
HIM 1990-2015

2012

Pepsin and amylase in oral and tracheal secretions of patients with standard versus continuous subglottic suctioning endotracheal tubes

Katherine Allen
University of Central Florida

 Part of the [Nursing Commons](#)

Find similar works at: <https://stars.library.ucf.edu/honorstheses1990-2015>

University of Central Florida Libraries <http://library.ucf.edu>

This Open Access is brought to you for free and open access by STARS. It has been accepted for inclusion in HIM 1990-2015 by an authorized administrator of STARS. For more information, please contact STARS@ucf.edu.

Recommended Citation

Allen, Katherine, "Pepsin and amylase in oral and tracheal secretions of patients with standard versus continuous subglottic suctioning endotracheal tubes" (2012). *HIM 1990-2015*. 1341.
<https://stars.library.ucf.edu/honorstheses1990-2015/1341>

PEPSIN AND AMYLASE IN ORAL AND TRACHEAL SECRETIONS OF
PATIENTS WITH STANDARD VERSUS CONTINUOUS SUBGLOTTIC
SUCTIONING ENDOTRACHEAL TUBES

by

KATHERINE HAY ALLEN

A thesis submitted in partial fulfillment of the requirements
for the Honors in the Major Program in Nursing
in the College of Nursing
and in The Burnett Honors College
at the University of Central Florida
Orlando, Florida

Fall Term 2012

Thesis Chair: Dr. Mary Lou Sole

© 2012 Katherine Hay Allen

ABSTRACT

The aspiration of oral and gastric substances is a well-known risk for ventilator associated pneumonia (VAP) in the intubated, mechanically ventilated (MV), patient of the intensive care unit (ICU) population. The gastric biomarker pepsin and the oral biomarker salivary amylase have been identified as evidence of aspiration prior to the manifestation of acute pulmonary illness. In an effort to decrease the risk for aspiration, several evidence based nursing practices are in place. Actions include 30 degree head of the bed positioning, oral care, suctioning, and circuit change interval protocols, as well as the administration of medication with the objective of reducing acid reflux. Additional recommendations concern the type of endotracheal tube (ETT) used to ventilate the intubated patient. The continuous subglottic suctioning endotracheal tube (CSS-ETT) features an additional port which continually suctions secretions that accumulate above the inflated endotracheal cuff. Patients with standard endotracheal tubes (S-ETT) receive manual, as needed suctioning of accumulated secretions in the mouth and the oropharynx per agency protocol. Research of the critical care population has demonstrated a decreased instance of VAP using CSS-ETT as compared to S-ETT utilization. This study sought to compare the incidence of the biomarkers pepsin and salivary amylase in the suctioned oral and tracheal secretions of patients with S-ETT compared to patients with CSS-ETT.

Part of the protocol of a descriptive, comparative study of the clinical indicators for suctioning established the collection of the paired suctioned oral and tracheal aspirates. Those collected aspirates were analyzed for a pilot study of pepsin and amylase analysis. This study compares the incidence of aspirates in oral and tracheal secretions by endotracheal tube type.

Tracheal aspirates were obtained with a closed tracheal suction device while oral secretions were obtained with a suction catheter designed to reach the oropharynx. Biomarkers assayed were the gastric marker pepsin and the oropharyngeal marker salivary amylase. Assays of pepsin and salivary amylase were performed using standard procedures in a specialty diagnostic laboratory.

Specimens were obtained from 11 subjects: 8 male and 3 female. The majority were Caucasian (n=9), had a CSS-ETT (n=8), were on mechanical ventilation in the synchronized intermittent mandatory ventilation mode, and on tube feedings (n=9) located in the stomach (n=7). The mean age was 56 years. Feeding tubes were placed in 9 patients, and the majority of the tubes were Dobhoff. Pepsin was found in the oral secretions of 62.5% (n = 5) of the CSS-ETT subjects, while 50.0% (n = 4) had pepsin in the tracheal aspirate. Pepsin was found in the oral secretions of 66.7% (n = 2) of the S-ETT subjects, and 66.7% (n = 2) had pepsin in their tracheal aspirate. All subjects of both groups (n = 11) had oral salivary amylase detected. Salivary amylase was detected in the tracheal aspirate of 100% (n = 3) of the S-ETT subjects versus 62.5% (n = 5) in CSS-ETT group.

Based on the results of this study, there was a reduction in the number of subjects who had oral compared to tracheal aspirate pepsin in the CSS-ETT group (n = 5 oral versus n = 4 tracheal) tube type. The S-ETT group had equal number of subjects with oral (n = 2) and tracheal pepsin detected (n = 2). However, the results when comparing the S-ETT and the CSS-ETT groups were not statistically significant (p = 0.898 pepsin oral and 0.621 tracheal pepsin).

There may be clinical significance. It appears that the CSS-ETT was beneficial in that group; two fewer subjects had pepsin in their tracheal aspirate (n = 5 oral versus n = 4 tracheal

aspirate pepsin). The intention of this study was that it would assist in demonstrating beneficial aspects of the selection of the CSS-ETT. It is considered that further investigation with a larger population group could add statistical significance.

DEDICATION

This thesis is dedicated to my mother and father who unfailingly believed in me,
giving me the support and courage to pursue my dreams.

“To dare is to lose one’s footing momentarily. Not to dare is to lose oneself.”
Søren Kierkegaard

To Aurea, who taught me so much about true friendship.
Keep your eye on the sky for the signal. We have much more to come.

“Our friends interpret the world and ourselves to us, if we take them tenderly and truly.”
Amos Bronson Alcott

ACKNOWLEDGEMENTS

It has been my great fortune to be associated with Dr. Mary Sole, researcher, mentor, and consummate professional nurse. Dr. Sole's passion for research and boundless energy gave life to my little idea. Happy am I to have experienced her universe which she so graciously shared.

Thank you, Dr. Steven Talbert and Dr. Bari Ruddy, for agreeing to serve as committee members. Your professional expertise and your insight continue to be greatly appreciated.

I am truly appreciative of Melody Bennett, Suzanne Ashworth, and Dr. Devendra Mehta of Orlando Health. Your efforts are outstanding and immeasurable in value to me.

Being a part of The Burnett Honors College at UCF has been an extraordinary experience. Not only have I felt supported continually by Denise Crisafi and Kelly Astro, the path was so well laid out that I was bound to succeed in meeting my commitments.

Finally, I wish to express my gratitude for the opportunity provided through the UCF College of Nursing by inviting Seminole State College/UCF concurrent nursing students to apply for Honors in the Major. Dr. Victoria Loerzel provided encouragement and assistance during these three semesters, and I am most appreciative of her support.

TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION	1
Background	1
Need for Mechanical Ventilation	1
Inflatable Cuff	1
Risk for Aspiration	2
Statement of the Problem	2
Maintain Patent Airway	2
Pooling Secretions	3
Professional and Agency Recommended	3
Nursing Actions	4
Purpose of the Study	4
Hypothesis	5
Research Question	5
Summary	5
CHAPTER 2: REVIEW OF LITERATURE	6
Literature Search	6
Subglottic Suctioning and Decreasing the Risk for Aspiration	6

Lowering the Incidence of Ventilator-Associated Pneumonia	8
Major Heart Surgery Patients and Lower VAP Rate with CSS-ETT	8
Mean Hospital Charges Less for CSS-ETT Group	9
Reduction in VAP Rate per 1,000 Ventilator Days	10
Lower Rates of Early and Late Onset VAP	10
Incidence of VAP Reduced in CSS-ETT Group	11
Dezfulian et al.'s Meta-Analysis of 16 Randomized Clinical Trials	11
Muscedere et al.'s Meta-Analysis of 13 Randomized Clinical Trials	13
Leasure et al.'s Meta-Analysis: Mortality not Affected by Tube Type	14
Wang et al.'s CSS-ETT Future Research Suggested	15
Summary	16
CHAPTER 3: METHODS AND PROCEDURES	18
Design	18
Subjects	18
Inclusion Criteria	18
Exclusion Criteria	18
Sample Size Determinants	18
Variables	19

Procedures	19
Demographic Data	19
Specimen Collection	19
Biomarkers	20
Endotracheal Tubes	21
Handling of Specimens.....	21
Maintaining Confidentiality.....	21
Informed Consent	21
Data Analysis	21
CHAPTER 4: FINDINGS	22
Hypothesis.....	22
Research Question	22
Results.....	22
Study group demographics	22
Laboratory Analysis of Amylase and Pepsin Specimens	23
CHAPTER: 5: DISCUSSION	27
Hypothesis.....	27
Research Question	27

Findings	27
Limitations of the Study	29
Time Constraints	30
Limited Number of Participants.....	30
Absence of a Randomized Control Group	30
Implications for Further Research	30
Clinical Implications	31
Summary	32
APPENDIX A: LITERATURE REVIEW TABLE.....	34
APPENDIX B: UCF IRB APPROVAL	38
APPENDIX C: ORLANDO HEALTH IRB APPROVAL.....	40
APPENDIX D: INFORMED CONSENT	43
APPENDIX E: UCF HUMAN RESEARCH PROTOCOL	46
REFERENCES	55

LIST OF TABLES

Table 1: Demographic Characteristics of Sample: Frequencies and Median	23
Table 2: Salivary Amylase Incidence by Sample Location and Type of ETT	24
Table 3: Pepsin Incidence by Sample Location and Type of ETT	25
Table 4: Results and Description by Subject	26

LIST OF FIGURES

Figure 1: Drawing of a Subglottic Suctioning Endotracheal Tube (CSS-ETT)	7
--	---

Terms and Definitions

Terms	Operational and Conceptual Definitions
amylase	an enzyme that splits starch; amylase in humans is distinguished by salivary or pancreatic type
aspiration	entry of gastric or oropharyngeal secretions due to absence of protective mechanisms (i.e. when intubated)
biomarker	a biochemical or molecular indicator used to screen for disease
CSS-ETT	continuous subglottic suctioning endotracheal tube; double lumen tube featuring a separate dorsal lumen allowing accumulated secretions from above the tracheal cuff to be removed continually through holes
early onset pneumonia	pneumonia that occurs prior to day five of hospitalization
ETCO ₂	end tidal carbon dioxide; an indicator of pulmonary ventilation
ETT	endotracheal tube
gastric reflux	regurgitation from stomach into the upper gastrointestinal tract
ICU	intensive care unit in a hospital
late onset pneumonia	pneumonia that occurs after day five of hospitalization; frequently associated with drug resistant organisms
LOS	length of stay
microaspiration	aspiration of oropharyngeal and gastric secretions into the airways of intubated and mechanically ventilated patients
MV	mechanical ventilation
oropharyngeal	the part of the pharynx between the soft palate and the upper edge of the epiglottis
pepsin	the chief gastric enzyme used to break down proteins
S-ETT	standard endotracheal tube; endotracheal tube comprised of a central lumen with an inflatable cuff
SIMV	Synchronized Intermittent Mandatory Ventilation; periodic assisted mechanical ventilation synchronized with the patient's breathing which maintains a preset rate if the patient fails to self-ventilate
sputum	a respiratory tract specimen of mucus obtained with suction and collected in an inline trap
tracheal	pertaining to the trachea which carries air from neck through upper chest
tracheal aspirates	secretions removed from the trachea by suctioning that area
ventilator-associated pneumonia	pneumonia that occurs after endotracheal intubation
ventilator days	used by agencies to compare incidence of VAP

CHAPTER 1: INTRODUCTION

Background

Need for Mechanical Ventilation

If deemed medically necessary to support adequate oxygenation and tissue perfusion, critically ill patients are intubated and mechanically ventilated. Airway patency is maintained via an artificial airway while the work of ventilation can be regulated by a mechanical source when the patient is unable to execute this effort naturally. One type of artificial respiration is delivered through an endotracheal tube which passes into the patient's mouth, past the oropharyngeal area, through the epiglottis into the trachea where an inflated cuff creates positive pressure for ventilation and secretions often pool above the cuff. The semi rigid endotracheal tube is made of a plastic, polymer type material and has been tested to conform to established specifications regarding size and performance (Simmons & Scanlon, 2009). The patient ventilation circuit connects the mechanical ventilation source to an endotracheal tube providing pathways for inspiration and expiration.

