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Original article

Subglottic secretion drainage for preventing ventilator associated pneumonia: A meta-analysis

Rong Wang, Xiang Zhen*, [1], Bao-Yi Yang**, [1], Xue-Zhen Guo, Xue Zeng, Chun-Yan Deng

Department of Intensive Care Unit, Taihe Hospital, Hubei University of Medicine, Shiyan, Hubei 442000, China

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ABSTRACT

Objective: Ventilator associated pneumonia (VAP) has been shown to be associated with significant morbidity and mortality (Chastre and Fagon, 2002; Klompas, 2007) among mechanically ventilated patients in the intensive care unit (ICU), with the incidence ranging from 9% to 27%; crude mortality ranges from 25% to 50% (Rello, Ollendorf, Oster, et al., 2002; Tablan, Anderson, Besser, Bridges, Hajjeh, 2003). A meta-analysis of published studies was undertaken to combine information regarding the effect of subglottic secretion drainage (SSD) on the incidence of ventilated associated pneumonia in adult ICU patients.

Methods: Reports of studies on SSD were identified by searching the PUBMED, EMBASE, and COCHRANCE LIBRARY databases (December 30, 2010). Randomized trials of SSD compared to usual care in adult mechanically ventilated ICU patients were included in this meta-analysis.

Results: Ten RCTs with 2314 patients were identified. SSD significantly reduced the incidence of VAP (relative risk [RR] = 0.52, 95% confidence interval [CI]: 0.42–0.64, $p < 0.00001$). When SSD was compared with the control groups, the overall RR for ICU mortality was 1.00 (95% CI, 0.84–1.19) and for hospital mortality was 0.95 (95% CI, 0.80–1.13). Overall, the subglottic drainage effect on the days of mechanical ventilation was −1.52 days (95% CI, −2.94 to −0.11) and on the ICU length of stay (LOS) was −0.81days (95% CI, −2.33 to −0.7).

Conclusions: In this meta-analysis, when an endotracheal tube (ETT) with SSD was compared with an ETT without SSD, there was a highly significant reduction in the VAP rate of approximately 50%. Time on mechanical ventilation (MV) and the ICU LOS may be reduced, but no reduction in ICU or hospital mortality has been observed in published trials.

1. Introduction

Patients who require invasive mechanical ventilation (MV) are at risk for ventilator-associated pneumonia (VAP).[1] It has been shown to be associated with significant morbidity and mortality[2,3] among mechanically ventilated patients in the intensive care unit (ICU). It also has been proved to be associated with prolonged durations of MV, ICU stay and hospital stay, in addition to increased healthcare costs.[4,5] For all of these reasons, the prevention of VAP has been important in ICU clinician research.

Colonization of the upper respiratory tract (oropharaynx and trachea) secretions with potentially pathogenic organisms has been recognized as being a key factor in the pathogenesis of VAP.[2,3] These secretions have been shown to pool above the cuff of endotracheal tubes (ETT) prior to entering the lower respiratory tract as micro-aspirations.[6] Therefore, subglottic secretion drainage (SSD) with a specialized ETT that incorporates a suction port above the cuff has been proposed and tested as a method to attempt to reduce the incidence of VAP in ICU patients.[7]

Since the introduction of SSD into medical practice, many studies have examined the efficacy and effectiveness of SSD in preventing VAP.[8] It is necessary to update the studies to provide more solid evidence and to minimize the potential bias that is caused by limited publications. Thus, we performed an updated meta-analysis to investigate the results of published SSD trials and the effect of SSD on the incidence of VAP, ICU and hospital mortality, ICU length of stay (LOS), and duration of MV.

* Corresponding author.
** Corresponding author.
E-mail address: yangbaoyigodfred@163.com (B.-Y. Yang).
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[1] Xiang Zhen and Bao-Yi Yang contributed equally to this study.

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2. Materials and methods

2.1. Search strategy

We followed the PRISMA guideline for reporting our meta-analysis.[9] Related articles that were published in English or Chinese were identified and selected by searching PUBMED, EMBASE, CINAHL and the Cochrane Central Register of Controlled Trials (December 31, 2013). All of the bibliographies were also identified in the reference lists. Search strategies were adapted for all databases, and the following search terms were used: (1) glottis or suction or drainage and respiration, and (2) artificial or ventilation or intubation, and (3) mechanical, and (4) pneumonia.

2.2. Study selection criteria

All of the potential studies were retrieved and reviewed. We included studies if they: (1) were randomized controlled studies (RCTs), (2) studied adult critically ill patients who required invasive MV, (3) included ETTs with SSD in an experimental group compared to standard ETTs in a control group, and (4) reported on the incidence of VAP as defined by the investigators. Pregnant or lactating women and patients who were children were excluded.

