Comparison of Standard Endotracheal Tube and Endotracheal Tube with Subglottic Secretion Drainage in Patients Undergoing Open Heart Surgery; Risk of Developing Postoperative Nosocomial Pneumonia

ABSTRACT

Objective: Postoperative nosocomial pneumonia (PoNP) is the pneumonia that develops 48 hours after the surgery. The risk of PoNP is 3-20 times higher when endotracheal tube (ET) was used. Therefore ETs with drainage lumens allowing subglottic secretion were produced (SSD-ET). The risk of PoNP has increased in cardiac surgery. There are limited number of studies on SSD-ET and VAP in the literature on patients under going fast-track cardiac anesthesia protocol. The aim of our study is to compare the protective effect of the SSD-ET on the extubation time and the development of PoNP in the patients having open heart surgery under going fast-track cardiac anesthesia protocols.

Method: A prospective, non-blind, randomized trial was conducted. Patients scheduled for cardiac surgery were randomly assigned to receive Standard Tube Group (Group 1) or Subglottic Aspiration Tube Group (Group 2). 60 patients were included in the study. The diagnosis of PoNP is determined according to the diagnostic criteria of 2015 “Centers for Disease Control and Prevention (CDC)”(1). A two-sided p-value <0.05 was considered as statistically significant.

Results: Extubation time was 12.65 h in group SSD-ET, it was revealed as 16.88 h in the S-ET group. SSD-ET group showed statistically shorter extubation time (<0.027) and less incidence of PoNP (<0.027).

Conclusion: Our study has showed that SSD-ETs decreased the extubation time in patients who underwent open heart surgery, although they did not directly affect the development of PoNP.

Keywords: subglottic secretion tubes, open heart surgery, postoperative nosocomial pneumonia

ÖZ

Amaç: Postoperatif nosokomial pnömoni (PoNP), ise ameliyatın 48 saat sonra gelişen pnömoniler olarak tanzim edilmektedir. PoNP riski, endotrakeal tüp (ET) kullanılması ve 3-20 kat daha fazla görülmektedir. Bu nedenle, subglotik sızıntı alerjisi olan hastalarda ET ile hastalıkların riski artmaktadır. Etude etekendir. Literatürde hızlı cerrahi protokolleri uygulanan hastalarda SSD-ET ve VAP ile ilgili sınırlı sayıda çalışma vardır. Çalışmanın amaç, hastalarda endotrakeal tüp kullanılarak açık kalp cerrahisi geçiren hastalarda SSD-ET’nin ektubasyon süresi üzerindeki etkisini ve PoNP gelişimini karşılaştırmaktır.

YÖNTEM: Prospektif, kör olmayan, rastgele bir çalışma planlandı. Açık kalp cerrahisi geçiren hastalarda, Standard Tüp Grubu (Grup 1) veya Subglottik Aspirasyon Tüp Grubu (Grup 2) alınmak üzere rastgele seçilen hastaların ektubasyon süresi ve PoNP gelişimine etkisi incelenmiştir.

Bulgular: SSD-ET grubunda ektubasyon süresi 12.65 saat, S-ET grubunda 16.88 saat olarak belirlenmiştir. SSD-ET grubunda ektubasyon süresi 12.65 saat, S-ET grubunda 16.88 saat olarak belirlendi. S-ET grubunda PoNP riski 3-20 kat daha yüksek görülmekteydi. SSD-ET grubunda ise PoNP riski 3-20 kat daha düşük görülmektedir.

Sonuç: Çalışmamız, açık kalp cerrahisi geçiren hastalarda SSD-ET’den PoNP riski düşürdüğü ve ektubasyon süresi ve ektubasyon süresi ile ilgili sınırlı sayıda çalışma vardır. Çalışmamızın amacı, SSD-ET’lerin ektubasyon süresine ve PoNP riskine etkisi incelenmektedir.