Inflatable Cuff

Endotracheal tubes create an open airway through the patient's mouth and oropharyngeal area to the trachea where the tube is held in place by an inflatable cuff. The cuff of the endotracheal tube serves to seal the space between the central lumen and the walls of the trachea which allows proper lung expansion by positive pressure inflation of the patient's lungs when using mechanical ventilation. The inflated cuff also helps to prevent aspiration of secretions that without a barrier could enter the lower part of the respiratory tract (Pierce & Sole, 2009).

However, the cuff does not form a perfect seal in the trachea, and upper airway, pooled, and collected substances are aspirated into the patient's lower airway.

Risk for Aspiration

Life sustaining mechanical ventilation and endotracheal tubes pose inherent risks, such as risk for microaspiration into the lower airway of substances accumulated in the upper airway. Mechanically ventilated patients often experience gastric reflux which is the reverse flow of gastrointestinal substances into the oropharyngeal area. Oral or gastric secretions are normally cleared by coughing or expectorating. However, in the mechanically ventilated patient, substances often accumulate subglottically above the inflated cuff of endotracheal tubes. The cuff does not form a perfect seal; microaspirates such as oropharyngeal secretions and substances of gastric origin enter the trachea from above the cuff and can seep into the lower airway via leaks and folds (Nseir, Zerimech, Jaillette, Artru, & Balduyck, 2011).

Statement of the Problem

Maintain Patent Airway

Critically ill patients undergoing mechanical ventilation with an endotracheal tube are unable to effectively clear their airway of accumulated oral secretions or gastrointestinal substances. Secretions typically consist of the patient's oropharyngeal endogenous mucus and microbes, but may also contain gastric enzymes or substances, and these potential aspirates are a well-known risk for ventilator-associated pneumonia (Bouza et al., 2008; Pierce & Sole, 2009). Respiratory therapists and nurses clear airway secretions by using negative pressure to suction the fluids through a catheter which empties the contents into a collection container. This is

accomplished in order to prevent aspiration of the secretions, maintain the airway, and reduce the risk of ventilator-associated pneumonia.

Pooling Secretions

Nurses or respiratory therapists suction the central lumen of endotracheal tubes on an as needed basis and per agency schedule to clear tracheal secretions. A specialized tube known as the continuous subglottic suctioning endotracheal tube (CSS-ETT) contains an additional dorsal lumen that allows constant or intermittent removal of the contents that pool above the cuff. The standard endotracheal tube (S-ETT) consists of a single, central lumen. Research has shown that the risk for aspiration of the pooled, accumulated secretions, which creates a risk for ventilator-associated pneumonia, is greater for patients with the S-ETT (Bouza et al., 2008).

Professional and Agency Recommended

According to the Institute for Healthcare Improvement (IHI), ventilator-associated pneumonia increases the number of days spent on the mechanical ventilator, increases the length of stay in the hospital, costs an additional \$40,000, and ranks highest in number of deaths from hospital-acquired infections (2011, n.p.). Use of the CSS-ETT has shown a 52% decrease in the incidence of ventilator-associated pneumonia, shorter patient hospital stays, and, additionally, patients were extubated and moved out of the intensive care unit sooner than when compared to the S-ETT data (Leasure, Stirlen, & Lu, 2012). The American Association of Critical Care Nurses (AACN) includes the recommendation of using a CSS-ETT in a ventilator-associated pneumonia practice alert (2008). Moreover, recommendations from the Centers for Disease Control (CDC) included the use of the CSS-ETT (Tablan, Anderson, Besser, Bridges, & Hajjeh, 2004).

Nursing Actions

Nurses are responsible for ameliorating the risk of aspiration in the mechanically ventilated patient and frequently assess the patient for signs that suctioning of secretions is needed in order to maintain a clear airway (Pierce & Sole, 2009). Since the two types of endotracheal tubes are in use in the clinical setting, there may be differences in the incidence of aspirates when comparing S-ETT and CSS-ETT suctioned secretions. When analyzed, the data may indicate an additional or amended nursing intervention recommendation. Some current nursing interventions include maintaining a 30 degree head of the bed positioning, completing an auscultation assessment for suctioning need, providing regular oral care, and ensuring that any pooled secretions are removed prior to balloon deflation when extubating the patient from the endotracheal tube (Pierce & Sole, 2009).

Purpose of the Study

This study compared the incidence of pepsin and amylase which was collected via the routine oropharyngeal and tracheal suctioning of critical care patients mechanically ventilated with either S-ETT or CSS-ETT. Suctioned specimens collected were analyzed to compare the incidence of pepsin and salivary amylase in oral and sputum samples by tube type. Based on the results of this study, more insight may be gained in order to guide future nursing actions. Additionally, based on the incidence of aspirate analysis, additional support of the recommendation which advocates the use of the CSS-ETT could be demonstrated (AACN, 2008). The overarching goal is the prevention of ventilator-associated pneumonia by meeting the objective of decreased risk for aspiration as indicated by a reduced incidence of designated markers of aspiration in oral and sputum suctioned samples.

Hypothesis

The hypothesis of this study is that there will be a difference in the incidence of pepsin and amylase in the oral and tracheal aspirate by endotracheal tube types. It is anticipated that due to the subglottic suctioning feature of the CSS-ETT, a reduced incidence of pepsin and amylase will be recorded.

Research Question

Will there be a difference in the incidence of pepsin and amylase when comparing by the endotracheal tube type?

Summary

To support adequate oxygenation and tissue perfusion, critically ill patients are intubated and mechanically ventilated via an endotracheal tube forming the artificial airway. The endotracheal tube's inflatable cuff serves to seal the space between the wall of the tube and the trachea. The patient is unable to effectively cough and expectorate because the epiglottis is kept open by the tube passing through into the trachea. Gastric reflux or oral secretions tend to pool above the inflated cuff of endotracheal tubes. These pooled substances are potential aspirates and are a well-known risk for ventilator-associated pneumonia. Research has shown that the risk for aspiration is greater for patients with the S-ETT. Governmental agencies and professional organizations have recommended the use of the CSS-ETT. Even so, Krein et al. (2008) found in a nationwide survey of more than 500 hospital infection control professionals, only 21% reported using subglottic suctioning tubes. This study may add to the body of knowledge related to the mechanical ventilation and intubation risk of the ICU patient for VAP.

CHAPTER 2: REVIEW OF LITERATURE

Literature Search

A literature search was performed in using the Cumulative Index to Nursing and Allied Health Literature (CINAHL) and MEDLINE databases. The date range was 2002 to 2012. The goal of the literature searches was to locate studies comparing incidence of aspiration by endotracheal tube types with the biomarkers salivary amylase and pepsin identified. The overarching goal in identifying markers of aspiration in the mechanically ventilated patient is to prevent disease, so a key word for the respiratory disease was included. The following terms were used: *aspiration*, *ventilator-associated pneumonia*, *subglottic suctioning*, *endotracheal tube type*, *pepsin*, and *amylase*. The searches were performed in combinations and yielded no results that studied pepsin or amylase as biomarkers for aspiration and comparing endotracheal tube types. It should be noted that aspiration in this context signifies microaspiration into respiratory tract of exogenous substances such as gastric or oropharyngeal substances.

Subglottic Suctioning and Decreasing the Risk for Aspiration

Pepsin and salivary amylase can be detected in tracheal aspirate specimens in laboratory settings, are indicators of aspiration, and as such their incidence can be useful when comparing tube types in an effort to prevent ventilator-associated pneumonia. One study discussed the silent aspect of aspiration, the damage that can rapidly occur to lung tissue, and that more detection efforts are warranted in order to prevent complications. Nseir, Zerimech, Jaillette, Artru, and Balduyck (2011) reviewed numerous interventions currently in practice such as patient positioning, maintenance of cuff pressure, feeding tube function surveillance, and different designs of endotracheal tubes. Subglottic suctioning tubes show promise in removing the

potential aspirates regurgitated from the gastrointestinal tract or other secretions that emanated from the oropharyngeal region. Subglottic suctioning tubes remove potential oral or gastric substances that have accumulated above the cuff of the endotracheal tube through an additional dorsal lumen. The conventional or standard tube features a central lumen which is suctioned distally from the inflated cuff. Aspiration of the accumulated secretions which pool around the cuff of the S-ETT is a well-known risk factor for ventilator-associated pneumonia. This study compared the standard versus continuously suctioning subglottic endotracheal tubes and the incidence of pepsin and amylase as biomarkers of aspiration. No studies were located during the review of literature that compared endotracheal tube type and marker of aspiration incidence. A diagram of a subglottic suctioning endotracheal tube (CSS-ETT) is shown below. The black line represents the additional, dorsal lumen tube that removes pooled secretions above the cuff from the subglottic space. The standard endotracheal tube (S-ETT) features a single, central lumen with no subglottic suction lumen.

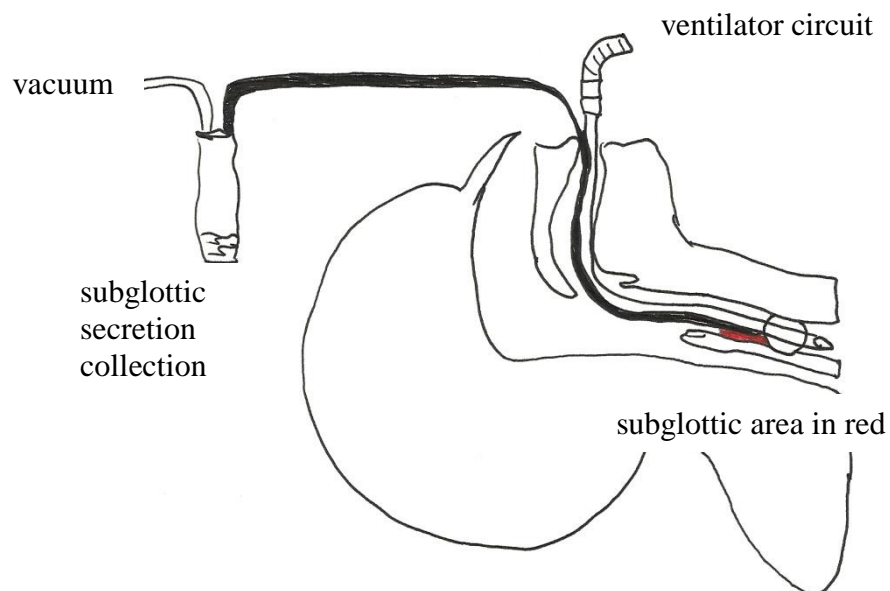


Figure 1: Drawing of a Subglottic Suctioning Endotracheal Tube (CSS-ETT)

Lowering the Incidence of Ventilator-Associated Pneumonia

The search for a comparison of endotracheal tube types produced results which were retained if the study compared standard to subglottic suctioning tube types or focused on the prevention of aspirates entering the lower airways as a risk for ventilator-associated pneumonia by using subglottic suctioning tubes. Ten articles include original research in the form of retrospective records reviews ($n = 2$) or randomized clinical controlled trials ($n = 4$) and systematic, meta-analysis reviews ($n = 4$). Taking the four meta-analyses as a unit, the findings of 16 total, not duplicated studies are detailed. The publication dates of the articles range from 1995 to 2010. The studies present data gathered during the hospitalization of 3,032 intubated, mechanically ventilated, critical care patients in the United States, Europe, China, and India. The subglottic suctioning groups from the original research studies utilized either intermittent ($n = 4$) or continuous ($n = 2$) subglottic suctioning. The meta-analyses incorporated both intermittent and continuous subglottic suctioning methods in their reviews. Antibiotic use, nosocomial infections, and cost analysis were measured in some studies. Other secondary outcome measures in the majority of studies were days to ventilator-associated pneumonia onset, duration of mechanical ventilation, length of ICU and hospital stay, and mortality. However, overall, the primary objective of the included studies was a comparison of standard endotracheal tubes to subglottic suctioning tubes and quantification of the incidence of ventilator-associated pneumonia.

