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Preintubation Application of Oral Chlorhexidine Does Not Provide Additional Benefit in Prevention of Early-Onset Ventilator-Associated Pneumonia

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BACKGROUND: Daily application of oral chlorhexidine gluconate (CHX) following intubation to reduce the risk of ventilator-associated pneumonia (VAP) is now the standard of care in many ICUs. This randomized clinical trial evaluated the benefit of adding a preintubation CHX dose to the known benefit of postintubation CHX to reduce the risk of early-onset VAP. A secondary aim was to test the effect of a preintubation oral application of CHX on early endotracheal tube (ETT) colonization.

METHODS: Subjects (N = 314) were recruited from two teaching hospitals and were randomly assigned to oral application of 5 mL CHX 0.12% solution before intubation (intervention group, n = 157), or to a control group (n = 157) who received no CHX before intubation. All subjects received CHX bid after intubation. Groups were compared using a repeated-measures model with Clinical Pulmonary Infection Score (CPIS) as the response variable. In a planned subset of subjects, ETTs were cultured at extubation.

RESULTS: Application of a preintubation dose of CHX did not provide benefit over the intervention period beyond that afforded by daily oral CHX following intubation. ETT colonization at extubation was < 20% in both groups (no statistically significant difference). Mean CPIS remained below 6 (VAP threshold score) in both groups.

CONCLUSIONS: Although it is feasible to deliver CHX prior to intubation (including emergent or urgent intubation), the results suggest that preintubation CHX may be inconsequential when the ventilator bundle, including daily oral CHX, is in place. During the preintubation period, providers should focus their attention on other critical activities.

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ABBREVIATIONS: APACHE = Acute Physiology and Chronic Health Evaluation; CHX = chlorhexidine gluconate; CPIS = Clinical Pulmonary Infection Score; ET = endotracheal; ETT = endotracheal tube; IHI = Institute for Healthcare Improvement; IRB = institutional review board; USF = University of South Florida; VAP = ventilator-associated pneumonia; VCU = Virginia Commonwealth University

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Hospital-acquired infections in critically ill adults are associated with increased morbidity, mortality, and cost. Reduction of ventilator-associated pneumonia (VAP) has been a target for quality improvement. Over the past decade, multiple interventions have been tested to reduce the risk of VAP. The Institute for Healthcare Improvement (IHI)[1] has published guidelines for the care of patients who are mechanically ventilated; the ventilator bundle incorporates interventions with evidence of effectiveness in reducing VAP risk, including 30° to 45° elevation of the head of the bed to reduce the risk of aspiration, and daily oral care with an antiseptic agent such as chlorhexidine gluconate (CHX). Many institutions have reported drastic reductions in VAP rates following implementation of a ventilator bundle.[2] However, VAP has not been eliminated, and additional interventions to further prevent risk would be beneficial.

CHX is a broad-spectrum antibacterial agent that is widely used as an oral rinse in outpatient dental care for the prevention and treatment of oral diseases such as gingivitis and periodontitis. Evidence supporting the inclusion of CHX in the daily oral care of patients who are mechanically ventilated to reduce the risk of VAP was reported in our initial investigations[3] and was confirmed by others in subsequent clinical trials and meta-analyses.[4,5] We also found that early application of a single dose of CHX (immediately after intubation) reduced early-onset VAP.[6] A Cochrane review concluded that chlorhexidine, either as a mouthwash or as a gel, is associated with a 40% reduction in the odds of developing VAP in critically ill adults.[7] However, studies have failed to show that oral CHX is associated with a difference in patient outcomes such as mortality, duration of mechanical ventilation, or duration of ICU stay.[4,7] Daily oral CHX was added to IHI guidelines for the care of the patient who is mechanically ventilated in 2010 and is now the standard of care in many ICUs. In contrast, a recent meta-analysis by Klompas et al[8] indicated that although patients undergoing cardiac surgery derived benefit from CHX, other types of critically ill patients did not; it is interesting to note that CHX is generally begun prior to intubation in patients undergoing elective cardiac surgery, but is begun following intubation in other critically ill patients.

During intubation, the endotracheal tube (ETT) must pass through the microbially rich environment of the oropharynx. In other clinical procedures in which a tube is inserted (for example, a urinary or IV catheter), decontamination procedures are performed at the insertion site to reduce the risk of subsequent colonization or infection. Endotracheal (ET) intubation generally proceeds without any preparation of the mouth other than suctioning of secretions and removal of dentures; loose teeth may be incidentally removed. Earlier studies in subjects undergoing elective cardiac surgery demonstrated a reduction in infections (including respiratory and surgical) in subjects who used CHX as an oral rinse before hospital admission,[9-11] but preintubation administration of CHX, including emergent or urgent intubations, has not been well studied in other patient populations. It is plausible that during urgent or emergent ET intubation, microbes in the pharynx may be dragged into the trachea and lower respiratory tract, potentially predisposing to pneumonia. Preintubation chlorhexidine, but not postintubation chlorhexidine, could potentially mitigate this. We reasoned that reducing the number of microorganisms in the mouth before intubation by application of CHX, added to continual microbial suppression by CHX applied after intubation, would reduce the risk of early-onset VAP in critically ill adults.

This project focused on evaluating the benefit of adding a preintubation CHX dose to the known benefit of postintubation CHX to reduce the risk of VAP. The primary aim was to test the effect of a preintubation oral application of CHX on the development of VAP in a variety of critically ill adults who were mechanically ventilated. Because colonization of the ETT provides a habitat for microorganisms and may contribute to the development of VAP, a secondary aim was to test the effect of a preintubation oral application of CHX on early ET colonization.

Materials and Methods

Subjects (N = 314) (Fig 1, Table 1) were enrolled from two large urban teaching medical centers in the Southeast (214 subjects at Virginia Commonwealth University Health System, an affiliate of Virginia Commonwealth University [VCU] in Richmond, Virginia, and 100 subjects at Tampa General Hospital, an affiliate of the University of South Florida [USF] in Tampa, Florida). The biostatistician investigator conducted an a priori power analysis to determine the sample size required to detect a difference in Clinical Pulmonary Infection Score (CPIS) of 1 between the two groups (intervention and control). Subjects were recruited in multiple clinical areas just prior to intubation, including critical care units, EDs, preoperative areas, procedural areas, and medical-surgical units during rapid response or code calls. Standard ETTs were selected by the clinical providers at each site. Neither site used subglottic suction tubes nor antimicrobial (eg, silver-coated) tubes. Patients with a clinical diagnosis of pneumonia at the time of intubation were excluded, because the determination of nosocomial pneumonia was confounded in subjects with preexisting pneumonia. Approval for involvement of human subjects was obtained from institutional review