Anahtar kelimeler: subglottik secreson tubes, open heart surgery, postoperative nosocomial pneumonia
INTRODUCTION

Nosocomial pneumonia is defined as pneumonia developing 48 hours after being admitted and is not in incubation period. Ventilator-associated pneumonia (VAP) is the pneumonia that occurs in those who are on mechanical ventilation for more than 48 hours \[1\]. Postoperative nosocomial pneumonia (PoNP) develops 48 hours after surgery \[2\]. PoNP may be preventable in many cases but increases health care cost and has high mortality and morbidity. The risk of PoNP has been reported to be 3-20 times greater when an endotracheal tube (ET) is used in conjunction with mechanical ventilation \[3\]. The insertion of an ET may cause airway injury and introduce endogenous oropharyngeal bacteria to the lower respiratory tract. Airway mucociliary clearance and cough reflex are often impaired in the presence of an ET. Airway mucosal damage and biofilm formation are other factors that will contribute to ET-associated PoNP development \[4-7\]. Although various methods are available for preventing nosocomial pneumonia in intubated patients, ET derived factors are important. Hence, ETs with drainage lumens allowing subglottic secretion drainage have been produced. This type of ET possesses two lumens so that while the cuff of one lumen is inflated, it is possible to drain subglottic secretions, continuously or intermittently, from the non-inflated cuff. Several studies have shown that VAP rates decrease with the use of ET with subglottic secretion drainage (SSD-ET) \[8-12\].

The risk of PoNP is increased following cardiac surgery \[12\]. Postoperative pulmonary complications are estimated to occur in 5-20% of patients undergoing cardiac surgery. However, there are few studies investigating the post-operative use of SSD-ET in cardiac surgery. Kollef et al. reported that the incidence of VAP is similar in SSD-ET compared with a normal ET but the VAP episodes occur later \[12\]. Bouza et al. also reported the incidence of VAP to be similar with both types of ET but there was a decrease in the use of antibiotics \[13\].

There are a limited number of studies in the literature of SSD-ET and VAP in patients undergoing a fast-track cardiac anesthesia protocol. Studies investigating SSD-ET generally report on the frequency of VAP in patients undergoing mechanical ventilation for at least 48 hours. The extubation time in open-heart surgery patients with fast track cardiac anesthesia protocols is less than 48 hours and they remain in the Intensive Care Unit (ICU) for a shorter period \[14\]. SSD-ET not only reduces the risk of VAP but also shortens the duration of mechanical ventilation \[9-12\]. Since longer extubation time is one of the risk factors for the development of PoNP, SSD-ET can also minimize the risk of the development of PoNP by shortening extubation time in cardiac surgery patients having fast track cardiac anesthesia \[15\].

The aim of our study was to compare SSD-ET with standard ET in patients having open-heart surgery undergoing fast-track cardiac anesthesia protocols in terms of extubation time and the risk of PoNP.

MATERIAL and METHOD

A prospective, non-blind, randomized trial was conducted. Ethical approval was obtained for the study from the local ethics committee of the university (KOU-KAEK 2017-405, NCT number: 03483285). The patients were informed about the study bedside one day prior to the procedure and their informed consent was obtained. Exclusion criteria included: abnormal respiratory function test; hypoxia or hypercapnia in arterial blood gas; prior infections; left main coronary artery disease; poor ventricular ejection fraction (EF<50%); congestive heart failure; anemia (defined as hemoglobin <10 gr/dL); renal insufficiency (serum creatinine >1.8 mg/dL); morbid obesity (Body mass index >35 kg/m\(^2\)); and smoking history up to two months prior to procedure. One researcher and the study microbiologist were not blinded to patient group. Patients scheduled for cardiac surgery were randomly assigned to receive standard polyvinyl chloride ET (Mallinckrodt Inc, Hazelwood, Mo., USA) (30 patients), which was des-
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ignated (Group S-ET,) or a TaperGuard Evac ET (Mallinckrodt, Covidien) (30 patients), designated the (SSD-ET group,) at intubation (Figure 1). Both groups contained the same number of patients. For both groups a cuffed ET with an internal diameter (ID) of 7.0 mm was used in women and 8.0 mm ID in men and the cuff pressure of the ET was maintained at 20 cm H$_2$O in both groups. In the SSD-ET group, subglottic aspiration was performed continuously with a negative inspiratory force of 20 cm H$_2$O in the intraoperative and postoperative periods until the patient was extubated. Subglottic pores were irrigated with 10 ml of sterile distilled water every six hours and irrigation was maintained until the aspiration area was clean, as recommended by the manufacturer.