Major Heart Surgery Patients and Lower VAP Rate with CSS-ETT

Bouza et al. (2008) studied of rate of ventilator-associated pneumonia by tube type. In this prospective, randomized study of 714 major heart surgery patients in Spain, at induction of anesthesia, patients were assigned to either the standard or continuous aspiration of subglottic

secretions group (CSS-ETT). The CSS-ETT group experienced lower rates of ventilator-associated pneumonia, shorter duration of mechanical ventilation, fewer days in the length of stay in the intensive care unit and the hospital, lower rates of antibiotic use, and fewer nosocomial infections. Mortality rates were similar with the standard group (n = 21) and the CSS-ETT group (n = 20).

Mean Hospital Charges Less for CSS-ETT Group

Speroni et al. (2011) compared the two tube types utilizing the continuous suctioning subglottic device. In this retrospective records review, 154 adult intensive care unit patients were intubated with either standard (n = 77) or continuous subglottic suctioning (n = 77) tubes. The primary outcome measure was the cost in total hospital charges for the patient based on tube type, if there was a ventilator-associated pneumonia diagnosis during the hospital stay, and if the two costs offset each other. The mean charges were \$103,600 for the S-ETT group and one ventilator-associated pneumonia diagnosis was made. None of the CSS-ETT patients were diagnosed with ventilator-associated pneumonia and the mean charges were \$88,500. The number of intensive care unit and mechanical ventilation days was greater for the CSS-ETT group, but one ventilator-associated pneumonia incident in the standard group incurred additional cost making the CSS-ETT more cost effective. Speroni et al. (2011) offered an explanation for the greater ICU and MV days in the CSS-ETT groups compared to the S-ETT groups. The patients with CSS-ETT were forecasted at the time of intubation to require more MV support days than the patients with S-ETT. Another study has found that physicians are 60-80% accurate in determining a need for prolonged mechanical ventilation at the time of intubation (Dezfulian et al., 2005).

Reduction in VAP Rate per 1,000 Ventilator Days

In 2011, Junega et al. reviewed the records to compare standard and intermittent subglottic suctioning endotracheal tubes to incidence of ventilator-associated pneumonia per 1,000 ventilator days during a three year period on an eight bed medical intensive care unit in India. The incidence of ventilator-associated pneumonia was 15.7 episodes per 1,000 ventilator days with a closed system, intermittent subglottic suctioning group to 25 episodes of VAP per 1,000 ventilator days with an open system, standard endotracheal tube control. No other results were deemed significant by the researcher.

Lower Rates of Early and Late Onset VAP

In a 24 bed medical-surgical intensive care unit in Spain, 280 patients assessed to require more than 24 hours mechanical ventilation were randomly assigned to intubation with either a standard or intermittent subglottic suctioning endotracheal tube. Lorente, Lecuona, Jiménez, Mora, and Sierra (2007) compared the incidence of ventilator-associated pneumonia and the days to onset. The control group experienced higher rates of ventilator-associated pneumonia (22.1%) versus the subglottic drainage group (7.9%). Rates of early and late ventilator-associated pneumonia onset were also lower in the subglottic secretion drainage group.

Lacherade et al. (2010) randomly assigned patients requiring more than 48 hours of mechanical ventilation to either standard or subglottic suctioning endotracheal tube intubation at four intensive care units in France. The results of this multicenter study of 333 subjects revealed that patients with the subglottic secretion drainage had lower rates of ventilator-associated pneumonia (14.8% vs. 25.6%), lower rates of early onset ventilator-associated pneumonia (1.2%

vs. 6.1%), and late onset ventilator-associated pneumonia (18.6% vs. 33.0%). Neither hospital mortality nor duration of mechanical ventilation results was significant between the two groups.

Incidence of VAP Reduced in CSS-ETT Group

In 2002, Smulders et al. randomly assigned 150 adult intensive care unit patients in the Netherlands expected to receive mechanical ventilation for longer than 72 hours to be intubated with either standard or subglottic suctioning tubes. The primary objective determining incidence of ventilator-associated pneumonia demonstrated a rate of 16% in the standard group and 4% in the subglottic drainage group. The other outcome measures of duration of days on mechanical ventilation, length of intensive care unit and hospital stay and mortality were not significant in the study.

Dezfulian et al. 's Meta-Analysis of 16 Randomized Clinical Trials

The four meta-analyses reviewed 16 randomized clinical trials that compared standard endotracheal tubes to either intermittent or continuous suctioning subglottic endotracheal tubes. Dezfulian et al. (2005) selected five studies comprising 896 patients four of which were targeted at patients expected to receive mechanical ventilation for greater than 72 hours. The fifth study concerned patients undergoing cardiothoracic surgery with a mean mechanical ventilation time of 1.5 days. The five sites included three medical-surgical intensive care units, one cardiothoracic intensive care unit, and one surgical intensive care unit. Other interventions to prevent the occurrence of VAP were included by the researchers. All studies included medication selected for stress ulcer prophylaxis and the use of antibiotics as well. Endotracheal cuff pressure checks were assessed at four or eight hour intervals in three studies. One study included head of the bed elevation protocols and a minimization of mechanical ventilation circuit changes. The

methods of subglottic drainage varied among the studies. Two studies utilized continuous wall suction, two studies utilized intermittent wall suctioning, one low intermittent, one high intermittent, and the fifth study removed subglottic secretions with a syringe on an hourly interval. Secondary outcome measures were early onset VAP, late onset VAP days on mechanical ventilation, length of stay in the ICU, and mortality. Early onset VAP is pneumonia occurring by day five after intubation. Late onset VAP occurs on day five or later. One of the five studies was excluded after the data were analyzed and it was found to be contrary to the other four. It was determined that this was due to the fact the excluded study concerned postoperative patients anticipated to require mechanical ventilation less than two days for whom the review concludes that subglottic suctioning is not beneficial as with longer intubations.

Dezfulian et al. (2005) reported that the frequency of ventilator associated pneumonia was decreased by almost 50%, and early onset VAP and the number of days on MV and ICU LOS were also decreased in the subglottic suctioning group compared to the standard endotracheal tube type group. There were also increased number of days to diagnosis of VAP in the subglottic drainage group, but there was no significant effect on mortality between the groups. The benefit of the subglottic suctioning tube is greatest realized by the patients MV for greater than 72 hours and in this meta-analysis, prevention of early onset of pneumonia is the most significant contribution. Dezfulian et al. (2005) suggests that late onset pneumonia may be due to other factors such as adherence of bacteria to the endotracheal tubes via the formation of biofilm. Subglottic suctioning would have no effect in the removal of that type of threat since the area of entry is the central lumen of the endotracheal tube. The cost savings comparing the higher cost of the subglottic suctioning tube to the cost of one VAP diagnosis amounted to

\$3,535 according to the researchers' calculations. Dezfulian et al. (2005) additionally concluded that physicians are 60-80% accurate in determining at time of intubation a need for prolonged mechanical ventilation. As the review surveyed three different types of intensive care units (cardiothoracic, surgical and medical-surgical) the results obtained are generalizable to different settings. This meta-analysis concludes that the most benefit is realized by those receiving greater than 72 hours of mechanical ventilation where two day shorter mechanical ventilation and a three day shorter ICU stay were demonstrated. Dezfulian et al. (2005) offers that tube type selection could be made with consideration of which group of patients most benefit from the subglottic suctioning option during their hospital stay.

Muscedere et al. 's Meta-Analysis of 13 Randomized Clinical Trials

In 2011, Muscedere et al. published a meta-analysis of 13 randomized controlled studies reporting the incidence of VAP as the primary outcome. Adult ICU patients were initially intubated with either S-ETT in the control group or CSS-ETT in the experimental group. The studies differed in the expected mechanical ventilation requirements at the time of intubation. The anticipated time frames ranged from greater than 24 hours to greater than five days mechanical ventilation. Secondary outcomes measured by the studies and analyzed by the reviewers included length of stay in the ICU and in the hospital, duration of MV, onset of VAP, the use of antibiotics, and mortality. In all of the studies, VAP was diagnosed radiographically; however, some studies included bronchoalveolar lavage quantification or endotracheal aspirate cultures. It should also be noted that three studies did not require an additional microbiological confirmation for the diagnosis of VAP. Twelve of the thirteen studies reported reduced rates of VAP with the use of a CSS-ETT. Reduction of VAP was similar between the intermittent and

continuous suctioning methodology compared to the standard tube type. Dezfulian et al (2005) had also concluded in their study that subglottic secretion removal was the key determinant in prevention of VAP. Overall, the CSS-ETT group experienced an ICU stay of 1.52 fewer days, MV was reduced by 1.08 days, and the onset of VAP was delayed by 2.66 days compared to the standard group. Neither hospital length of stay nor mortality was affected. The potential cost avoidance benefit calculating the low cost of the subglottic suctioning tube versus the higher cost of one occurrence of VAP was stressed by the reviewer. The issue of determining which patient should be intubated by which tube type was discussed as well. It was suggested that all patients in either an emergency situation or forecasted to require postoperative MV should be intubated with a subglottic suctioning tube. There was discussion regarding the practice of changing from a standard to a subglottic suctioning tube in an effort to reduce VAP risk. More research is required examining the benefit of reducing VAP risk versus the repeated intubation and the potential complications therewith. Muscedere et al. (2011) suggests further research is required in how to increase the use of CSS-ETT into practice given the evidentiary benefits.

Leasure et al.'s Meta-Analysis: Mortality not Affected by Tube Type

Leasure et al. (2012) reviewed 12 out of the 13 random clinical trials that Muscedere et al. (2011) analyzed and four of the five that Dezfulian et al. (2005) had reviewed. The primary outcome measured was incidence of VAP comparing standard versus subglottic suctioning endotracheal tubes, and the secondary outcomes were days to ventilator-associated pneumonia onset, duration of mechanical ventilation, and length of ICU and hospital stay. Again, a 50% decrease in ventilator-associated pneumonia rates was assessed in the experimental group, shorter ICU stays, and fewer days with mechanical ventilation which is equivalent to what had

been noted in the previous two meta-analyses. Leasure et al. (2012) suggests that additional research focus on one interventional change in studies in order to clarify that the improvements were directly attributable to that intervention. As also seen in Muscedere et al. (2011) and Dezfulian et al. (2005), mortality was not affected by tube type, and Leasure et al. (2012) suggests that mortality may be more attached to the overall poor condition of the patient rather than tube type. In other words, consistently, tube type has been shown to be inconsequential to mortality.

