Increased Risks of Endotracheal Tube Cuff Colonization after Prolonged Intubation

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Abstract

Mechanical ventilation using endotracheal tube (ETT) intubation is crucial in saving life but may also cause ventilator-associated pneumonia resulting in morbidity and mortality. The purpose of this study was to examine the effects of intubation duration on pathogen colonization rates of ETT cuff region, and its association with the subsequent re-intubation and tracheostomy. We enrolled 92 patients who were successfully weaned from ventilator and were extubated within 20 days of intubation duration. Patients were divided into Group I and II based on intubation for 1-9 days and 10-20 days, respectively. Pathogen colonization over ETT cuff region and extra-cuff region (including sputum and ETT aspirates) were assessed. As compared to Group I patients, Group II patients had a significant higher pathogen colonization rate (100% vs. 69.2%; P < 0.001) in the ETT cuff samples, but not in the extra-cuff samples (92.6% vs. 84.8%; P = 0.442). Further studies demonstrated that there was no difference between Group I and II patients in the percentages of patients with the same pathogen over both the cuff and extra-cuff samples (35.5% vs. 30.8%; P = 0.925), suggesting that the increased pathogen colonization rate over the ETT cuff region was least likely from the extra-cuff region. In addition, the results showed that longer intubation was also associated with increased tracheostomy rate from 9.3% to 28.9% for Group I and Group II respectively (P = 0.025). We conclude that longer intubation has a higher pathogen colonization rate over the ETT cuff region in patients receiving mechanical ventilation support; longer intubation also increases the trend of receiving re-intubation and tracheostomy. Our findings indicate that it is crucial to remove ETT as soon as possible and perform pathogen culture over the ETT cuff regions immediately after extubation.

Key Words: endotracheal tube cuff, re-intubation, tracheostomy, ventilator-associated pneumonia

Introduction

To date, nosocomial or hospital-acquired infections remain to be the main causes of morbidity and mortality in critically ill patients (8, 9, 16, 33). Among all the hospital-acquired infections, lungs are extremely susceptible if patients receive mechanical ventilation frequently resulting in ventilator-associated pneumonia (VAP) (28, 32). VAP is defined by the occurrence of nosocomial pneumonia after two days of mechanical ventilation (13), and is one of the most common nosocomial infections seen in the intensive care unit (ICU). VAP is generally categorized as either early onset (occurred within 4 days) or late onset (occurred after 4 days of mechanical ventilation) (1, 10). The development of VAP seriously prolongs ICU stay and increases morbidity and mortality (9, 16, 28). However, it is hard to accurately diagnose
VAP and there is lacking a gold standard of VAP diagnostic procedure (1, 2, 9). This is due, at least in part, to varied pathogens, diverse sampling methods and different antibiotic resistance profiles in different hospital settings. Moreover, whether endotracheal tube (ETT) cuff colonization contributes to the development of VAP is still unclear. In order to address this question, we collected ETT cuff and aspirate samples from patients who had received extubation within 20 days of mechanical ventilation. Patients were divided into two groups (Group I: 1-9 days of intubation; Group II: 10-20 days of intubation) to determine the effects of intubation duration on ETT cuff colonization, and its association with subsequent re-intubation or tracheostomy.

### Materials and Methods

#### Protocols

This study was approved by the Institutional Review Board of Taipei Medical University. Each subject was informed and consented prior to sample collection. Enrolled in this study were 92 patients in an ICU setting, who had successfully weaned from mechanical ventilator treatment and were extubated within 20 days of intubation period. Patients were supported with ventilators due to unstable vital sign and/or respiratory failure. Characteristics and causes for endotracheal intubation of the patients are shown in Table 1. Patients were divided into Group I and II, based on intubation duration for 1-9 days and 10-20 days, respectively.

#### Samples

Cuff samples were collected immediately from ETT cuffs after the extubation procedure. Smears were done by rotating the swab on the upper side of the ETT cuff using the Collection & Transport System (BBL™ CultureSwab™, Becton Dickinon, MD, USA). For extra-cuff (including sputum and ETT aspirate) samples, sputum samples were collected from ETT aspirates from endotracheal tubes while the patients were still in the intubation period. Both sets of collected samples were tested for microbial growth in culture dishes.

### Data Analysis

Comparison of the extra-ETT cuff colonization (including sputum and ETT aspirate) and ETT cuff colonization between Group I and Group II was analyzed by using Chi-square test. $P < 0.05$ was considered statistically significant.