Patients were pre-medicated with intravenous (iv) midazolam (0.03 mg/kg) before being transferred to the operating room. Next 5 L/min oxygen was given, via a face mask, and peripheral venous access was achieved in the antecubital area using an 18-gauge catheter. Heart rate (HR) was determined by5-channel electrocardiography (ECG), and standard peripheral oxygen saturation (SpO$_2$) and noninvasive blood pressure monitoring were performed. After local anesthesia with lidocain 2% and iv fentanyl (1 μg/kg), an arterial catheter was placed before anesthesia induction. After anesthesia induction, using 0.05-0.1 mg/kg midazolam, 5-7 μg/kg fentanyl, 0.1 mg/kg rocuronium and 2-3 mg/kg thiopental, the patients were intubated. Following endotracheal intubation, volume controlled mechanical ventilation was started. Tidal volume was set at 8 ml per kilogram of predicted body weight, inspiration/expiration ratio was adjusted 1:2, respiratory rate to 10/minute, and fresh gas flow was set at 3 L/minute in all patients. Positive end expiratory pressure of 5cmH2O was applied. All patients were ventilated with the same equipment (Draeger, Primus, Draeger Medical AG&Co, Germany). Anesthesia was maintained with 40%/60% O2 /air + desflurane and remifentanil infusion. The fentanyl dose was limited to a maximum of 20 μg/kg during anesthesia.

In the case of hypotension, defined as a (decrease in systolic arterial pressure of more than 20% from the baseline) during induction, the patient was first placed in the Trendelenburg position. In non-responsive patients, 250 mL of colloid was infused, and in the case of further unresponsiveness bolus administration of 5–10 mg of iv ephedrine was performed. If hypertension occurred, defined as an (increase in systolic arterial pressure of more than 20% from the baseline)
baseline), anesthesia was deepened and 2 µg/kg fentanyl was applied. For bradycardia, defined as (an HR < 50 beats/minute), the patients were administered 0.5 mg of iv atropine. Post-operatively all patients, still intubated, were transferred to the cardiovascular ICU. The same postoperative mechanical ventilation strategy was maintained as in the intraoperative period.

All patients were administered 0.1 mg/kg iv morphine (Morfin Hidroklorür 0.02 gr/ml, Osel) 15 minutes before the end of the operation. All patients received PCA with continuous infusion of tramadol (100 mg/2 ml vial Menta pharma) 16 mg/h during a 24 h period and paracetamol 1 gr in 100 ml (parol 10mg/10ml vial, Atabay) at 6 hours intervals for 72 postoperative hours.

Lansoprazol and ranitidin were preferred for gastric ulcer protection. Antibiotic prophylaxis of patients was performed with Cefazolin unless or until contraindicated. The diagnosis of PoNP was based on the 2015 diagnostic criteria of the “Centers for Disease Control and Prevention (CDC; see)” (Table 1) [1]. Pneumonia was diagnosed by evaluating the clinical features and symptoms, indications of fever and laboratory findings of the patients, in whom any infiltration, consolidation or cavitation was identified on chest X-ray.