Wang et al. 's CSS-ETT Future Research Suggested

The reviewer of the fourth meta-analysis compared standard versus subglottic suctioning endotracheal tubes from 10 randomized controlled trials, five of which postdated Dezfulian et al.'s work in 2005. These results were compared to primarily focus on incidence of VAP and secondarily to days to onset, duration of mechanical ventilation, length of ICU and hospital stay, and mortality (Wang et al., 2012). Consistent with the previous meta-analyses discussed, VAP incidence was decreased in the subglottic suctioning group, early onset VAP was decreased, days to onset were increased, and mechanical ventilation days were decreased. No significant differences were found related to mortality, late onset VAP, length of stay in the ICU or in the hospital overall. Wang et al. (2012) separated the intermittent and continuous suctioning patients into a sub group and after analysis discovered that the VAP rates for each were again similar as found in Dezfulian et al.'s (2005) study. Also similar to the other three meta-analyses were the findings that there was no effect on mortality, late onset VAP, or duration of ICU or hospital stay. Wang et al.'s (2012) meta-analysis raises the issue of the safety of subglottic suctioning in light of concerns regarding post extubation laryngeal edema and animal study tracheal injury.

Additionally, future research investigating the prevention of late onset VAP is warranted in order to fully evaluate the findings by Lacherade et al. (2010) and Lorente et al. (2007) which were not observed in any of the meta-analyses.

Summary

The mechanically ventilated, intensive care unit patient is at risk for development of VAP for several reasons. Interventions are in place to decrease the risk for this life threatening complication. Researchers have investigated many variables such as head of the bed positioning, maintenance of cuff pressure, prophylactic use of antibiotics and gastric reflux inhibitors, and endotracheal tube type with mode of subglottic suctioning, intermittent or continuous. Reduction of VAP was similar between the intermittent and continuous suctioning methodology. Two researchers found decreased rates of late onset VAP comparing the tube types which was contrary to the results of the other studies. This is possibly due to the larger sample size revealing the late onset benefit which was absent in other smaller studies (Lacherade et al., 2010). The accumulation of biofilm has been postulated as the cause of the development of late onset VAP.

The literature review confirms that there is a distinct difference in the rate of VAP between the standard versus subglottic suctioning groups. Consistently, there was about a 50% decrease in the incidence. Furthermore, the cost of the subglottic tubes is offset by the finding that of every 100 patients intubated with a subglottic suctioning endotracheal tube, 11 cases of VAP are avoided (Lacherade et al., 2010).

Biomarkers may be used as proof of silent microaspiration delivering data clinicians can use to implement additional VAP precautions. Detection of substances exogenous to the lower respiratory tract provides information that may be useful in order to prevent VAP from occurring

(Nseir, 2011). At least, the selection of the CSS-ETT may prolong the number of days to VAP onset which could buy time for recovery and an opportunity for extubation.

CHAPTER 3: METHODS AND PROCEDURES

Design

This study was a secondary, retrospective review of data collected during a descriptive, comparative study examining the clinical cues for ETT suctioning.

Subjects

The 11 subjects for this study were critically ill patients intubated with either a CSS-ETT or S-ETT and receiving MV. All subjects were also participants in the primary suctioning cues study (Sole & Bennett, 2012).

Inclusion Criteria

The inclusion criteria for this secondary study were adult, critical care patients who met the requirements of the primary study for periodic suctioning by a closed system and that traditional mechanical ventilation was provided through an ETT.

Exclusion Criteria

This study excluded participants of the primary study if mechanical ventilation was provided via tracheostomy. Study participants were excluded if endotracheal suctioning was contraindicated on the patient's medical record, suctioning was performed by open method, non-traditional ventilation modes were in use, or if they were already enrolled in another research study.

Sample Size Determinants

The sample size was determined by the number of subjects who met the criteria and consented to participate from June 1, 2012 through August 31, 2012. During that time, 11 subjects were enrolled in the study.

Variables

The independent variable was tube type, CSS-ETT or S-ETT, and the dependent variables were presence of pepsin or salivary amylase in oral or tracheal suctioned secretions.

Procedures

Demographic Data

Demographic data were obtained including diagnoses, type of airway, presence of a feeding tube and placement location, duration of intubation and MV, Glasgow Coma Scale, type of mechanical ventilation supplied, age, gender, and ethnicity. Characteristics are shown in Table 1.

Specimen Collection

The research protocol included paired sampling of oral and tracheal specimens. While an oral secretion sample was obtained using a deep suctioning catheter, an endotracheal aspirate was also obtained. A baseline suctioning event (with paired specimen collection) marked the beginning of the study. The study endpoint was the completion of one to four hours of assessment data. The study participants were assessed every hour for up to four hours for ETT suctioning need based on clinical indicators such as ventilator waveform, coarse crackles auscultated over the trachea, inability of the patient to generate an effective cough, deteriorating oxygen saturation values, visible secretions in the airway, or signs of respiratory distress. Closed tracheal suction system was used for tracheal specimen collection. The patients were hyperoxygenated prior to suctioning with the suction pass lasting 15 seconds or less. The number of passes was recorded as to how many it took to clear the airway of secretions. Tracheal secretions were collected into a specimen trap. Five (5) mL of normal saline for respiratory use

cleared the suction catheter after every suctioning event. Following the tracheal suction, the mouth was suctioned with a deep suction catheter and the secretions were collected in the sputum trap.

Tracheal aspirate volume was measured by the graduated markings on the aspirate trap, less any saline volume that had been instilled. The aspirate traps were weighed after the suction event with the weight of the trap and saline subtracted in order to arrive at a net aspirate weight for that suctioning event. Posts suctioning physiological data were recorded. ETCO₂ waveform tracings and digital photographs of the ventilator waveform were taken post suctioning. The assessments were repeated every hour up to four hours. The study period ended after four hours post initial suction event or after completion of one additional ETT suctioning event, whichever came first. If assessment indicated that there was no need for suctioning, after four hours the patient was suctioned per protocol.

Biomarkers

By suctioning the oral cavity as well as the airway in a paired manner, biomarkers in the collected secretions were assessed for origin. Salivary amylase is oropharyngeal in origin while pepsin is endogenous to the stomach. Established enzymatic assay procedures for the detection of biomarkers of aspiration, pepsin and salivary amylase, were utilized (Appendix E). Pepsin was determined by measuring total pepsin.

In order to quantify salivary amylase present in the specimen samples, substrate was added to tint the end product of the samples through a process of metabolic breakdown. The rate of absorbance was calculated at 405 nm proportional to the activity of total amylase in the sample. Then, acarbose was used to inhibit salivary amylase in the sample; and the remaining

activity was pancreatic amylase activity only. The amount of salivary amylase was derived by subtracting the pancreatic activity from the total amylase activity in the specimen.

Endotracheal Tubes

Patient demographic data included the ETT type (Table 2). Oropharyngeal and tracheal aspirate specimens were collected, measured, recorded, and analyzed from each tube type in the same manner.

Handling of Specimens

All specimens were placed in a biohazard bag and kept chilled on ice. The specimens were transported by one of the primary study investigators to the agency research laboratory at the completion of data collection.

Maintaining Confidentiality

No patient identifying information or images were recorded. All oral or tracheal aspirate sample specimens were labeled with unique identifying numbers without any HIPAA identifiers.

Informed Consent

The research study was explained to persons with the authorization for the healthcare consent each participant. Informed consents were obtained for all subjects.

Data Analysis

Statistical Package for the Social Sciences (SPSS) version 19.0 was used for data analysis. Demographic data were summarized with frequencies and descriptive statistics. Descriptive, quantitative analysis assessed the collected oropharyngeal and tracheal suctioned secretions of patients comparing each by tube type for the presence of pepsin and amylase using the cross tabulation procedure.

CHAPTER 4: FINDINGS

Hypothesis

The hypothesis of this study is that there will be a difference in the incidence of pepsin and amylase in the oral and tracheal aspirate by endotracheal tube types. It is anticipated that due to the subglottic suctioning feature of the CSS-ETT, a reduced incidence of pepsin and amylase will be recorded.

Research Question

Will there be a difference in the incidence of pepsin and amylase when comparing by the endotracheal tube type?

Results

Study group demographics

Pepsin and amylase assays were performed on oropharyngeal and tracheal samples from 11 subjects ranging from 19 to 91 years old with the median age 62. This subgroup of the primary suctioning cues study were mostly male (n = 8), non-Hispanic (n = 9), and were on tube feeds (n = 9). The majority of the tube feeds were Dobhoff (n = 5) ending in the stomach (n = 7). Most of the subjects were mechanically ventilated with a CSS-ETT (n = 8) with the majority operating in SIMV mode (n = 9). The Glasgow Coma Scale median value was 10.0. The median value for endotracheal intubation and mechanical ventilation was 5.5 days, and ranged from one to 15 days. Table 1 summarizes the clinical and demographic data of the 11 subjects.

Table 1: Demographic Characteristics of Sample: Frequencies and Median

Demographic	Participants (n =11)
Gender	8 male 3 female
Age	62.0 years
Ethnicity	9 Non-Hispanic 2 Hispanic
Type of ETT	3 Standard 8 Subglottic
ETT Size	7.5
Duration ETT Duration MV	5.5 days 5.5 days
Mode of MV	9 Synchronized Intermittent Mandatory Ventilation (SIMV) 2 Other
GCS	10.0
Tube Type	1 no tube 5 Dobbhoff 1 nasogastric 4 orogastric
Tube Placement	7 stomach 3 post-pyloric 1 no tube

Laboratory Analysis of Amylase and Pepsin Specimens

Paired oropharyngeal and tracheal aspirate specimens were collected during the same suctioning event. The sample volumes were recorded, and analyzed from each of the 11 subjects in this study. The incidence of amylase in the oral and tracheal samples by tube type is reported in Table 2.

Table 2: Salivary Amylase Incidence by Sample Location and Type of ETT

Endotracheal Tube Type	Amylase Oral Detected	Amylase Tracheal Detected
S-ETT (n = 3)	Yes = 3 (100%)	Yes = 3 (100%)
	No = N/A	No = N/A
CSS-ETT (n = 8)	Yes = 8 (100%)	Yes = 5 (62.5%)
	No = N/A	No = 3 (37.5%)
p value	oral amylase constant	0.214
Oral = oropharyngeal samples; Tracheal = tracheal aspirate sample		

In the S-ETT group, amylase was detected in 100% of the subjects oropharyngeal samples while amylase was detected in 100% of the subjects' the tracheal aspirate sample as well. In the CSS-ETT group, amylase was also detected in 100% of the subjects' oropharyngeal samples. The tracheal aspirate sample had amylase detected in 62.5% in the CSS-ETT subjects (n = 5).

The incidence of pepsin in the oral and tracheal aspirate samples is reported on Table 3.

Table 3: Pepsin Incidence by Sample Location and Type of ETT

Endotracheal Tube Type	Pepsin Oral Detected	Pepsin Tracheal Detected
S-ETT (n = 3)	Yes = 2 (66.7%)	Yes = 2 (66.7%)
	No = 1 (33.3%)	No = 1 (33.3%)
CSS-ETT (n = 8)	Yes = 5 (62.5%)	Yes = 4 (50.0%)
	No = 3 (37.5%)	No = 4 (50.0%)
p value	0.898	0.621

Oral = oropharyngeal samples; Tracheal = tracheal aspirate sample

Comparing the incidence between the tube type groups, 66.7% of the S-ETT group (n = 2) had pepsin detected in oropharyngeal samples versus 62.5% of the CSS-ETT group (n = 5). Pepsin was detected in the tracheal aspirate samples of 50.0% of the CSS-ETT group (n = 4) and 66.7% of the S-ETT group (n = 2).

The 11 subjects can be viewed according to their endotracheal tube type, day of mechanical ventilation with an endotracheal tube, cuff pressure, feeding tube type and placement, feeding rate, and the head of the bed position on Table 4. Subjects varied according to day of mechanical ventilation, tube type, cuff pressure, tube feeding location and the head of the bed positioning. Additionally, time one (T1) and time two (T2) are shown which record the detection (+) or absence of detection (-) of amylase or pepsin in oropharyngeal or tracheal secretion samples. T1 indicates the result from the first suctioning event, and T2 represents the result for the second suctioning event. Oropharyngeal and tracheal suctioning events were paired throughout the study.

