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ALPHA AMYLASE AS AN EMERGING BIOMARKER OF
MICROASPIRATION IN MECHANICALLY VENTILATED PATIENTS: AN
INTEGRATIVE REVIEW OF THE LITERATURE

by

CHLOE A. CHASE

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

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Thesis Chair: Dr. Mary Lou Sole, PhD, RN, CCNS, CNL, FAAN, FCCM

Abstract

Aims: The purpose of this thesis was to synthesize the current literature on alpha amylase as an emerging biomarker of microaspiration in mechanically ventilated patient.

Methods: The methodology included a review and synthesis of pertinent research articles from 1981-2018, written in English language. Criteria for inclusion in the review were all articles that evaluated α - amylase in tracheal secretions or bronchoalveolar lavage fluid (BAL) as a diagnostic tool for identifying microaspiration. The search yielded 11 studies that were reviewed.

Findings: The findings suggest that once aspiration occurs, the duration of α -amylase in the lungs requires further exploration to assist in interpretation of positive values. After these values are identified they need be used consistently used throughout practice of mechanically ventilated patients. Inconsistencies in the defining parameters of α -amylase were used with the thirteen studies.

Conclusion: Testing amylase levels can require financial stability, standardized training, and timeliness of collecting the specimen. Alpha-amylase is a biomarker of microaspiration. Further research should be conducted to evaluate the biomarker capabilities of α -amylase to assist in early identification and/or prevention of microaspiration in mechanically ventilated patients. Implications for nursing policy practice, education, and considerations for upcoming research of α -amylase were reviewed with limitations to the study.

Key words: Mechanical ventilation, nursing, ventilator associated events, pneumonia, α -amylase, aspiration biomarker, aspiration

DEDICATIONS

This thesis is dedicated to my family and friends who always supported me through my undergraduate career and the beginning of my nursing career. Thank you, mom, for all the sacrifices that you made in your life to be able to get me through schooling. Your love and appreciation are limitless.

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INTRODUCTION

Microaspiration is a potentially serious complication that can occur in intubated patients who are in critical conditions. Microaspiration entails the seepage of subglottic secretions around the endotracheal tube (ETT) (Blot, Poelaert, and Kollef, 2014; Nseir, Zerimech, Jaillette, Artru, & Balduyck, 2011), VAP results in increased lengths of stay in the intensive care unit (ICU) and hospital and requires a team of ICU staff to provide around the clock care to affected patients. Rather than focus on VAP, current practice is to monitor for complications known as Ventilator Associated Events (VAE). VAE occur from a decline in oxygenation after a patient has previously stabilized, positive cultures of a respiratory infection, and diagnostic tests indicating infection or inflammation of the lungs (Center for Disease Control and Prevention, 2018). Critically ill patients are susceptible to aspirating on their own oral secretions while confined in their hospital beds (VanBlarcom & McCoy, 2018). Microaspiration can cause damage and contamination to the respiratory tract. This can leave patients with various secondary diseases: decreased cardiac output, respiratory alkalosis, increased intracranial pressure (ICP), distended abdomen, pneumothorax, and hospital- acquired infections, among other issues (Drašković & Rakić, 2011). The secretions that seep past the ETT tube may be found within the lungs of patients on mechanical ventilators.

Amylase is an enzyme that is found usually in saliva or pancreatic secretions. Amylase converts starch into simple sugars inside the body (Medline, 2019). Patients are susceptible to many infections and complications when they are on a ventilator. More research needs to be conducted on the prevalence of α -amylase when found in the lungs compared to other locations in the human body. As well as, what a safe amount of α -amylase to have in the body before it

becomes a problem. Patients can aspirate both oral and/or gastric secretions. Aspiration of oral contents may be identified by detecting levels of α -amylase on tracheal secretion. Patients with α -amylase do not have protocols in place to identify the degree of severity in their lungs. α -amylase has been associated with patients who have experienced microaspiration (Dewavrin et al, 2014).

New research is suggesting α -amylase in tracheal secretions as a potential biomarker for detection of microaspiration of secretions around a breathing tube into the lungs; however, defined limits of its use have not been described. Few studies have acknowledged α - amylase as an imperative biomarker for aspiration pneumonia patients (Rouzé, Jaillette, and Nseir, 2018).

Purpose

The purpose of this thesis was to analyze the research that has been conducted on α -amylase in tracheal secretions of intubated patients.