Extubation time and PoNP development were considered as the primary endpoints in this study. In the postoperative period, the decision to extubate was taken by a multidisciplinary team, including the anesthesiologist and cardiovascular surgeon. In addition clinical characteristics of each patient were taken into account including arterial blood gas results, mechanical ventilator parameters, hemodynamic stability, degree of consciousness, body temperature and drainage that requiring red blood cell transfusion. Patients were followed closely in terms of infection parameters (clinical findings, daily hemogram, C-reactive protein (CRP) levels and, chest x-ray) in the ICU and in the ward for 120 hours after the operation.

**Statistical Analysis**
All statistical analyses were performed using SPSS for Windows, version 20.0 (IBM Inc., Chicago, IL, USA). Kolmorogov-Smirnov test was used to assess normality of data distribution. Continuous variables were expressed as mean±standard deviation or median (25th -75th. percentile). Categorical variables were summarized as counts (percentages). Comparison of continuous variables between groups was performed using Mann Whitney U test. Relationships between categorical variables were examined by Chi-Square test. A two-sided p-value <0.05 was considered statistically significant.
Table 1. Diagnosis of clinical nosocomial pneumonia.

| Radiological Findings | Signs and Symptoms |
|-----------------------|--------------------|
| At least one of the following must be present on two or more chest x-rays of the series: | At least one of the following: |
| • New or progressive and permanent the infiltration | • Fever (> 38°C) |
| • Consolidation | • Leukopenia (≤4000/mm³) or leukocytosis (≥12000/mm³) |
| • Cavitation | Unexplained change of mental state ≥70 years |

*NOTE:*
In patients without underlying cardiac or pulmonary disease (respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), a single chest radiograph with one of the above findings is sufficient

Table 2. Demographic characteristics and intraoperative and postoperative data of the patients

| Gender n (%) | S-ET groupe (n:30) | SSD-ET groupe (n:30) | p value |
|--------------|---------------------|----------------------|---------|
| Female | 11 (36.7) | 7 (23.3) | 0.398 |
| Male | 19 (63.3) | 23 (76.7) | |
| Age, years average (min-max) | 59.6 (32.0-70.0) | 56.3 (21.0-70.0) | 0.279 |
| BMI, Kg/m² average (min-max) | 27.59 (25.86-31.30) | 29.23 (25.18-31.32) | 0.882 |
| CCT, min median (IQR) | 76.00 (54.75-108.75) | 72.00 (55.00-100.50) | 0.544 |
| CPBT, min median (IQR) | 130.50 (108.50-175.25) | 114.00 (100.75-162.75) | 0.167 |
| Hypertension n (%) | 18 (60) | 18 (60) | 1.00 |
| Diabetes n (%) | 17 (56.7) | 22 (73.3) | 0.279 |
| ES average (min-max) | 3 (1.6) | 3 (2.5) | 0.963 |
| Coronary artery bypass grafting n (%) | 19 (63.3) | 19 (63.3) | 1.00 |
| Open Valve Surgery n (%) | 11 (36.7) | 11 (36.7) | 1.00 |
| EuroSCORE n (%) | 12 (40.0) | 13 (43.3) | 0.334 |
| Low 15 (56.7) | Median 17 (56.7) | High 21 (65.7) |
| PAP>30 mmHg n (%) | + | - | + | - |
| Low 7 (23.3) | 23 (76.7) | 6 (20.0) | 24 (80.0) | 1.00 |
| EF, % median (IQR) | 60.00 (50.00-65.00) | 61.00 (50.00-65.00) | 0.342 |
| ICU time, days median (IQR) | 3.31 (2.0-13.0) | 3.0 (2.0-12.0) | 0.075 |
| Extubation time, hours median (IQR) | 16.88 (5.0-77.5) | 12.65 (6.0-41.3) | <0.027 |
| PONP n(%) | 5 (16) | 3 (10) | 0.706 |

BMI: Body mass index; CCT: Cross-clamp time; IQR: interquartile range; CPBT: Cardiopulmonary bypass time; ES: Erythrocyte Suspension; PAP: Pulmonary artery pressure; EF: Ejection fraction; ICU: Intensive care unit; PONP: Post-operative nosocomial pneumonia
RESULTS