Table 4: Results and Description by Subject

Subjects			Amylase				Pepsin				Day ETT/ MV	Cuff Press	Tube Type	Tube Place	Tube Feed rate	HOB
			Oral		Trach		Oral		Trach							
			T1	T2	T1	T2	T1	T2	T1	T2						
Endotracheal Tube Type	S-ETT	35	+	+	+	-	+	+	+	+	9	24	NG	stomach	50	30
		39	+	+	+	+	-	+	+	+	10	28	OG	stomach	0	30
		40	+	+	+	+	-	-	-	-	4	26	OG	stomach	35	30
	CSS-ETT	31	+	+	-	-	-	-	-	-	1	26	DH	stomach	45	15
		32	+	+	-	+	-	-	-	-	15	22	DH	stomach	40	20
		33	+	+	+	+	+	+	-	-	1	24	DH	postpyloric	55	90
		34	+	+	-	-	+	+	+	+	7	24	DH	postpyloric	40	30
		36	+	+	-	-	+	+	+	+	11	24	OG	stomach	50	30
		37	+	+	+	+	+	+	+	+	10	24	OG	stomach	65	30
		38	+	+	-	-	+	+	+	+	11	24	DH	postpyloric	60	30
		41	+	+	-	-	+	+	+	-	8	22	No Tube Feed Placement			30

Notes: + = presence of amylase or pepsin (any); - = no amylase or pepsin detected (none)

T1 = time one, first suctioning event of the study; T2 = time two, second suctioning event of the study

Oral = suctioned oropharynx specimen; Trach = suctioned tracheal aspirate specimen

Day ETT/MV = endotracheal intubation and mechanical ventilation day

Cuff press = endotracheal cuff pressure in cm H2O.

DH = Dobbhoff, NG = Nasogastric, and OG = Orogastric.

Tube feed rate in mL/hour.

HOB = head of the bed positioning in degrees.

CHAPTER: 5: DISCUSSION

Hypothesis

The hypothesis of this study is that there will be a difference in the incidence of pepsin and amylase in the oral and tracheal aspirate by endotracheal tube types. It is anticipated that due to the subglottic suctioning feature of the CSS-ETT, a reduced incidence of pepsin and amylase will be recorded.

Research Question

Will there be a difference in the incidence of pepsin and amylase when comparing by the endotracheal tube type?

Findings

Five of the total study group (subjects 35, 36, 37, 38, and 39) had amylase and pepsin detected in both the oropharyngeal and tracheal secretions (S-ETT = 2; CSS-ETT = 3). Two subjects (31 and 41) had only amylase detected in the oropharyngeal secretions, none detected in the tracheal aspirates, and no pepsin detected in either location (CSS-ETT = 2). Comparing T1 and T2 differences in the subject data revealed that one S-ETT subject (35) had amylase detected in tracheal aspirate in T1 but not in T2. CSS-ETT subject 32 had no amylase detected in T1, but it was present in T2. S-ETT subject 39 did not have pepsin detected in the oropharyngeal sample in T1, but in T2, there was pepsin detected in the oropharyngeal secretion sample. In CSS-ETT subject 41, the T1 tracheal aspirate sample had pepsin detected that was not detected in the T2 sample. All other subject oropharyngeal and tracheal aspirate samples that were detected or not detected in T1 were the same status in T2.

Although differences were noted, there is no statistical significance. In the S-ETT group, pepsin was detected in the oral secretions of 66.7% of the subjects ($n = 2$) while pepsin was also detected in the tracheal aspirates of 66.7% of the subjects ($n = 2$). In the CSS-ETT group, pepsin in oral secretions was detected in 50.0% of the subjects ($n = 4$) while pepsin was detected in the tracheal aspirate of 50.0% of the subjects ($n = 4$). Comparing the S-ETT and the CSS-ETT pepsin findings, it is apparent that a smaller percentage of the CSS-ETT subjects experienced tracheal aspiration of pepsin. In the S-ETT group, oral and tracheal pepsin was detected in an equal number of subjects ($n = 2$).

Salivary amylase was detected in the oral sample 100% of both groups' subjects. This is an expected finding as salivary amylase is endogenous to the oropharyngeal region. All tracheal samples from the subjects in the S-ETT group ($n = 3$) had salivary amylase detected in the tracheal aspirate. In the CSS-ETT group, detection of salivary amylase in the subjects' tracheal aspirate sample decreased ($n = 5$) compared to the oral salivary amylase detected ($n = 8$). While the amylase tracheal aspirate comparison between tube types is not statistically significant, it could be clinically significant. Fewer subjects with the CSS-ETT had amylase detected in their tracheal aspirate samples than in their oropharyngeal samples (62.5%, $n = 5$ versus 100%, $n = 8$). This can be compared to the entire S-ETT group which had amylase detected in the oropharyngeal and tracheal aspirate samples (100%, $n = 3$). This comparison remains outside statistical significance ($p = 0.214$), however, it may be clinically significant.

The dorsal, subglottic suctioning port of the CSS ETT may have demonstrated its effectiveness in this study. Fewer CSS-ETT subjects had tracheal aspirate biomarkers than oropharyngeal biomarkers. The absence of statistical significance is likely attributable to the to

the small sample size. Microaspiration has been estimated to occur in almost 90% of mechanically ventilated patients. Endotracheal tube cuffs do not form a perfect seal. Pooled secretions tend to leak through the folds of the cuff. The utilization of an endotracheal tube featuring an additional dorsal, subglottic suctioning tube removing the above the cuff, pooled secretions has shown substantial promise in reducing VAP rates (Nseir, 2011). Several meta-analyses have found reduced VAP rates of up to near 50% with use of the CSS-ETT (Dezfulian et al., 2005; Leasure et al., 2012; Muscedere et al., 2011; Wang et al., 2012). The literature review confirms that there is a distinct difference in the rate of VAP between the standard versus subglottic suctioning groups. Consistently, there was about a 50% decrease in the incidence. Furthermore, the cost of the subglottic tubes is offset by the finding that of every 100 patients intubated with a subglottic suctioning endotracheal tube, 11 cases of VAP are avoided (Lacherade et al., 2010).

The biomarkers pepsin and amylase were detected in the tracheal aspirate of fewer subjects intubated with the CSS-ETT than with the S-ETT. It may be that the reduction in number of subjects' aspirates positive for pepsin and salivary amylase shown in this study may be one reason for the lower levels of VAP reported by researchers. The findings of this secondary study demonstrate differences, but are not statistically significant. The incidence of pepsin and salivary amylase by comparison of tube types, but there may be clinical significance.

Limitations of the Study

This study has recognized limitations. Time constraints, a limited number of participants, a single center study, and the absence of a randomized control group are all identified

limitations. The small number of participants is judged to be the most significant identified limitation.

Time Constraints

Since the primary suctioning cues study had been operational for several months by the time the secondary study was instigated, this study was limited by a three month primary study end point time frame.

Limited Number of Participants

The 11 subjects at one ICU comprised the entire group. It can be argued that the study's statistical significance may have been limited by the small number of participants. However, the study was designed for a small number group.

Absence of a Randomized Control Group

This study is descriptive in nature and describes the results from the patients intubated with S-ETT or CSS-ETT. There was no randomization in the selection of type of tube used during the patient's stay. However, there were two groups, a standard group and a subglottic suctioning group.

Implications for Further Research

Future, expanded research with multiple study sites could attain statistical significance. A larger sample size is another recommendation for future research. The study of a larger group may potentially reveal differences indistinguishable in this study comparing incidence of pepsin and salivary amylase aspiration by tube type in a group of 11 subjects. Lacherade et al. (2010) utilized a relatively larger sample size of 333 subjects which were then randomized to either S-ETT or CSS-ETT intubation. The multicenter study revealed a decrease in late onset pneumonia

which the researchers directly relate to having a larger study group. The greater number of participants undergoing mechanical ventilation for longer than five days may have revealed the relationship (Lacherade et al., 2010).

Clinical Implications

This study adds information to the body of knowledge in an effort to prevent VAP. It appears that the use of CSS-ETT instead of S-ETT may offer protection against secretions seeping into the patient's lower airway region as indicated by reduced incidence of biomarkers in the CSS-ETT group compared to the S-ETT group. However, the comparison is not statistically significant as was discussed earlier. Even though tracheal ($n = 4$) versus oral 9 ($n = 5$) pepsin was detected in fewer patients, the data is not significant by tube type ($p = 0.898$). Salivary amylase was decreased from oral ($n = 8$) versus tracheal ($n = 5$) in the CSS-ETT group, but this was not statistically significant ($p = 0.214$). In the S-ETT group, pepsin tracheal aspirate ($n = 2$) incidence was equal to the oral ($n = 2$) incidence in suctioned secretions. The salivary amylase oropharyngeal and tracheal aspirate were the same, comprising the entire subgroup ($n = 3$). Data gathered from this group size ($n = 11$) did not permit a relationship, if any, to be observed between incidence of pepsin and amylase as markers of aspiration and tube type.

The overarching aim of the primary suctioning cues study was to improve patient outcomes and reduce the risk for VAP. The patients in this study were accessed hourly for suctioning need which is more frequently than the usual suctioning need assessment interval. Additionally, multiple visual (waveform patterns or visually apparent mucus), auditory (tracheal auscultation), and other assessment data (blood gas, decreased O_2 saturation, or increased peak airway pressure) were implemented by the researchers as suctioning cues (Sole & Bennett,

2012). Perhaps, the primary study's protocol of at least hourly assessment as well as the implementation of multiple clinical cues rendered tube type statistically insignificant.

Summary

Researchers have studied many interventions in order to reduce the risk for VAP. Head of the bed positioning, hand washing, use of prophylactic antibiotic and gastric acid reducing medications, ventilator circuit change intervals, and providing oral care to the intubated, mechanically ventilated critical care patient are all part of the prevent VAP strategy (Coffin et al., 2008). The subglottic suctioning endotracheal tube has been recommended for use as part of the VAP practice alert by the AACN (2008). Based on the literature review for this study, VAP rates were shown to have been reduced by approximately half (Appendix A). Additionally, from the clinical results of this study, there was a reduction in the number of patients who had tracheal compared to oral suctioned pepsin and salivary amylase by tube type. However, the results were not significant. The intention of this study was that it would assist in demonstrating beneficial aspects of the endotracheal tube type selection. However, incidence of the selected biomarkers by tube types was not statistically significant. It could be that the other factors, suctioning cues, at least hourly assessment, and now standard interventions, such as head of the bed positioning, are more significant in this study than endotracheal tube type.

Although the results are not statistically significant when comparing pepsin detected in the oropharyngeal samples ($p = 0.898$) and tracheal aspirate samples ($p = 0.621$) by tube type, there may be clinical significance. In the CSS-ETT group the number of subjects that had pepsin oral decreased from six to four individuals with tracheal pepsin detected in their aspirate. There was no difference in the number of S-ETT subjects that had oral or tracheal pepsin detected ($n =$

2). Therefore, statistically speaking, any differences in the incidence of biomarkers by tube types in this study have a high chance of being unrelated to the tube type.

Potentially, future investigation with a larger population group could add the missing statistical significance to tube type absent in this study. A larger group may reveal a significance unseen at this study size ($n = 11$). On the other hand, perhaps, the clinical implication from this study is that the microaspiration prevention protocols in place in the critical care setting and the primary study's clinical suctioning protocol made tube type selection insignificant.

