ICU. One such measure is the use of endotracheal tubes with subglottic secretion drainage (SSD), which claim to reduce the incidence of VAP by preventing the formation of micro-aspirations around the cuff of the endotracheal tube. In our country, the use of this type of endotracheal tube is not a common practice, varies significantly between different centers, and is associated with a significant increase in cost compared to the standard endotracheal tubes. To our best knowledge, a comparative study with this type of tube has not been conducted in our country. In this study, we aimed to compare standard endotracheal tubes with those with SSD function with regard to their impact on the prevention of VAP.

## Materials and Methods

This randomized, multicenter study was conducted prospectively and included 42 patients who were admitted to the pulmonary ICUs of Yedikule Hospital for Chest Disease and Thoracic Surgery and Bezmialem Vakif University Faculty of Medicine hospitals between April 2012 and January 2013. Patients older than 18 years with no pneumonia at admission to the ICU and who were mechanically ventilated for at least 48 h were included in this study. Of these, standard endotracheal tubes were used on 30 patients and endotracheal tubes with SSD function were used on 12 patients. Patients under 18 years, patients who were mechanically ventilated for <48 h, and patients with a pulmonary infection at admission to the ICU were excluded.

The following criteria were used to diagnose VAP in the study subjects:

- Newly developed or progressive and persistent infiltration, consolidation, and/or cavitation on at least two consecutive chest X-rays
- Fever, leukopenia (<4000/mm$^3$) or leukocytosis (>12,000/mm$^3$), changes in the character of the aspirate, increased need for aspiration, new-onset cough, tachypnea or dyspnea, rale, rhoncus, or bronchial breathing sounds on lung auscultation, impaired gas exchange (increased oxygen need or ventilation need) on physical examination or laboratory tests that cannot be linked to other causes
- Blood culture positivity that cannot be explained with another microbiological focus
- Positive growth on the pleural fluid culture
- Infective agent isolated on endotracheal aspirate and/or bronchial lavage culture.

On admission to the ICU, the heart rhythm, arterial oxygen saturation, hourly urine output, and invasive or noninvasive blood pressure of the subjects were monitored.

Concomitant endotracheal aspirate and blood and urine samples were sent for culture at the time of intubation, on day 2 and 4, and then routinely every week, and whenever an infection was suspected. After a gross examination under appropriate conditions, the samples were prepared with Gram, Ehrlich-Ziehl–Neelsen, and Giemsa stains. Standard aerobic and anaerobic culturing methods were used. APACHE II score of the subjects was determined based on the physiological parameters identified during the first 24 h. Any potential use of antibiotics throughout the hospital admission was recorded. Arterial blood gases, complete blood count, and electrolytes were monitored daily, and chest X-rays were obtained every 24–48 h. Body temperature was monitored to guide the clinical assessment. If the body temperature exceeded 38.4°C, fresh culture samples were sent to the laboratory. Endotracheal aspirates were obtained using an open and sterile process. Subjects with endotracheal tubes with SSD were manually aspirated every 2 h. Empirical antibiotic therapy was introduced based on the baseline clinical findings at the time of admission to the ICU. Antibiotic therapy was later adjusted according to patient's antibiogram results and clinical condition. For all patients, the head of bed was elevated to 30°–45°. To facilitate enteral feeding, a nasogastric tube was inserted to all patients included in the study. Parenteral feeding was used in patients who could not tolerate tube-feeding. All patients received standard doses of intravenous ranitidine, an H2-receptor blocker, for stress ulcer prophylaxis. Subcutaneous low-molecular weight heparin at a prophylactic dose was administered to all patients who had no contraindication.

Informed consent was obtained from all subjects or their legal representatives. Approval from the Ethics Committee was obtained in November 2011, and the study was conducted in compliance with the Helsinki Human Rights Declaration.

### Statistical analysis of data

When reviewing the data collected in the study, statistical package software was used for the statistical analysis. The study data were analyzed using descriptive statistical

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methods (frequency, percentage, mean, and standard deviation) and Kolmogorov–Smirnov test was utilized to study the normal distribution. Qualitative data were compared using the Chi-square test, Cox regression analysis was used for the VAP-related survival data, and multiple regression analysis was used to study the significance of factors associated with VAP. Within the confidence interval (CI) of 95%, the results were considered significant at $P < 0.05$ and highly significant at $P < 0.01$.