Sixty patients between the ages of 18 and 70 were included in the study. All eligible patients gave consent, and no patient needed to be excluded. There were 30 patients in each group. The demographic characteristics, co-morbid diseases, intraoperative surgery characteristics, the duration of cross-clamp time (CCT) and cardiopulmonary bypass time (CPBT), and the amount of erythrocyte suspension used in the patients were found to be similar in both groups. The extubation time in the SSD-ET group (12.65 hours) was significantly shorter than in the S-ET group (16.88 hours; p=0.027). PoNP developed in 5 (16.7%) patients in the S-ET group while in the SSD-ET group this occurred in 3 (10%) patients. The rate of PoNP did not differ between the groups (p=0.71). No mortality was observed during the study. No infection other than PoNP was observed (Table 2).

DISCUSSION

In this cohort the rate of PoNP was similar in the SSD-ET and S-ET groups, but extubation time was significantly shorter in patients with SSD-ET. One of the major causes of in-hospital mortality and morbidity after cardiac surgery is the development of postoperative infections [12]. The most common infection in the postoperative early period is PoNP. The most significant causes of PoNP are bronchial and gastrointestinal secretions that accumulate above the ET cuff. In addition, frequent tracheal aspirations also contribute to PoNP development [16]. Microaspiration and biofilm formation are the two principal features of ET which contribute to the development of PoNP and VAP [17]. The measures to prevent post-operative pneumonia development, both PoNP and VAP, and the features of ET which contribute to prevention are shown in Figure 2.

Use of S-ET may lead to both microaspiration and biofilm formation on the cuff. In order to minimize the risk of this, SSD-ET can be used, particularly for prolonged mechanical ventilation and associated VAP risk in ICUs. An SSD-ETs will enable continuous or intermittent aspiration of secretions accumulating on the cuff. In addition the ET cuff is made of either polyvinyl chloride (PVC) or polyurethane (PU). S-ET cuffs are generally made of PVC. However, PVC allows more microaspiration than PU. Dullenkopf et al showed that there was less secretion flow using PU cuffs compared with PVC cuffs, under the appropriate cuff pressure, because PU cuffs ultra-thin [18]. Studies have also highlighted the shape of the ET cuff as being important. Dave et al. reported that a conical shaped cuff lead to less secretion flow compared with cylindrical shaped cuffs in ET [19]. In conical shaped cuffs, the fluid flow decreases due to the sealing area where the cuff outer diameter and the internal diameter of the trachea meet [19].

The SSD-ET used in this study had a cuff of conical shape (Figure 3) while the S-ET had a cylindrical cuff structure (Figure 4). Thus it is possible that the difference in cuff shape used in the SSD-ET and S-ET groups may have contributed to differences in findings.

Cuff pressure is also important when considering infection prevention due to ET use. Both low and high cuff pressure may cause microaspiration. The use of a high-pressure cuff may damage the tracheal mucosa, due to exposure to high pressure gases, whereas in low-pressure cuffs, the barrier effect of the cuffs is less effective due to the lack of pressure. This has led to the production of, low-pressure, high-volume ET cuffs [17].