APPENDIX A: LITERATURE REVIEW TABLE

Appendix A: Literature Review Table

Author, Year	Population (n)	Study Design	Intervention Details	Outcome Measures	Results/Key Findings
Bouza et al., 2008	714	Prospective, randomized, comparative study	S-ETT vs. CSS-ETT	Incidence of VAP, ICU/ hospital LOS, non-pulmonary nosocomial infections, prophylactic antibiotics.	CASS group demonstrated lower rates of VAP, MV, ICU/hospital stay, C. diff infection, and reduced antibiotic consumption. The two groups experienced similar mortality (20 vs. 21).
Dezfulian et al., 2005	896	Systematic, meta-analysis of 5 RCTs	S-ETT vs. CSS-ETT	Incidence/onset of VAP, LOS ICU, Days on MV, Mortality.	Subglottic drainage tubes reduced VAP incidence by almost 50%, decreased early onset VAP, increased days to VAP onset, decreased MV days and ICU LOS. No effect on mortality.
Junega et al., 2011	311	Retrospective records review	S-ETT vs. CSS-ETT	Incidence of VAP/1000 ventilator days, Episodes of VAP, days on MV, length of stay, mortality.	VAP reduced from 25 to 15.7/1000 MV days comparing the closed system, intermittent subglottic suctioning group to the control. No other results were deemed significant.
Lacherade et al., 2010	333	Clinical randomized controlled trial	S-ETT vs. CSS-ETT	Overall incidence of VAP, early and late onset VAP, duration of MV, hospital mortality	Patients with the subglottic secretion drainage had lower rates of VAP than the standard group (14.8% vs. 25.6%), lower rates of early onset (1.2% vs. 6.1%) and late onset of VAP (18.6% vs. 33.0%). Results were not significant for duration of neither MV nor hospital mortality.

Author, Year	Population (n)	Study Design	Intervention Details	Outcome Measures	Results/Key Findings
Leasure et al., 2012	1,829	Systematic, meta-analysis of 13 RCTs	S-ETT vs. CSS-ETT	Incidence of VAP, days to onset of VAP, duration of MV, ICU/hospital LOS.	CSS-ETT group demonstrated lower rates of VAP, MV, ICU/hospital stay, C. diff infection, and reduced antibiotic consumption. The two groups experienced similar mortality (20 vs. 21).
Lorente et al., 2007	280	Clinical randomized controlled trial	S-ETT vs. CSS-ETT	Incidence/onset of VAP	VAP rates were 22.1% of S-ETT vs. 7.9% in CS-ETT, rates of early onset and late onset VAP were also lower in the CSS-ETT group
Muscedere et al., 2011	2,442	Systematic, meta-analysis of 13 RCTs	S-ETT vs. CSS-ETT	Incidence/onset of VAP ICU/hospital LOS, Antibiotic use, Intermittent vs. continuous suctioning, Mortality	CSS-ETT group experienced 50% reduction in VAP vs. S-ETT group, similar VAP reduction, decreased ICU, MV, onset of days to VAP, no effect on mortality or hospital LOS.
Smulders et al., 2002	150	Clinical randomized controlled trial	S-ETT vs. CSS-ETT	Incidence of VAP, duration of MV, ICU/hospital LOS, mortality	VAP rates were 16% of S-ETT vs. 4% in CSS-ETT group. The other outcome measures were not significant.
Speroni et al., 2011	154	Retrospective records review	S-ETT vs. CSS-ETT	Diagnosis of VAP Days on MV Length of stay Cost of stay	One case of VAP in the S-ETT group, none in the CSS-ETT group. ICU days and MV days greater for CSS-ETT group. Mean hospital charges \$103,600 (S-ETT) vs. \$88,500 (CSS-ETT).

Author, Year	Population (n)	Study Design	Intervention Details	Outcome Measures	Results/Key Findings
Wang et al., 2012	2,213	Systematic, meta-analysis of 13 RCTs	S-ETT vs. CSS-ETT	Incidence/onset of VAP, ICU/hospital LOS, MV duration, mortality.	Patients intubated with CSS-ETT had a decreased incidence of VAP, decreased incidence of early onset VAP, decreased MV days, and increased time to onset of VAP. No significant differences between tube type for late onset VAP, overall mortality, or LOS in the ICU or hospital overall.

APPENDIX B: UCF IRB APPROVAL



University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Human Research

From: **UCF Institutional Review Board #1**
FWA00000351, IRB00001138

To: **Mary L. Sole and Co-PI: Melody Bennett**

Date: **July 16, 2012**

Dear Researcher:

On 7/16/2011 the IRB approved the following modifications / human participant research until 7/15/2013 inclusive:

Type of Review: Submission Response for IRB Continuing Review Application Form
Project Title: Clinical Indicators for Endotracheal Suctioning in Adult Patients Receiving Mechanical Ventilation
Investigator: Mary L. Sole
IRB Number: SBE-11-07793
Funding Agency:
Grant Title:
Research ID: n/a

The Continuing Review Application must be submitted 30 days prior to the expiration date for studies that were previously expedited, and 60 days prior to the expiration date for research that was previously reviewed at a convened meeting. Do not make changes to the study (i.e., protocol, methodology, consent form, personnel, site, etc.) before obtaining IRB approval. A Modification Form **cannot** be used to extend the approval period of a study. All forms may be completed and submitted online at <https://iris.research.ucf.edu>.

If continuing review approval is not granted before the expiration date of 7/15/2013, approval of this research expires on that date. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

Use of the approved, stamped consent document(s) is required. The new form supersedes all previous versions, which are now invalid for further use. Only approved investigators (or other approved key study personnel) may solicit consent for research participation. Participants or their representatives must receive a copy of the consent form(s).

In the conduct of this research, you are responsible to follow the requirements of the Investigator Manual.

On behalf of Sophia Dziegielewski, Ph.D., L.C.S.W., UCF IRB Chair, this letter is signed by:

Signature applied by Patria Davis on 07/16/2012 11:31:56 AM EDT

IRB Coordinator

APPENDIX C: ORLANDO HEALTH IRB APPROVAL

FORM MUST BE
TYPED

CPA#

59165



Orlando Health Institutional Review Board
AMENDMENT OR REVISION APPROVAL REQUEST

RECEIVED
MAY 29 2012
IRB
ORLANDO HEALTH

IRB #: 11.071.07		Sponsor Protocol #: n/a	
<input type="checkbox"/> Version # / Amendment# / Date			
<input checked="" type="checkbox"/> ICF Revision Date: 05/29/12 <i>r40 -</i>			
PI Name: Mary Lou Sole		Department: Center Nursing Research	
Contact Person: Mary Lou Sole		Phone #: 407-823-5133 or 407-230-6905	Fax #: 407-823-5675
E-Mail: mary.sole@ucf.edu			
Project Title: Clinical Indicators for Endotracheal Suctioning in Adult Patients Receiving Mechanical Ventilation			

- I. ☒ Minor Change(s)/Minimal Risk

Requesting Expedited Review? ☒ Yes ☐ No : Review of Minor Changes by Expedited Procedure: Examples – minor changes that do not alter the risk/benefit relationship involved in the research; administrative/editorial changes; addition of qualified investigators. **If unsure, send for full Board review.**

- ☐ Significant Change(s)/Greater Than Minimal Risk (Full Board Review Required)

- II. Summarize and provide a rationale for the change(s). If request involves changes to the consent document, please also list the specific revisions or additions.

(The revisions must be summarized in this section. The IRB will not accept "see attached.")

Protocol was revised in March and approved along with revised consent form adding Dr. Mehta to protocol. When submitted to UCF IRB (since this went in as dual approval), IRB has requested minor modification to note that the oral and mucus specimens will be saved for analysis and not used for treatment. Minor modifications made to clarify and were reviewed by Janice Turchin at UCF.

What you will be asked to do in the study: You will begin the study after you have been suctioned by a staff member. At that point, as part of your standard of care, members of the study team will assess you each hour for cues that you need to be suctioned. If cues are found, you will be suctioned according to critical care standards. The exam will be done each hour for up to 4 hours. Exam findings and tracings from the ventilator and monitor will be written down each hour and collected for the study. We will collect and store the mucus secretions from your mouth and trachea and analyze for signs of aspiration. Up to two specimens will be obtained, and results will not be used to guide treatment. The patient or family member can ask that the study be stopped at any time.

Confidentiality: We will limit your personal data collected in this study to people who have a need to review this information. Each patient will have a code number assigned. No personal data will be written down. Data from all patients will be used to report study findings. No patient data or specimens will be labeled with personally identifiable information.

4/16/07, 06/2008, 10/2009
Orlando Health IRB (321) 841-5895

V:/aph/irb/irb/data/forms/amendmentrevisionform

III. Describe how this amendment will affect the risk to benefit ratio for subjects.

Does not change risk benefit ratio.

IV. ☐ Yes ☒ No Do changes require REVISION OF THE PROTOCOL? If **YES**, Refer to "How to Submit to the IRB" for submission requirements

V. ☒ Yes ☐ No Do changes require **REVISION OF ICF**? If **YES**, Refer to "How to Submit to the IRB" for submission requirements **clarification of content only (see summary)**

☐ Yes ☒ No Do changes require an **ADDITIONAL CONSENT FORM**? If **YES**, Refer to "How to Submit to the IRB" for submission requirements

VI. ☐ Yes ☒ No Are changes requested by a **STUDY SPONSOR**? If **YES**, enclose written verification from the sponsor.

VII. ☐ Yes ☒ No Have subjects been enrolled in this study? If **YES**, describe below how you will notify them of the change(s): _____

VIII. ☐ Yes ☒ No Change or Addition of Recruiting Materials/Advertising? If **YES**, attach copies to be used. Include one (1) original color copy and 20 copies with this form for Full Board Review (2 copies if being expedited).

Mary Lou Sole

5/29/2012

Signature of Principal Investigator

Date

(IRB Use Only)

☒ Approved on 5/30/12 as Minimal Risk

Signature of IRB Official

☐ Approved on _____ as Greater than Minimal Risk

Reported to IRB Meeting _____

APPENDIX D: INFORMED CONSENT



Clinical Indicators for Endotracheal Suctioning in Adult Patients Receiving Mechanical Ventilation

Principal Investigator(s): Mary Lou Sole, PhD, RN, CCNS, FAAN, FCCM

Sub-Investigator(s): Melody Bennett, MN, RN, CCRN
Suzanne Ashworth, MSN, RN, CCNS
Devendra Mehta, MD, MBBS, MRCP, MS

Investigational Site(s): Orlando Regional Medical Center

Introduction: Researchers at Orlando Health and the University of Central Florida (UCF) study many topics. To do this we need the help of people who agree to take part in a research study. You are being invited to take part in a research study which will include about 73 people. You have been asked to take part in this research study because you have a breathing tube in the mouth or the neck, are on a breathing machine, per your chart you can be suctioned, and you have a suction device attached to the breathing machine (closed suction). You must be 18 years of age or older to be included in the research study.

What you should know about a research study:

- Someone will explain this research study to you.
- A research study is something you volunteer for.
- Whether or not you take part is up to you.
- You should take part in this study only because you want to.
- You can choose not to take part in the research study.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- Feel free to ask all the questions you want before you decide.

Purpose of the research study: Many patients in the critical care unit have breathing tubes placed in the mouth (endotracheal tube) or neck (tracheostomy tube) so that breathing can be helped with a machine (ventilator). It is hard for patients with these breathing tubes to cough up secretions (mucus) that collects in the tube and lungs. When needed, the nurse or respiratory therapist (RT) suction the patient through the breathing tube to remove these secretions. The nurse or RT decides to suction the patient based on exam and cues.

The purpose of this study is to identify which exam findings and cues best identify the need for suctioning.

What you will be asked to do in the study: You will begin the study after you have been suctioned by a staff member. At that point, as part of your standard of care, members of the study team will assess you each hour for cues that you need to be suctioned. If cues are found, you will be suctioned according to critical care standards. The exam will be done each hour for up to 4 hours. Exam findings and tracings from the ventilator and monitor will be written down each hour and collected for the study. We will collect and store the mucus secretions from your mouth and trachea and analyze for signs of aspiration. Up to two specimens will be obtained, and results will not be used to guide treatment. The patient or family member can ask that the study be stopped at any time.