METHODOLOGY

A literature search was conducted, and findings are reported as a literature review. Multiple databases were searched: MEDLINE, CINAHL, PsycInfo and Academic Search. Key terms used were, “alpha-amylase or amylase* OR (MH "Amylases") AND (MH "Biological Markers") OR marker* or "bio* marker" or biomarker*) AND (aspirat* or Suctioning or bronch* or pulmonary or endotracheal or ventilat*. There were no restrictions on publication dates. Inclusion criteria consisted of the English language. All articles with α - amylase as a diagnostic tool for identifying microaspiration and indicators of α -amylase in bronchoalveolar lavage fluid (BAL) were included.

From the original search with MEDLINE, CINAHL, PsycInfo, and Academic Search, (n= 77) articles were identified. Articles excluded discussed various properties of α -amylase with investigative research on preventing various medical conditions and their complexities that follow asthma, organ failure, high-intensity stress, and motor vehicle accidents. Articles were excluded due to not meeting the inclusion criteria (n = 68) of relating specifically to mechanically ventilated patients. Articles specific to amylase and its clinical significance in ventilated patients (n=9). Additional studies were found through review of article reference lists (n=2). A total of eleven studies were included in this review. These eleven articles that discussed α -amylase in ventilated patients were further investigated for their credibility in this literature review.

FINDINGS

A comprehensive review of literature findings was completed to discuss the role of α -amylase as a biomarker for aspiration and complications of ventilation. Dewarvin et al, (2014) compared α -amylase levels in 109 patients in an ICU in a retrospective analysis. Of the patients that were included in the study there was 1055 tracheal aspirates. The value of a tracheal aspirate of α -amylase in a patient was >1688 IU/L to be deemed positive (Dewarvin et al, 2014).

Weiss et al (2011), measured α -amylase in 296 BAL specimens from 280 patients that classified with a minimum of one risk factor of aspiration. These risk factors were difficulty swallowing, a decreased level of consciousness, cardiac infarction, a problem while being intubated, and vomiting within sixty minutes of an ETT tube being placed. The values that were used for this study were based off three categories of patients. One risk factor had 70 IU/L (22 IU/L-17 IU/L; one risk factor, 253 IU/L (58 IU/L-623 IU/L), patients with a positive BAL gram stain (359 IU/L (154 IU/L-1453 IU/L) vs. 66 IU/L (26 IU/L-165 IU/L), $p<0.001$). Levels were higher in patients with a positive culture for bacteria, normal flora, or yeast compared to a negative culture, and patients with positive culture for bacteria, normal flora, or yeast 25.15 IU/L[94 IU/L-832 IU/L] vs.63 IU/L [22IU/L], $p<0.001$ (Weiss et al, 2011). Individuals who were intubated for at least 72 hours were found to have α -amylase. Dewarvin et al and Weiss et al, suggested that measuring α -amylase was an efficient diagnostic tool that would allow for testing of critically ill patients.

Samanta et al (2018) conducted a prospective observational study of 151 patients who were also intubated for at least 72 hours. α -amylase was evaluated in mini-BAL specimens and it was explored for association with VAP. OF the 151 patients 64.9% tested patients presenting with VAP. VAP patients had significantly higher median mini BAL α -amylase values than those

without VAP (287 IU/L vs. 94 IU/L, $p < 0.001$). Patients that had none or up to 4 pre-intubation risk factors were 65 IU/L, 200 IU/L, 867 IU/L, and 3453 IU/L ($p < 0.001$). Median amylase in patients with 1 and 2 post intubation risk factors were 472 IU/L and 731 IU/L ($p < 0.001$) (Samanta et al, 2018).

One of the 11 articles included a population of children. Abu-Hasan et al, utilized 67 chronically ill children with respiratory illnesses that needed a bronchoscopy (Abu-Hasan et al, 2014). α -amylase was found to be significantly higher in bronchoalveolar lavage (BAL) of gram stains in positive BAL cultures (1,632 vs. 84 IU/L; $p = 0.049$), and in positive BAL oral flora cultures (1,803 vs. 270 IU/L; $p = 0.004$) (Abu-Hasan et al, 2014).

Bai et al, expanded on the findings of the research Weiss et al (2013) investigating the effect of α -amylase as an indicator of aspiration. The study included 280 mechanically ventilated patients of these 296 BAL samples were accumulated (Bai et al, 2013). The predictors of high amylase had a limit of 125 IU/L (Bai et al, 2013). Bronchial secretions were also analyzed in a study with Bain, Clarke, Davies, Levin, and Lamber (1981). The patient population was 21 adults who acquired transtracheal aspiration chest infections. This exploratory/observational study found that amylase activity was 50,000 IU/L.