In order to prevent the development of PoNP, more recently designed ET allow for the removal of accumulated secretions above the cuff by either continuous or intermittent aspiration [20]. These are SSD-ET and the earliest studies comparing SSD-ET with S-ET showed a reduction in the incidence of VAP [8-12]. The aspiration method, continuous versus intermittent, has also been shown to affect morbidity. The incidence of injuries in patients with continuous aspiration of subglottic secretions was 8.1%, and located mostly in subglottic space [21]. In contrast,
Seguin et al reported a similar rate of tracheal damage in patients, regardless of the type of aspiration used [22]. Fujimoto et al. also reported that continuous or intermittent drainage aspiration did not change the effectiveness of the aspiration or likelihood of VAP development, but mechanical ventilation time was shortened in the group undergoing continuous aspiration [23]. Similar to the results of Fujimoto et al., the present study also showed significantly shorter extubation time in patients with SSD-ET [23]. While Fujimoto et al. found the incidence of VAP was similar, in our study it was shown that the rate of PoNP was similar in continuously aspirated patients. Moreover, in a meta-analysis performed by Muscedere et al., examining 2,442 patients, it was shown that SSD-ET reduced the development of VAP by 50% [24]. However, the patients included in this meta-analysis were maintained on mechanical ventilation for more than 48 hours. In the current study all patients underwent open-heart surgery with a fast-track anesthesia protocol. There are a limited number of studies in the literature with patients undergoing fast-track anesthesia protocol. Although there was no statistically significant difference in rates of PoNP between the SSD-ET and S-ET groups, the group sizes were relatively small. It is suggested that future studies should include larger group sizes to examine if significant differences in PoNP rates may appear given sufficiently powered studies.

The American Thoracic Society recommends SSD-ETs should be used in patients who will remain on mechanical ventilation for more than 48-72 hours [25]. However, the effect of SSD-ET use has not been rigorously investigated in procedures such as open-heart surgery, where fast-track extubation is performed. It has been shown that continuous aspiration SSD-ETs can reduce rates of VAP, duration of mechanical ventilation, and length of stay of patients in the ICU [26]. Wang et al. found in their meta-analysis that the rate of VAP development was 50% less with SSD-ET [27] which is in agreement with Muscedere et al. [24]. Wang et al also reported that mortality and the length of hospital stay were similar in both groups, the latter being in accord with our findings [27].

We found significantly shorter extubation time in the SSD-ET compared to the S-ET groups (p<0.027). Many studies have shown that prolongation of intubation constitutes a risk factor for both PoNP and VAP development [9-11]. It has been reported that shorter ventilation time, avoidance of reintubation and support with non-invasive ventilation all aid in minimizing the risk of PoNP [16]. In some studies in the literature, it has been stated that SSD-ET does not affect the extubation time but reduces the development of VAP in patients who have undergone cardiac surgery. However, interestingly, in our study, the extubation time was found to be significantly shorter with SSD-ET compared to S-ET. Although the surgical and anesthetic procedures applied to the patients were similar in both groups intraperatively and postoperatively, we could not explain for any reason which factors belonging to SSD-ET shorten the duration of extubation [13,28,29]. In our opinion SSD-ETs will prevent PoNP development by shortening extubation time in open-heart surgery patients, undergoing fast-track cardiac anesthesia protocol. The current study was conducted in patients with normal lung function and a low level of risk of PoNP development. We suggest that the effect of SSD-ET in patients having a high level of risk and poor lung functions should also be investigated.
Limitations
The limitations of this study include being single-centered and the assessors not being blinded to patient groups. This was because it is not possible to disguise the type of ET in use in each patient. In addition, monitoring for PoNP only occurred for the first 120 hours. Further studies should monitor the patients for more than five days.

Conclusion
Prolonged extubation period is risk factor for PoNP and VAP. This study has shown that SSD-ETs decreased the extubation time in patients undergoing open heart surgery, although there was no effect on the development rate of PoNP. Larger studies of both low and high risk patients using SSD-ET following open-heart surgery are warranted in terms of the possible beneficial effect on morbidity and mortality.