Risks: There are no known risks to you for participating in this research.

Benefits: You will not benefit from this study. However, you will be assessed every hour as opposed to normal standard of care practices which is usually every 2 to 4 hours.

Compensation or payment:

There is no compensation or other payment to you for taking part in this study.

Confidentiality: We will limit your personal data collected in this study to people who have a need to review this information. Each patient will have a code number assigned. No personal data will be written down. Data from all patients will be used to report study findings. No patient data or specimens will be labeled with personally identifiable information..

Study contact for questions about the study or to report a problem: If you have questions, concerns, or complaints, or think the research has hurt you, talk to Mary Lou Sole at 407-823-5133 or 407-823-2744 or mary.sole@ucf.edu.

IRB contact about your rights in the study or to report a complaint: Research at Orlando Health involving human participants is carried out under the oversight of the Institutional Review Board (IRB). This research has been reviewed and approved by the IRB. For information about the rights of people who take part in research, please contact: the Orlando Health IRB at 1414 Kuhl Ave. MP #21 Orlando, FL 32806 or by telephone at 321-841-5895 or the IRB at the University of Central Florida, Office of Research & Commercialization, 12201 Research Parkway, Suite 501, Orlando, FL 32826-3246 or by telephone at (407) 823-2901. You may also talk to them for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You want to get information or provide input about this research.

APPENDIX E: UCF HUMAN RESEARCH PROTOCOL



Human Research Protocol Template

IRB Template Version Date 11/19/2010

1) Protocol Title

Clinical Indicators for Endotracheal Suctioning in Adult Patients Receiving Mechanical Ventilation

2) Investigator(s)

Mary Lou Sole, PhD, RN, CCNS, FAAN, FCCM

Co-I: Melody Bennett, MN, RN, CCRN

3) Objectives

3.1 Primary Objective

To identify clinical indicators for endotracheal suctioning

3.2 Secondary Objectives

To compute sensitivity and specificity of suctioning cues

To describe characteristics of those who do not show clinical cues for the need for suctioning within a 4-hour period

To compare ratings of need for endotracheal suctioning between two investigators

To analyze mucus samples from mouth and trachea for presence of markers of potential aspiration.

4) Background

Many patients in the critical care setting receive mechanical ventilation as part of their treatment. Mechanical ventilation is delivered via an artificial airway, either an endotracheal tube (ETT) or tracheostomy tube. Nurses and respiratory therapists assume responsibility for airway management and related patient care. Airway management includes oral care, oral suction, endotracheal tube cuff management, management of specialized endotracheal tubes, and endotracheal (ET) suctioning.

ET suctioning for those with artificial airways is essential to remove retained tracheobronchial secretions. Secretions are retained in the lower airway secondary to impaired cough reflex, decreased mucociliary clearance, and possible increased mucus production.[1] Retention of secretions in the lower airways is a risk factor for development of ventilator-associated pneumonia (VAP).[2-4]

The 2010 American Association of Respiratory Care (AARC) Clinical Practice Guidelines for Endotracheal Suction specify that ET suctioning should be done when clinically indicated (versus a routine). The AARC indications for ET suctioning are noted below: [5]

- ☐ Sawtooth pattern on flow-volume loop on ventilator monitor
- ☐ Coarse crackles auscultated over trachea
- ☐ Increased peak inspiratory pressure during volume control ventilation
- ☐ Decreased tidal volume during pressure-controlled ventilation
- ☐ Deterioration in oxygen saturation and/or arterial blood gas values
- ☐ Visible secretions in airway
- ☐ Patient's inability to generate an effective cough
- ☐ Acute respiratory distress
- ☐ Suspected aspiration of gastric or upper airway secretions

Guglielminotti and colleagues conducted a study to identify factors indicative of retained secretions and the need for ETT suctioning.[1] Retained secretions were defined by retrieval (suctioning) of ≥ 0.5 ml of secretions. They found that both changes in the flow-volume waveform and respiratory sounds over the trachea were the best indicators of retained secretions. They also concluded that absence of sawtooth waveforms on the ventilator flow-volume waveform may rule out retained secretions.

Wood conducted a study to identify differences in ET suctioning outcomes between patients who had routine (every 2 hours) suctioning and ET suctioning performed on the basis of nursing assessment following specialized training. ET suctioning was done every 2.6 hours in the assessment group as compared to 2.1 hours in the routine group. Those who were suctioned per nursing assessment had significantly more secretions retrieved per suction episode, and a greater change in peak airway pressure following the procedure. Assessment indicators most often used by the nurses were chest auscultation (crackles, gurgles, and wheezes) or patient coughing. Other clinical indicators were recorded in documentation notes (desaturation, changes in arterial blood gases, and increased peak airway pressure); however, these cues were not used by the nurses to determine the need for ET suction.[6] A limitation of Wood's study is that neither auscultation over the tracheal, nor inspection of the ventilator flow-loop pattern, were included as part of the nursing assessment.[6]

Appropriate ET suctioning (suctioning when deemed clinically necessary) may reduce the risk for VAP. Caruso and colleagues found that routine suctioning along with instillation of normal saline reduced the risk for VAP by 54% in a sample of critically ill patients. They hypothesized that suctioning and or coughing that was induced after the saline instillation may have contributed to the reduced risk for infection.[7] Blamoun and colleagues included regular ET suctioning, defined as every 4 hours, as part of an expanded ventilator bundle and were successful in reducing the VAP rates to zero.[8]

ET suctioning is considered a necessary procedure for those with artificial airways. Recommendations for the need for ETT suctioning have been published, but may not be widely incorporated. In clinical practice, we have observed variation in assessments that are done to determine the need for suctioning. The purpose of this study is to expand upon the work of Guglielminotti [1] and Wood [6] to assist in determining the best practices for assessing the need for ETT suctioning. The overarching aim is to determine the best practices that improve patients' outcomes.

Addendum:

Secretions from the stomach and mouth often leak around the cuff of the artificial airway. The cuff is a balloon that theoretically seals the airway. However, secretions often leak around the cuff secondary to folds that develop in the cuff, tube movement, or underinflation of the cuff. This leakage of small amounts of secretions is termed microaspiration. When microaspiration occurs, selected biomarkers of aspiration, such as pepsin, may be detected in the sputum.[10, 11] As part of this study, we will be suctioning patients as clinically indicated; therefore we propose that rather than throwing away the mucus samples from the mouth and ETT, that we analyze the samples that are obtained for markers of aspiration. This will provide pilot data to support a future clinical study to test strategies to reduce the risk for microaspiration. Having readily available specimens enables us to expand this study without increasing burden or risk to the subject.

5) Setting of the Human Research

Critical care units at Orlando Health (4B Trauma ICU, 5B Medical, Surgical, Neuro, Cardiac)

6) Resources available to conduct the Human Research

Sole (PI), Bennett (Co-I) will collect data. Have time, supplies, needed to dedicate to the study. Dr. Devendra Mehta's research laboratory has the resources need to analyze the sputum specimens.

7) Study Design

Descriptive, comparative design.

a) Recruitment Methods We will enroll 73 subjects in the study who meet criteria as delineated below.

b) Inclusion and Exclusion Criteria

Inclusion criteria:

- ☐ Patients hospitalized in the critical care unit who have either an ETT or tracheostomy and require periodic ET suctioning
- ☐ Receiving volume or pressure mechanical ventilation (e.g, assist/control, SIMV, or APRV)
- ☐ Ventilator has screen and/or end-tidal CO₂ (ETCO₂) for waveform analysis
- ☐ Closed ET suction used for secretion removal

Exclusion criteria:

- ☐ Documented contraindications for ET suctioning in the medical record
- ☐ Routine suctioning with open method of ET suctioning rather than closed system
- ☐ Non-traditional modes of mechanical ventilation, such as the oscillator
- ☐ Enrolled in another research study

c) Study Endpoints

Completion of 4 hours of assessment data

d) Procedures involved in the Human Research.

Subjects who meet inclusion and exclusion criteria will be enrolled in the study. All procedures are part of the standard of care for the intubated, mechanically ventilated patient:

1. Obtain baseline demographic values.
2. Determine baseline suction event. Establish a mechanism for communicating with nurses and RTs to identify when an ET suctioning event is done (baseline) by staff members; obtain post-ET suction baseline data.
3. Following baseline, assess the patient for clinical indicators for need for ET suctioning every hour for up to 4 hours.
 - a. Drain water and/or secretions from the ventilator circuit tubing prior to assessment of the ventilator waveform.[1]
 - b. Conduct clinical assessment for parameters noted in the above table.
 - c. Take digital photograph of ventilator waveform (without any patient identifying information or images)
4. If clinical assessment indicates the need for ET suctioning, perform ET suction (PI or Co-I) per standard protocol[9]
 - a. Use closed tracheal suctioning (suction catheter is attached to ETT and ventilator circuit and remains attached).
 - b. Set suction regulator between 100 and 120 mm Hg.
 - c. Attach sputum trap to the closed suctioning circuit to retrieve secretions.
 - d. Hyperoxygenate the patient via the ventilator prior to suctioning and between suction passes.
 - e. Suction for no longer than 15 seconds per suction pass.
 - f. Repeat procedure until airway is cleared of secretions; record number of suction passes.
 - g. Rinse closed suction catheter with 5 mL of normal saline for respiratory use
 - h. Suction the mouth, if indicated, (presence of mucus audible or visible). This is part of standard of care for all patients with artificial airways and done every 2 hours or more frequently by the nurses, often in conjunctions with ET suctioning. Collect secretions in sputum trap as possible.
 - i. Record tracheal sputum volume from graduated markings on sputum trap (total minus volume of
 - j. Weigh tracheal sputum trap upon completion of suction event. Determine weight of secretions retrieved (total weight minus weight of sputum trap and normal saline rinse).
 - k. Collect post ET suctioning physiological data.
 - l. Take digital photograph of ventilator waveform (without any patient identifying information or images) to identify differences post suctioning.
 - m. Obtain waveform of ETCO₂ tracing (without any patient identifying information or images).
5. Repeat assessments every hour up to 4 hours after the initial ET suctioning.
6. If the patient is deemed to need suctioning by the nurse or RT prior to the hourly assessment, the procedure will be done by the staff and assessment data will be obtained for sub-analysis. Patients are eligible to begin another 4-hour study period.
7. Enrollment in the study ends upon completion of one ET suctioning event or 4 hours post initial ET suctioning, whichever comes first.

8. At the end of 4-hours, if ET suctioning was not performed, the patient will be suctioned using standard procedures and secretions will be weighed and measured to assess specificity of assessment cues.
9. All mucus specimens will be labeled with a unique ID number without any HIPAA identification. Specimen will be stored in a biohazard bag and kept on ice. Specimens will be transported on ice by one of the investigators to Dr. Devendra Mehta's Orlando Health research laboratory on Bonnie Loch at the completion of data collection. Established procedures for the detection of pepsin and other potential biomarkers of aspiration will be followed according to Policy # APH PSDL-00 (with the exception of omitting patient identification). Specimens are for research pilot testing only and results will not be used to treat the patient; therefore, no information will be logged other than unique ID #, type of specimen (oral or tracheal), and date/time of collection. All specimens will be discarded according to laboratory protocol once analyses are completed.
10. For the first 10 patients, both the PI and Co-I will be conduct independent assessments of the need for suctioning. If one or both indicate an assessment that warrants suctioning, step 4 will be done.[1] If assessments are concordant, then the remainder of subjects will be assessed by either PI or Co-I. If concordance is not established, then data will be collected on an additional 10 patients concurrently for re-evaluation.