### Results

In this study, all the Group II patients had pathogen colonization over their ETT cuff regions (Table 2), and the pathogen colonization rate over ETT cuff samples was significantly higher in the Group II patients than in Group I patients (100% vs. 69.2%; $P < 0.001$). However, there was no significant difference in the pathogen colonization rate over the extra-ETT cuff samples between Groups I and II patients ($P = 0.442$). Our results further indicate that Group II patients had a significant higher tracheostomy rate (28.9% vs. 9.3%; $P = 0.025$) as well as a higher tendency of re-intubation rate (47.4% vs 31.5%; $P = 0.152$). These results also suggest potential harmful effects of longer

### Table 1. Characteristics of patients

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>92</td>
<td>54</td>
<td>38</td>
</tr>
<tr>
<td>Age</td>
<td>72.5 ± 15.7</td>
<td>70.9 ± 16.2</td>
<td>74.8 ± 14.3</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>51/35</td>
<td>28/22</td>
<td>23/13</td>
</tr>
<tr>
<td>White blood cells ($\times 10^9$/l)</td>
<td>11.9 ± 5.9</td>
<td>11.7 ± 5.5</td>
<td>12.1 ± 6.4</td>
</tr>
<tr>
<td>Red blood cells ($\times 10^9$/l)</td>
<td>3.6 ± 0.8</td>
<td>3.5 ± 0.9</td>
<td>3.7 ± 0.7</td>
</tr>
<tr>
<td>Platelet ($\times 10^9$/l)</td>
<td>243.8 ± 153.3</td>
<td>226.4 ± 133.5</td>
<td>267.9 ± 176.3</td>
</tr>
<tr>
<td>Underlying diseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>66.3%</td>
<td>35.9%</td>
<td>30.4%</td>
</tr>
<tr>
<td>Cardiorespiratory failure</td>
<td>34.8%</td>
<td>21.7%</td>
<td>13.0%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>21.7%</td>
<td>9.8%</td>
<td>12.0%</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>19.6%</td>
<td>9.8%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Chronic heart disease</td>
<td>17.4%</td>
<td>10.9%</td>
<td>6.5%</td>
</tr>
<tr>
<td>Cerebral vascular injury</td>
<td>14.1%</td>
<td>6.5%</td>
<td>7.6%</td>
</tr>
<tr>
<td>Drug overdose</td>
<td>2.2%</td>
<td>2.2%</td>
<td>0%</td>
</tr>
<tr>
<td>Renal disease</td>
<td>5.5%</td>
<td>3.3%</td>
<td>2.2%</td>
</tr>
</tbody>
</table>
We further compare the cultured microorganism between the ETT cuff and extra-ETT samples from each patient. There was no significant difference between Groups I and II samples in the ratio of patients with the same species of pathogen (35.5% vs. 30.8%, \( P = 0.925; \) Chi-square test) (Table 2), suggesting that the increased pathogen colonization rate over the ETT cuff region was least likely from colonization over sputum and ETT aspiration samples. In addition, normal pharyngeal flora were identified in the ETT cuff region among 30.8% of Group I patients (Table 2), but in none of Group II patients.

The species of germs identified in the extra-cuff and cuff samples are shown in Figs. 1 and 2. The infection rate of *Klebsiella pneumonia*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, *Enterobacter aerogenes*, *E. coli*, *MRSA*, *Staphylococcus aureus*, *Providencia stuartii*, *Calcoaceticus complex*, and *Pantoea agglomerans* were identified in the ETT cuff and extra-cuff samples.

### Table 2. Cultured of the endotracheal tube cuff and extra-cuff samples

<table>
<thead>
<tr>
<th>Group</th>
<th>Intubation (days)</th>
<th>ETT cuff samples</th>
<th>Extra-cuff samples***</th>
<th>Same pathogen flora in cuff and extra-cuff</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1-9 (n = 54)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No. Non-pathogen</td>
<td>Pathogen (%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>52 16*</td>
<td>36 69.2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>33 5**</td>
<td>28 84.8%</td>
<td>35.5% (11/35)</td>
</tr>
<tr>
<td>II</td>
<td>10-20 (n = 38)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>37 0</td>
<td>37 100.0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>27 2*</td>
<td>25 92.6%</td>
<td>30.8% (8/26)</td>
</tr>
<tr>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

\*: normal pharyngeal flora  
**: no growth  
***: including sputum and ETT aspirate samples

Fig. 1. Pathogen colonization over ETT cuff region in Group I (black bar) and Group II patients (grey bar). Cuff samples were collected immediately after the procedure of pulling out ETT. Smear was done by rotating the swab on the upper side of the ETT cuff and tested for microbial infection in culture dishes.
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baumannii, Stenotrophomonas maltophilia and Serratia marcescens increased by 2-5 folds over the ETT cuff region in Group II than in Group I patients (Fig. 1).