REFERENCES
1. CDC/NHSN Surveillance Definitions for Specific Types of Infections, January 2015. Available at https://www.cdc.gov/pneumonia/management-prevention-guidelines.html
2. Méndez GE, Calderón CHR. Risk factors for nosocomial pneumonia in patients with abdominal surgery. Factores de riesgo para neumonía nosocomial en pacientes con cirugía abdominal. Cirugía y Cirujanos (English Edition) Volume 2016;84(1):21-7. https://doi.org/10.1016/j.circir.2015.05.051
3. Chastre J, Fagon JY. Ventilator-associated pneumonia Am J Respir Crit Care Med. 2002;165:867-903. https://doi.org/10.1164/ajrccm.165.7.2105078
4. Zanella A, Scaravilli V, Isgrò S, et al. Fluid leakage cross tracheal tube cuff, effect of different cuff material, shape, and positive expiratory pressure: a bench-top study. Intensive Care Med. 2011;37:343-7. https://doi.org/10.1007/s00134-010-2106-z
5. Yia-Ting Li, Yao-Chen Wang, Jung-Hsing Tang, Chun Hui, Min-Chi Lu, Shun-Fa Yang. The association of ventilator-associated pneumonia with the frequent exchange of endotracheal tube. Int J Clin Exp Med. 2017;10(3):5252-60. https://doi.org/10.1183/13993003.congress-2016.PA2640
6. Coppadoro A, Berra L, Bigatelto LM. Modifying endotracheal tubes to prevent ventilator-associated pneumonia. Curr Opin Infect Dis. 2011;24:157-62. https://doi.org/10.1097/QCO.0b013e328343b733
7. Berra L, Sampson J, Fumagalli J, Panigada M, Kolobow T. Alternative approaches to ventilator-associated pneumonia prevention. Minerva Anestesiol. 2011;77:323-33.
8. Mahul P, Auboyer C, Jospe R, et al. Prevention of nosocomial pneumonia in intubated patients: respective role of mechanical subglottic secretions drainage and stres ulcer prophylaxis. Intensive Care Med. 1992;18:20-5. https://doi.org/10.1007/BF01706421
9. Zheng RQ, Lin H, Shao J, Chen QH, Lu NF, Yu JQ. A Clinical study of subglottic secretion drainage for prevention of ventilatation associated pneumonia. Zhongguo Wei Zhong Bing Ji Jiu Yi Xue Chinese critical care medicine 2008;20(6):338-40.
10. Dezfulian C, Shojania K, Collard HR, Kim HM, Matthy MA, Saint S. Subglottic secretion drainage for preventing ventilator-associated pneumonia: a meta-analysis. Am J Med. 2005;118:11-8. https://doi.org/10.1016/j.amjmed.2004.07.051
11. Lacherade JC, Azaïs MA, Pouplet C, Colin G. Subglottic secretion drainage for ventilator-associated pneumonia prevention: an under used efficient measure. Ann Transl Med. 2018 Nov;6(21):422. https://doi.org/10.21037/atm.2018.10.40
12. Kollef MH, Skubas NJ, Sundt TM. A randomized clinical trial of continuous aspiration of subglottic secretions in cardiac surgery patients. Chest. 1999 Nov;116(5):1339-46. https://doi.org/10.1378/chest.116.5.1339
13. Bouza E, Pérez MJ, Muñoz P, Rincón C, Barrio JM, Hortal J. Continuous aspiration of subglottic secretions in the prevention of ventilator-associated pneumonia in the postoperative period of major heart surgery. Chest. 2008 Nov;134(5):938-46. https://doi.org/10.1378/chest.08-0103
14. Myles PS, McIlroy D. Fast-track cardiac anesthesia: choice of anesthetic agents and techniques. Semin Cardiothorac Vasc Anesth. 2005 Mar;9(1):5-16. https://doi.org/10.1177/10892532050090102
15. Donlan RM, Costerton JW. Biofilms: Survival mechanisms of clinically relevant microorganisms. Clin Microbiol Rev. 2002;15(2):167-93. https://doi.org/10.1128/CMR.15.2.167-193.2002
16. Hortal J, Muñoz P, Cuerpo G, Litvan H, Rosseel P M, Bouza E. The European Study Group on Nosocomial Infections, the European Workgroup of Cardiothoracic Intensivists. Ventilator-associated pneumonia in patients undergoing major heart surgery: an incidence study in Europe. Crit Care. 2009;13(3):R80. https://doi.org/10.1186/cc7896
17. Fernandez JF, Levine SM, Restrepo MI. Technologic advances in endotracheal tubes for prevention of
ventilator-associated pneumonia. Chest. 2012 July; 142(1):231-8.
https://doi.org/10.1378/chest.11-2420