2.3. Data extraction

Two reviewers independently extracted the following data: first author's surname, year of publication, setting of trials, number of participants in studies, method of subglottic drainage (intermittent or continuous and frequency), and definition of VAP and other interventions. The quality of trials was assessed with the method recommended by the Cochrane Collaboration for assessing the bias risk.[10]

2.4. Data synthesis and analysis

All of the data that were extracted were entered in the freeware program Review Manager (RevMan) Version 5.2 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012). Differences were expressed as relative risks (RRs) with 95% confidence intervals (95% CIs) for dichotomous outcomes. Binary outcomes (i.e., VAP and mortality) are reported as Mantel–Haenszel style risk ratios (RRs), whereas continuous outcomes are reported as inverse variance weighted mean differences. A fixed-effect model was used in cases of homogeneity (p value of χ^2 test >0.10 and $I^2 \leq 50\%$), and a random-effects model was used in cases of significant heterogeneity (p value of χ^2 test >0.10 and I^2 >50%). Publication bias was assessed by the inspection of funnel plots, and asymmetry was assessed using the regression test suggested by Egger (a p-value <0.1 was considered to be evidence of funnel plot asymmetry).[11]

3. Results

From our search strategy, a total of 146 potential studies were selected for secondary review after excluding non-randomized trials and review articles; twelve published randomized trials were included in the analysis,[12,23] but 2 studies[12,13] were excluded because the interventions might have influenced the effectiveness of SSD in reducing VAP and were therefore ineligible. We reviewed and abstracted data from each study prior to discussing the results (Table 1 and Table 2).

The included studies, with a randomized total of 2314 patients, are summarized in Table 1. The main inclusion criterion was predicated on the duration of expected MV in 9 of the 10 studies: one study[18] had an expected duration of MV > 24 h, four studies[15,17,22,23] had an expected duration of MV > 48 h, and four studies[4,19–21] had an expected duration of MV > 72 h. In all of the studies, ETTs with SSD were placed at the time of original intubation. The definitions of VAP always included radiologic criteria (new or persistent infiltrates on a chest radiograph) along with clinical and microbiological criteria.[24] The methods used to drain the subglottic secretion ranged from intermittent aspiration with a syringe to continuous suction (Table 1).

The pooled analyses across studies are graphically expressed in Figs. 1 to 5. The vertical line in the centre indicates that the estimated effects are the same for both the intervention and control groups and is often called the line of no difference. The values on the left of the line favour SSD, and those on the right favour the control. The diamond on the lower aspect of the graph near the horizontal line represents pooled values.[25]

In the meta-analysis for the primary outcome, the overall risk ratio (RR) for VAP was 0.52 (95% CI: 0.42–0.64; $p < 0.00001$), with no heterogeneity ($I^2 = 0\%$) (Fig. 1). It showed that SSD significantly reduced the incidence of VAP. Nine studies reported on mortality (either ICU or hospital); seven reported on ICU LOS. There was no effect on mortality in either the ICU (RR, 1.00; 95% CI, 0.84–1.19; $p = 0.91$) or the hospital (RR, 0.95; 95% CI, 0.80–1.13; $p = 0.98$) (Figs. 2 and 3, respectively). There was a significant reduction of 1.52 days in the duration of ICU LOS (95% CI, −2.94 to −0.11; $p = 0.03$), although there was significant heterogeneity ($I^2 = 77\%$) When the study by Kollef and colleagues[17] was removed, $I^2 = 4\%$ with $z = 5.83$, $P < 0.00001$, which indicated adequate homogeneity for pooling the study results. The mean ICU stay length was 2.29 days shorter than that in the group that received subglottic drainage (Fig. 4). Six studies reporting on the MV duration were able to be aggregated, and in these, MV duration was reduced (0.81 days; 95% CI, −2.33–0.7; $p = 0.29$), although there was significant heterogeneity ($I^2 = 94\%$) (Fig. 5).

Moreover, two studies reported antibiotic utilization. Bouza et al[15] reported a reduction in the number of defined daily doses of antibiotics with SSD (1213 vs.1932; $p < 0.001$), whereas Lacherade et al[17] did not find any difference in antibiotic utilization. Additionally, the re-intubation rates were also available in three studies: Kollef et al[16] reported re-intubation rates of five out of 160 (3.1%) patients in the SSD group and six out of 183 (3.3%) patients in the control group, Bouza et al[15] reported that re-intubation rates were 12 out of 331 (3.6%) patients in the SSD group and 14 out of 359 (3.9%) patients in the control group, and Lacherade et al[17] reported re-intubation rates of 21 out of 169 (1.2%) patients in the SSD group and 20 out of 164 (1.2%) in the control group.

4. Discussion

The goal of this study was to examine the effectiveness of subglottic secretion aspiration in reducing the occurrence of VAP. In this meta-analysis, when an ETT with SSD was compared with an ETT without SSD, there was a highly significant reduction in the VAP rate of approximately 50% (RR = 0.52, 95% CI 0.42–0.64) and a reduction in the number of MV patients. No reduction in the risk of ICU or hospital mortality was observed in our study, although this may not be surprising given that adequately treated VAP may demonstrate little or no attributable mortality.[24] Although only a slight reduction in duration of MV (summary estimate nearly −1 days, 95% CI, −2.33 to 0.7) and ICU LOS (about −1.5 days, 95% CI, −2.94 to −0.11) was observed, significant variation existed among studies that were included in the meta-analysis. Although the number of RCTs increased to 10 and the number of randomized patients was over 2300, our findings are similar to those of a previous smaller meta-analysis that found a 50% reduction in VAP, but no benefit in reducing ICU or hospital mortality; the number of