## Results

We included 42 patients who were mechanically ventilated for at least 2 days (48 h) within the last 8 months in this study. Of these, standard endotracheal tubes were used in 30 patients and endotracheal tubes with SSD were used on 12 patients. The number of subjects included in the study within the established timeframe was fewer than anticipated. Of the two centers that participated in this study, one was a secondary respiratory ICU with five beds and the other was a tertiary general ICU with 14 beds. The limited number of patients admitted to these two units who met the inclusion criteria and the fact that the study was conducted in two different centers may explain the low number of patients who were intubated with endotracheal tubes with SSD. Twenty-seven of the subjects were male and 15 were female, with an age distribution between 34 and 92 years. The length of stay in the ICU varied between 5 and 45 days. The patients were divided into the standard tube group and the SSD tube group. The study groups were compared with regard to age, gender, APACHE II score, length of stay in the ICU, duration of mechanical ventilation, VAP incidence, and mortality rate [Table 1]; reason for admission to the ICU [Table 2]; and microbiologically proven infectious agent [Table 3].

There was no significant difference in terms of gender and mean age between the two groups ($P > 0.05$). The APACHE II scores were significantly different between the two groups ($P < 0.05$). Duration of mechanical ventilation was not significantly different between the groups ($P > 0.05$). The overall length of stay in the ICU was comparable for both groups ($P > 0.05$). The VAP incidence and VAP rate were 36.7% and 23%/1000 ventilator days versus 33.3% and 30%/1000 ventilator days in the standard endotracheal tube and endotracheal tube with SSD groups, respectively. This result suggests that there is no significant difference between the groups with regard to occurrence of VAP ($P > 0.05$) [Table 1]. The mortality rate was 70% versus 41.7% in the standard endotracheal tube and endotracheal tube with SSD groups, respectively. There was no statistically significant difference in the mortality rates between two groups ($P > 0.05$) [Table 1].

**Table 1: Age, gender, acute physiology and chronic health evaluation II scores, length of stay in the intensive care unit, duration of mechanical ventilation, ventilator associated pneumonia incidence, and mortality rates of subjects**

| | Standard endotracheal tube (*n*=30) | Endotracheal tube with SSD (*n*=12) | *P* |
|---|---|---|---|
| Age | 71±10.4 | 64.4±13.9 | >0.05 |
| Gender | | | |
| Male | 18 | 9 | >0.05 |
| Female | 12 | 3 | |
| APACHE II | 20.2±3.8 | 17.0±3.8 | 0.02 |
| Duration of mechanical ventilation | 15.9±11.5 | 11.0±8.1 | >0.05 |
| Length of stay in the ICU | 18.0±12.4 | 15.5±12.2 | >0.05 |
| Patients with VAP, *n* (%) | 11 (36.7) | 4 (33.3) | >0.05 |
| Mortality, *n* (%) | 21 (70) | 5 (41) | >0.05 |

VAP: Ventilator associated pneumonia, SSD: Subglottic secretion drainage, APACHE: Acute Physiology and Chronic Health Evaluation, ICU: Intensive care unit

**Table 2: Reason for hospital admission**

| Reason for admission | Standard endotracheal tube, *n* (%) | Endotracheal tube with SSD, *n* (%) |
|---|---|---|
| COPD | 13 (43.3) | 5 (41.7) |
| Asthma | 1 (3.3) | 0 |
| Lung cancer | 4 (13.3) | 3 (25) |
| Interstitial pulm. disease | 2 (6.7) | 1 (8.3) |
| Hemoptysis | 1 (3.3) | 1 (8.3) |
| Acute renal failure | 8 (26.7) | 0 |
| Other malignancies | 2 (6.7) | 0 |
| Cerebrovascular disorders | 3 (9.9) | 0 |