18. Dullenkopf A, Gerber A, Weiss M. Fluid leakage past tracheal tube cuffs: evaluation of the new Microcuff endotracheal tube. Intensive Care Med. 2003 Oct; 29(10):1849-53.
https://doi.org/10.1007/s00134-003-1933-6

19. Dave MH, Frotzler A, Spielmann N, Madjdpour C, Weiss M. Effect of tracheal tube cuff shape on fluid leakage across the cuff: an in vitro study. Br J Anaesth. 2010 Oct;105(4):538-43.
https://doi.org/10.1093/bja/aqe202

20. Bo H, He L, Qu J. Influence of the subglottic secretion drainage on the morbidity of ventilator associated pneumonia in mechanically ventilated patients. Chinese Journal of Tuberculosis and Respiratory Diseases. 2000 Aug; 23(8):472-4.

21. Vallés J, Millán S, Díaz E, et al. Incidence of airway complications in patients using endotracheal tubes with continuous aspiration of subglottic secretions. Ann Intensive Care. 2017;7:109. Published online 2017 Nov 2.
https://doi.org/10.1186/s13613-017-0331-0

22. Seguin P, Perrichet H, Le Pabic et al. Effect of Continuous versus Intermittent Subglottic Suctioning on Tracheal Mucosa by the Mallinckrodt Taper Guard Evac Oral Tracheal Tube in Intensive Care Unit Ventilated Patients: A Prospective Randomized Study. Indian J Crit Care Med. 2018 Jan; 22(1):1-4.
https://doi.org/10.4103/ijccm.IJCCM_350_17

23. Fujimoto H, Yamaguchi O, Hayami H, et al. Efficacy of continuous versus intermittent subglottic secretion drainage in preventing ventilator-associated pneumonia in patients requiring mechanical ventilation: A single-center randomized controlled trial. Oncotarget. 2018 Mar 23; 9(22):15876-82.
https://doi.org/10.18632/oncotarget.24630

24. Muscedere J, Rewa O, McKechnie K, Jiang X, Laporta D, Heyland DK. Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: a systematic review and meta-analysis. Crit Care Med. 2011 Aug; 39(8):1985-91.
https://doi.org/10.1097/CCM.0b013e318218a4d9

25. American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med. 2005;171(1):388-416
https://doi.org/10.1164/rccm.200405-644ST

26. Chow MCM, Kwok SM, Luk HW, Law JWH, Leung BPK. Effect of continuous oral suctioning on the development of ventilator-associated pneumonia: A pilot randomized controlled trial. International journal of nursing studies June 2012;49(11):1333-1341
https://doi.org/10.1016/j.ijnurstu.2012.06.003

27. Wang R, Zhen X, Yang BY, GuoX Z, Zeng X, Deng CY. Subglottic secretion drainage for preventing ventilator associated pneumonia: A meta-analysis. Chinese Nursing Research Volume 2, Issues 2-3, June-September 2015, Pages 55-60.
https://doi.org/10.1016/j.cnre.2015.03.001

28. Nam K, Park JB, Park WB, et al. Effect of Perioperative Subglottic Secretion Drainage on Ventilator-Associated Pneumonia After Cardiac Surgery: A Retrospective, Before-and-After Study. Cardiothorac Vasc Anesth. 2020 Oct 2; 3053-0770(20):31044 2.
https://doi.org/10.1053/j.jvca.2020.09.126

29. Gopal S, Luckraz H, Giri R, et al. Significant reduction in ventilator-associated pneumonia with the Venner-PneuX System in high-risk patients undergoing cardiac surgery: The Low Ventilator-Associated-Pneumonia study Eur J Cardiothorac Surg. 2015;47(2015):e92-e96
https://doi.org/10.1093/ejcts/ezu483