Discussion

Our results indicated that a longer duration of intubation was associated with significantly higher pathogen colonization rates over the ETT cuff regions, and the increases were associated with an increased tendency of subsequent re-intubation and tracheostomy.

ETT cuff is intended to seal the tracheal lumen to achieve positive-pressure mechanical ventilation as well as to prevent leakage of oropharyngeal secretion into the lower airways. In this study, we demonstrated that longer intubation duration was associated with increased pathogen colonization over the ETT cuff regions. Our culture results also indicated that, in the ETT cuff region, normal pharyngeal flora was identified in 30.8% of Group I patients (Table 2), but in none of Group II patients, indicating that normal pharyngeal flora were replaced by pathogenic flora on the ETT cuff surface after longer intubation. In addition, extra-cuff samples were collected to determine the pathogen in both sputum or ETT aspiration in this study. However, the ratios of patients with the same pathogenic florae identified from both cuff and extra-cuff samples were similar between Group I and Group II patients. These finding suggested that the adequate sealing effect of ETT cuff among our patients had prevented communication between cuff and extra-cuff regions. Therefore, the observed increased pathogen colonization over cuff surfaces was unlikely to be caused by leakage from regions either above or below the cuff site.

There are no evidence-based predictors that can reliably identify patients who will require prolonged mechanical ventilation. Studies have sought to identify such predictors, but their results are difficult to generalize because these studies examined varying durations of mechanical ventilation and specific patient populations. In addition, attempts to validate potential predictors have found poor sensitivity and specificity. Common causes for weaning failure have been identified such as underlying source of the respiratory failure not being fully corrected, volume overload, cardiac dysfunction, neuromuscular weakness, delirium, anxiety, metabolic disturbances and/or adrenal insufficiency. Recently, it has been demonstrated that a longer duration of mechanical ventilation is associated with higher incidences of developing VAP in patients receiving mechanical ventilation for more than 48 h (21). Previous reports have demonstrated
that *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Acinetobacter baumannii* are frequently implicated in the pathogenesis of VAP (3, 22, 30, 31). In consistence with these reports, our results also demonstrated that *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Acinetobacter baumannii* and *Candida albicans* were frequently identified on the ETT cuff region of our study groups. In addition, previous studies have reported that longer intubation would also increase the risk of losing cuff pressure, and this is likely as cause of leakage of subglottic secretions across the ETT cuff region contributing to the development of VAP (1, 4, 7, 11, 15, 18, 20). Furthermore, we have demonstrated that patients with longer intubation were associated with a higher risk of receiving re-intubation or tracheostomy, suggesting recurrence of respiratory infections and/or respiratory failure among some of our patients after extubation. It is likely that pathogen colonization on the cuff surface is associated with ventilator-associated tracheobronchitis or sub-clinical stages of VAP at the time of extubation, which progresses to VAP and respiratory failure needing re-intubation and/or tracheostomy. However, our study was limited by lacking follow-up information regarding the pulmonary conditions after extubation. This warrants further clinical studies.

Prolonged intubation is also associated with increased risks of micro-aspiration and the formation of biofilm over ETT, which subsequently contributes to the development of VAP. It has been shown that microorganisms can adhere to the surface of ETT and some species exude an exopolysaccharide which acts as a slime-like adhesive (5, 12, 17, 19, 29). Bacteria encased in this matrix (biofilm) are relatively resistant to the action of antimicrobials and host defenses (6, 24, 26). It has been suggested that dissemination of such microorganisms from the biofilm into the airways may occur upon insertion of a suction catheter. Fragments of ETT biofilm may be dislodged and carried further into the lung by ventilator gas flow. Besides, coughing is also able to cause micro-aspiration below the cuff and contributes to the development of VAP in patients with mechanical ventilation support (16). Taken together from our current findings and reports of others, we propose that longer intubation is associated with higher colonization rates over the ETT cuff region, which may contribute to the development of VAP.

In the clinical setting, our results suggest that it is crucial to remove ETT as soon as possible once the patients are no longer receiving mechanical ventilation support to prevent pathogen colonization over the ETT cuff region and the development of VAP. Recently, Nseir *et al.* reported that antimicrobial treatment in patients with VAP is associated with a greater number of days free of mechanical ventilation and lower rates of VAP and ICU mortality; however, antimicrobial treatment has no significant impact on total duration of mechanical ventilation (22, 23). Based on our and others’ findings, we recommend routine culture procedure over the cuff surface immediately after extubation in daily practices to obtain important information regarding the pathogenic flora and to help clinicians in choosing the appropriate antibiotic treatment to prevent the development of VAP.

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**References**

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