COPD: Chronic obstructive pulmonary disease, SSD: Subglottic secretion drainage

**Table 3: Distribution of infectious agents**

| Agents | Standard endotracheal tube, *n* (%) | Endotracheal tube with SSD, *n* (%) |
|---|---|---|
| *Haemophilus influenzae* | 1 (3.3) | 0 |
| *Staphylococcus aureus* | 8 (26.7) | 2 (16.7) |
| *Klebsiella pneumoniae* | 4 (13.3) | 2 (16.7) |
| *Candida* spp. | 2 (6.7) | 0 |
| *Acinetobacter* | 7 (23.3) | 4 (33.3) |
| *Pseudomonas aeruginosa* | 4 (13.3) | 3 (25) |
| VRE | 2 (6.7) | 0 |
| *Stenotrophomonas maltophilia* | 1 (3.3) | 0 |

No conflict of interest was reported by the authors. VRE: Vancomycin-resistant *enterococci*, SSD: Subglottic secretion drainage

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The culture results of samples obtained from patients intubated with standard endotracheal tubes were positive for *Staphylococcus aureus* in 8 patients (26.7%), *Acinetobacter* spp. in 7 patients (23.3%), *Klebsiella pneumonia* in 4 patients (13.3%), *Pseudomonas aeruginosa* in 4 patients (13.3%), and vancomycin-resistant enterococci in 2 patients (6.7%). Of the culture results of samples obtained from patients intubated with endotracheal tubes with SSD, 4 (33.3%) were positive for *Acinetobacter* spp. and 3 (%25) for *P. aeruginosa* [Table 3].

## Discussion

In spite of advances in the diagnosis, management, and prevention of VAP, the condition still remains an important cause of nosocomial morbidity and mortality.[9] In recent years, a number of methods have been introduced to prevent the development of VAP, with the most popular ones being the use of the endotracheal tubes with SSD and oral antiseptic solutions. In this study, we found no significant difference in VAP incidence, duration of mechanical ventilation, or mortality between the standard tubes and endotracheal tubes with SSD function.

In the literature, reports on VAP incidence vary between 7% and 70% depending on the definition of VAP, type of hospital or ICU, study population, and calculation method.[10]

Recent reports from our country suggest that VAP is the most common type of infection among patients admitted to ICUs.[11] Recent studies report the incidence of VAP between 14.8 and 35.7/1000 ventilator days.[12,13] The study by Heyland *et al*. reports a VAP incidence of 10.8/1000 ventilator days while Rosenthal *et al*.[14] reported an incidence of 50.7/1000 ventilator days. In the study conducted in our country, Ergin *et al*.[15] reported that 49.6% of the patients develop VAP and the VAP incidence is 16.1/1000 ventilator days; Erbay *et al*.,[16] on the other hand, reported the incidence as 8.9/1000 ventilator days in their study. In this study, the VAP incidence in the ICU over a period of 8 months was 36.7% (VAP rate = 23/1000 ventilator days) versus 33.3% (VAP rate = 30/1000 ventilator days) in the standard endotracheal tube group and endotracheal tube with SSD group, respectively. This study illustrates that the VAP incidence may vary between centers. The VAP incidence in this study is comparable to reports from similar studies in our country.

One of the tools claimed to be effective in preventing VAP is related to the use of endotracheal tubes. Endotracheal tubes that are used in routine practice interfere with the host defense mechanism and mechanical cleaning of the respiratory tract, lead to local trauma and inflammation, and result in build-up of secretions around the cuff. The cuff pressure should be sufficient to prevent secretions that build up in the subglottic region from escaping into the lower airways. Continuous or intermittent aspiration of oropharyngeal and upper airway secretions from the endotracheal cuff helps to prevent the escape of these secretions into the lower airways. Endotracheal tubes that have been engineered with a separate dorsal lumen on the cuff to facilitate the suction of subglottic secretions are reported to reduce early-onset VAP rates.[17] On the other side, some randomized trials produced contradictory results with no benefits reported.[18] The use of this type of endotracheal tube is limited by its failure to reduce late-onset VAP rates and increased costs. In this study, we found significant difference in VAP incidence between standard endotracheal tubes and endotracheal tubes with SSD. In a meta-analysis that included 17 studies with 3369 patients, SSD tubes were found to be associated with lower VAP rates (risk ratio, 0.58; 95% CI, 0.51–0.67; $I^2$ = 0%), but no difference in the duration of mechanical ventilation, length of stay in the ICU, length of stay in the hospital, ventilator-associated events, and mortality was demonstrated.[19]