Instrument, including reliability and validity

Data will be collected in an Excel spreadsheet using variables identified by other researchers (Guglielminotti and Woods).[1, 6] See appendix. Established techniques for analysis of aspiration biomarkers will be followed per laboratory policies and procedures to ensure accuracy of results.

e) Data management

Data will be collected in an Excel spreadsheet using variables identified by other researchers (Guglielminotti and Woods).[1, 6] See appendix.

No HIPAA identifiers are being collected. All subjects will be issued a code number. Data will be stored in password protected computer.

SPSS version 19.0 will be used for data analysis. Demographic data will be summarized with frequencies and descriptive statistics. A p-value of $\leq .05$ will be considered statistically significant.

Primary Objective: To identify clinical indicators for endotracheal suctioning
Statistics:

- ☐ Descriptive statistics of clinical indicators used to determine need for suctioning
- ☐ Mean time to need for suctioning will be computed.
- ☐ Chi-square test (categorical variables) or t-test (continuous variables) will be done to identify clinical indicators that changed between baseline suction pass and ET suctioning event done based on clinical assessment. Calculations of sensitivity and specificity will be computed for variables that showed a significant difference.[1]
- ☐ All variables will be placed into a logistic regression model to determine odds ratios.

- Subanalysis: Characterize photographs of waveforms as having sawtooth flow pattern present or absent.

Secondary Objective: To compute sensitivity and specificity of suctioning cues
 Statistics: Sensitivity (true positive) and specificity (true negative) will be computed using standard epidemiological formulas.

Secondary Objective: To describe characteristics of those who do not show clinical cues for the need for suctioning within a 4-hour period.

Secondary Objective: To analyze mucus samples from mouth and trachea for presence of markers of potential aspiration.
 Statistics: Descriptive analysis of biomarkers that are present.

f) Provisions to monitor the data for the safety of participants (Required when Human Research involves more than minimal risk to participants.)

n/a. Study procedures fall within the standard of care.

g) Withdrawal of participants

Those who provide consent may ask that subjects may be withdrawn. The PI or CO-I may withdraw subjects based on clinical judgment of the staff taking care of the patient.

8) Risks to participants

ET suctioning is part of the routine care of all mechanically ventilated patients. Although ET suction is not a benign procedure, there are no absolute contraindications for the procedure if suctioning is indicated. In fact, the AARC Guidelines emphasize that ETT suctioning when should not be withheld when indicated.[5] Standardized procedures to minimize/prevent complications of ET suctioning will be in place (e.g., hyperoxygenation before and during the procedure and use of closed system endotracheal suction devices.)

9) Potential benefits to participants

Assessment of the need for ET suctioning will be done every hour for a 4-hour period. This is more frequent than the every 2 to 4 hour assessments done in the critical care setting. Identification of the need for ET suction may occur sooner.

10) Provisions to protect the privacy interests of participants

All subjects will be issued a unique code number. No HIPAA-related data are collected.

11) Provisions to maintain the confidentiality of data

All subjects will be issued a unique code number. No HIPAA-related data are collected.

12) Medical care and compensation for injury

All patients will be receiving care and treatment that is part of the day-to-day management. No injury is anticipated in that all procedures are part of the standard care that all patients receive.

13) Cost to participants

No cost

14) Consent process

The study will be explained to family member/proxy of eligible subjects by members of the study team. Their decision to allow the family member to participate will be made. Waiver of written documentation of consent is requested since the study is considered minimal risk and falls within the standard of care for the patient population. Family members of critically ill patients are often stressed, so having a consent sheet with waiver of documentation is desired. Assent will be obtained from patients who are able to communicate.

15) Process to document consent in writing

See above. Request to waive written documentation of consent.

16) Vulnerable populations (Pregnant Women, Minors, Prisoners, Decisionally compromised adults, others)

Patients are those hospitalized in critical care units. Most are sedated.

17) Drugs or Devices

N/a

18) Multi-site Human Research

n/a

19) Sharing of results with participants

Results will be shared with staff members upon completion of the study.

20) References

1. Guglielminotti, J., et al., *Bedside detection of retained tracheobronchial secretions in patients receiving mechanical ventilation: is it time for tracheal suctioning?* Chest, 2000. **118**(4): p. 1095-9.
2. Garcia, R., et al., *Reducing ventilator-associated pneumonia through advanced oral-dental care: a 48-month study.* Am J Crit Care, 2009. **18**(6): p. 523-32.
3. Chao, Y.F., et al., *Removal of oral secretion prior to position change can reduce the incidence of ventilator-associated pneumonia for adult ICU patients: a clinical controlled trial study.* J Clin Nurs, 2009. **18**(1): p. 22-8.

4. Tsai, H.H., F.C. Lin, and S.C. Chang, *Intermittent suction of oral secretions before each positional change may reduce ventilator-associated pneumonia: a pilot study*. Am J Med Sci, 2008. **336**(5): p. 397-401.
5. AARC Clinical Practice Guidelines. *Endotracheal suctioning of mechanically ventilated patients with artificial airways 2010*. Respir Care. **55**(6): p. 758-64.
6. Wood, C.J., *Can nurses safely assess the need for endotracheal suction in short-term ventilated patients, instead of using routine techniques?* Intensive Crit Care Nurs, 1998. **14**(4): p. 170-8.
7. Caruso, P., et al., *Saline instillation before tracheal suctioning decreases the incidence of ventilator-associated pneumonia*. Crit Care Med, 2009. **37**(1): p. 32-8.
8. Blamoun, J., et al., *Efficacy of an expanded ventilator bundle for the reduction of ventilator-associated pneumonia in the medical intensive care unit*. Am J Infect Control, 2009. **37**(2): p. 172-5.
9. Chulay, M. and M.A. Seckel, *Suctioning: Endotracheal or tracheostomy tube*, in *AACN Procedure Manual for Critical Care*, D.L.-M. Wiegand, Editor. 2011, Elsevier-Saunders: Philadelphia.
10. Nseir S, Zerimech F, Jaillette E, Artru F, Balduyck M. *Microaspiration in intubated critically ill patients: diagnosis and prevention*. Infect Disord Drug Targets. 2011;11(4):413-23.
11. Jaoude, PA, Knight PR, Ohtake P, El-Solh AA. *Biomarkers in the diagnosis of aspiration syndromes*. Expert Rev Mol Diagn, 2010, 10:309-19.

REFERENCES

- American Association of Critical Care Nurses [AACN] (2008). *AACN Practice Alert: Ventilator Associated Pneumonia*. Retrieved on July 4, 2012 from <http://www.aacn.org/WD/Practice/Docs/PracticeAlerts/Ventilator%20Associated%20Pneumonia%201-2008.pdf>
- Bouza, E., Perez, M. J., Munoz, P., Rincon, C., Barrio, J. M., & Hortal, J. (2008). Continuous aspiration of subglottic secretions in the prevention of ventilator-associated pneumonia in the postoperative period of major heart surgery. *Chest*, 134(5), 938-946.
- Coffin, S., Klompas, M., Classen, D., Arias, K., Podgorny, K., Anderson, D., & ... Yokoe, D. (2008). Strategies to prevent ventilator-associated pneumonia in acute care hospitals. *Infection Control and Hospital Epidemiology*, 29(Suppl 1), S31-S40.
- Dezfulian, C., Shojania, K., Collard, H., Kim, H., Matthay, M., & Saint, S. (2005). Subglottic secretion drainage for preventing ventilator-associated pneumonia: A meta-analysis. *The American Journal of Medicine*, 118(1), 11-18.
- Institute for Healthcare Improvement (2011). *Implement the IHI ventilator bundle*. Retrieved on July 4, 2012 from <http://www.ihl.org/knowledge/Pages/Changes/ImplementtheVentilatorBundle.aspx>
- Junega, D., Javeri, Y., Singh, O., Nasa, P., Pandey, R., & Uniyal, B. (2011). Comparing influence of intermittent subglottic secretions drainage with/without closed suction systems on the incidence of ventilator associated pneumonia. *Indian Journal of Critical Care Medicine*, 15(3), 168-172.

- Krein, S. L., Kowalski, C. P., Damschroder, L., Forman, J., Kaufman, S. R., & Saint, S. (2008). Preventing ventilator-associated pneumonia in the United States: A multicenter mixed methods study. *Infection Control and Hospital Epidemiology*, 29(10), 933-940.
- Leasure, A. R., Stirlen, J., and Lu, S. H. (2012). Prevention of ventilator-associated pneumonia through aspiration of subglottic secretions: A systematic review and meta-analysis. *Dimensions of Critical Care Nursing*, 31(2), 102-107.
- Lacherade, J., De Jonghe, B., Guezennec, P., Debbat, K., Hayon, J., Monsel, A., & ... Bastuji-Garin, S. (2010). Intermittent subglottic secretion drainage and ventilator-associated pneumonia: A multicenter trial. *American Journal of Respiratory & Critical Care Medicine*, 182(7), 910-917.
- Lorente, L., Lecuona, M., Jimenez, A., Mora, M., & Sierra, A. (2007). Influence of an endotracheal tube with polyurethane cuff and subglottic secretion drainage on pneumonia. *American Journal of Respiratory and Critical Care Medicine*, 176(11), 1079-1083.
- Muscedere, J. Rewa, O., McKenzie, K., Jiang, X., Laporta, D. & Heyland, D. K. (2011). Subglottic secretion drainage for the prevention of ventilator assisted pneumonia: A systematic review and meta-analysis. *Critical Care Medicine* (39), 8, 1985-1991.
- Nseir, S., Zerimech, F., Jaillette, E., Artru, F., & Balduyck, M. (2011). Microaspiration in intubated critically ill patients: Diagnosis and prevention. *Infectious Disorders Drug Targets*, 11(4), 413-423.

- Pierce, L. N. B. & Sole, M. L. (2009). Ventilatory assistance. In M. L. Sole, D. G. Klein, & M. J. Moseley (Eds.), *Introduction to critical care nursing* (5th ed., pp. 173-229). St. Louis, MO: Saunders Elsevier
- Simmons, K. F. & Scanlan, C. L. (2009). Airway management. In R. L. Wilkins, J. K. Stoller, & R. M. Kacmarek (Eds.), *Egan's fundamentals of respiratory care* (9th ed., pp.693-741). St. Louis, MO: Mosby Elsevier
- Sole, M. L. & Bennett, M. (2012, March 26). *Clinical indicators for endotracheal suctioning in adult patients receiving mechanical ventilation* (Version No. 2, Amendment No. 2).
- Smulders, K., H, Weers-Pothoff, I., & Vandenbroucke-Grauls, C. (2002). A randomized clinical trial of intermittent subglottic secretion drainage in patients receiving mechanical ventilation. *Chest*, 121(3), 858-862.
- Speroni, K. G., Lucas, J., Dugan, L., O'Meara-Lett, M., Putman, M., Daniel, M., & Atherton, M. (2011). Comparative effectiveness of standard endotracheal tubes vs. endotracheal tubes with continuous subglottic suctioning on ventilator-associated pneumonia rates. *Nursing Economic\$*, 29 (1), 15-37.
- Tablan, O., Anderson, L., Besser, R., Bridges, C., & Hajjeh, R. (2004). Guidelines for preventing health-care-associated pneumonia, 2003: Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *Morbidity and Mortality Weekly Report*, 53(RR-3), 1-36.

Wang, F., Bo, L., Tang, L., Lou, J., Wu, Y., Chen, F., & ... Deng, X. (2012). Subglottic secretion drainage for preventing ventilator-associated pneumonia: An updated meta-analysis of randomized controlled trials. *Journal of Trauma and Acute Care Surgery*, 72(5), 1276-1285.