A review of the correlation between the duration of mechanical ventilation and VAP indicates that prolonged mechanical ventilation is a significant risk factor for developing VAP.[20] In the literature, the risk of pneumonia in patients on mechanical ventilation is reported as 6.5% for the first 10 days versus 19% for 20 days and longer.[21,22] In the study by Bodur *et al*.,[23] VAP rate was 32.1%, mean length of stay in the was 26.8 days, and the mean duration of mechanical ventilation was 17.7 days, and VAP developed on the 11$^{st}$ day of mechanical ventilation. The average day of developing VAP was reported as 12.5 days by Bregeon *et al*.,[24] 5 days by Marik *et al*.,[8] and between 5 and 10 days by Heyland *et al*.[25] In this study, the mean duration of mechanical ventilation and mean length of stay in the ICU were 15.9 and 18.9 days versus 11 and 15.5 days with the standard endotracheal tube and endotracheal tube with SSD, respectively. There were no significant differences in the length of stay in the ICU and duration of mechanical ventilation between the two groups.

Crude mortality rate associated with VAP is reported between 24% and 76%. Bodur *et al*.[23] reported the crude mortality rate associated with VAP as 76.9%. Bregeon *et al*.[24] reported a mortality rate of 79% among patients with VAP. In this study, the crude mortality rate associated with VAP was 70% versus 41.7% in standard tube and SSD tube groups, respectively. There was no significant difference in mortality between the two groups. The statistical analysis, however, indicated a higher mortality rate in subjects with a higher mean APACHE II score which suggests that APACHE II

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score is an independent risk factor for mortality. On the other hand, the limited sample size may explain why no statistical significance was reached in spite of the lower mortality rate in patients intubated with SSD tubes. To anticipate the number of patients needed to treat to demonstrate the benefits of a method to reduce the VAP risk, one should refer to similar studies conducted previously. Based on the assumption of an incidence around 4%, 33 patients have to be intubated using an endotracheal tube with SSD to prevent VAP in one patient.[26]

Microorganisms that are involved in the etiology of VAP vary depending on the hospital, microbial flora of the admitting ICU, and patient characteristics.[1] In most of the studies, Gram-negative bacilli are reported as causative organism in 71%–74% of the cases. This was also confirmed in this study with positive growth of *S. aureus* in 8 patients (26.7%), *Acinetobacter* spp. in 7 patients (23.3%), *K. pneumonia* in 4 patients (13.3%), and *P. aeruginosa* in 4 patients (13.3%) who were intubated with standard endotracheal tubes. In patients intubated using endotracheal tubes with SSD, 4 (33.3%) had *Acinetobacter* spp. and 3 (25%) had *P. aeruginosa* growth on their culture samples.

The microorganisms associated with VAP appear similar in this study as well as in reference reports. Their distribution, however, varies according to the diagnostic methods and studied patient population.

## Conclusion

VAP is a preventable infectious disease with high morbidity and mortality, which leads to extended length of stay in the hospital and increased healthcare costs and puts a significant burden on national economy.

Although many different diagnostic, management, and preventive strategies are recommended, there is no single method that is widely accepted.

Many strategies to prevent VAP are still controversial and under investigation. Endotracheal tubes with SSD are among those strategies. Many studies and meta-analyses report positive effects on the VAP incidence, length of stay in the ICU, and duration of mechanical ventilation in favor of endotracheal tubes with SSD compared to standard endotracheal tubes.[17]

In this study, we observed no significant difference in the VAP incidence, length of stay in the ICU, duration of mechanical ventilation, or mortality rates between the standard endotracheal tube and endotracheal tube with subglottic secretion ventilation groups.

To prevent VAP, we believe that a full assessment of the patient, including a review of laboratory data, from the time of admission to the unit is required to identify potential risks and appropriate preventive measures in combination with infection control programs must be implemented.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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