In France there were 10 ICU's that were incorporated into a study conducted by Jaillette, et al. Pepsin and α -amylase were evaluated in 2739 tracheal aspirates from 303 patients in the hospitals. Amylase levels that were > 1685 IU/mL in $> 30\%$ of tracheal aspirated per patient (Jaillette et al, 2017). A prospective study was initiated that comprised of 26 intubated patients that were sedated for at least 48 hours and had a HiLo ETT (Filloux et al, 2019). These 26 patients were considered a high risk for microaspirating. The oral amylase group compared between intubation groups of tracheal and subglottic study groups, oral had the highest numbers

of amylase accumulation of (307,606 [200,725-461,300] IU/L). Tracheal amylase was decreased in the control group of intubated patients where group where the median values IQR were as follows (191 [10–917] vs 6661 [2774–19,358] IU/L, $p < 0.001$). Subglottic amylase levels were (130,750 [55,257-157,717] IU/L (Filloux et al, 2019).

There were 15 patients that were mechanically ventilated with Shiley tracheostomy on low pressure and high-volume settings participated in a study on alpha-amylase activity in tracheobronchial secretions (Nandapalan et al, 1995). The α -amylase ranges that were used were (35-1125 IU/L; median 295 IU/L (Nandapalan et al, 1995). A retrospective analysis of 147 elderly patients associated with VAP were grouped into a study by Qu et Al (2018). Their analysis revealed that patients with 3 or more risk factors for having a complication that required intubation, having a Glasgow coma scale score of < 8 , without subglottic secretions, and had α -amylase levels of $> 4,681.5$ IU/L (Qu et al, 2018).

Sole et al (2014) conducted a descriptive study to review the existence of pepsin and amylase in oral-tracheal secretions of mechanically ventilated adult patients. From a study not yet published levels of aspiration of α -amylase were no aspiration (0 to 392 IU/L), low aspiration (392 to 1,499 IU/L), moderate (1,500 to 4,999 IU/L), high ($\geq 5,000$ IU/L). These levels were used to categorize patients for risk for complications from a different study (Sole, et al unpublished data).

DISCUSSION

Each of these articles utilized a different range of values to help quantify the amount of α -amylase in patients' secretions. Filloux et al, had used oral, subglottic, and tracheal secretions of α -amylase to determine the difference in each section of the upper airway. Whereas, Dewarvin, Weiss, Bain, and Abu-Hassan focused on the location of BAL secretions. A weakness in Dewarvin's study included their sample size of tracheal aspirates from patients and that their cut-off range of 1688 IU/L could have falsely reinforced the results. The patients that were on the ventilators in the hospital also did not have their markers for microaspiration consistently trended during their hospital stay (2014). Sole et al, reiterates that microaspiration of oral and gastric secretions occur often even though pepsin was more commonly detected in the 2014 study. Qu et al, found that α -amylase can be a prognostic tool for identifying VAP. The higher the levels of tracheal aspirates the higher the likelihood of VAP occurring. Tracheal aspirate α -amylase levels exceeded more than 4681.5 IU/L elderly patients.

An acceptable level of secretions containing α -amylase must be established to set standardized parameters in practice (Gatell et al, 2012). Samanta et al, agrees that the lack of a gold standard limits the diagnosis for aspiration. Small sample sizes of intubated patients need to be expanded to further validate α -amylase analytic abilities. Once aspiration occurs, the duration of α -amylase in the lungs requires further exploration to assist in the interpretation of positive values. Researchers are still unaware of how long α -amylase occurs in the lungs which calls for uncertainty of its destruction leading to VAP. An exact range for positive aspiration has yet to be defined.

IMPLICATIONS FOR NURSING

Education

Currently nursing education in some areas does not consist of information on α -amylase and its biomarker capabilities. As evidence-based practice continues to be updated in the research setting this information needs to be transferred from the bedside to the classroom. Student nurses have a right to be informed and brought in on new data. Nurses swear an oath to become a patient advocate. A part of being a patient advocate means knowing the best possible form of treatment. Hospitals have nurse educators who are constantly providing informational packets and assignments to nurses to have current EBP. However, there are no values being taught in the hospitals for nurses to look for because more research must be done to find how significant these values are.

Practice

Applying α -amylase in the nursing profession requires commitment of the nurses and the hospitals to regulate the values of α -amylase. Once aspiration occurs, the duration of α -amylase in the lungs requires exploration to assist in the interpretation of positive values. This means that more work needs to be done to have an established cutoff level of α -amylase. An established cutoff level will facilitate comparison of patient populations, interventions, and outcomes.

Research

Weiss et al, stated that more research needs to be conducted on α -amylase as a biomarker for microaspiration (2013). At risk patients that have private health information such as a history of HIV/AIDS or risk factors that are unknown are unable to be identified within the hospital setting to prevent ventilator associated events (VAE) and VAP. Further funding would need to be

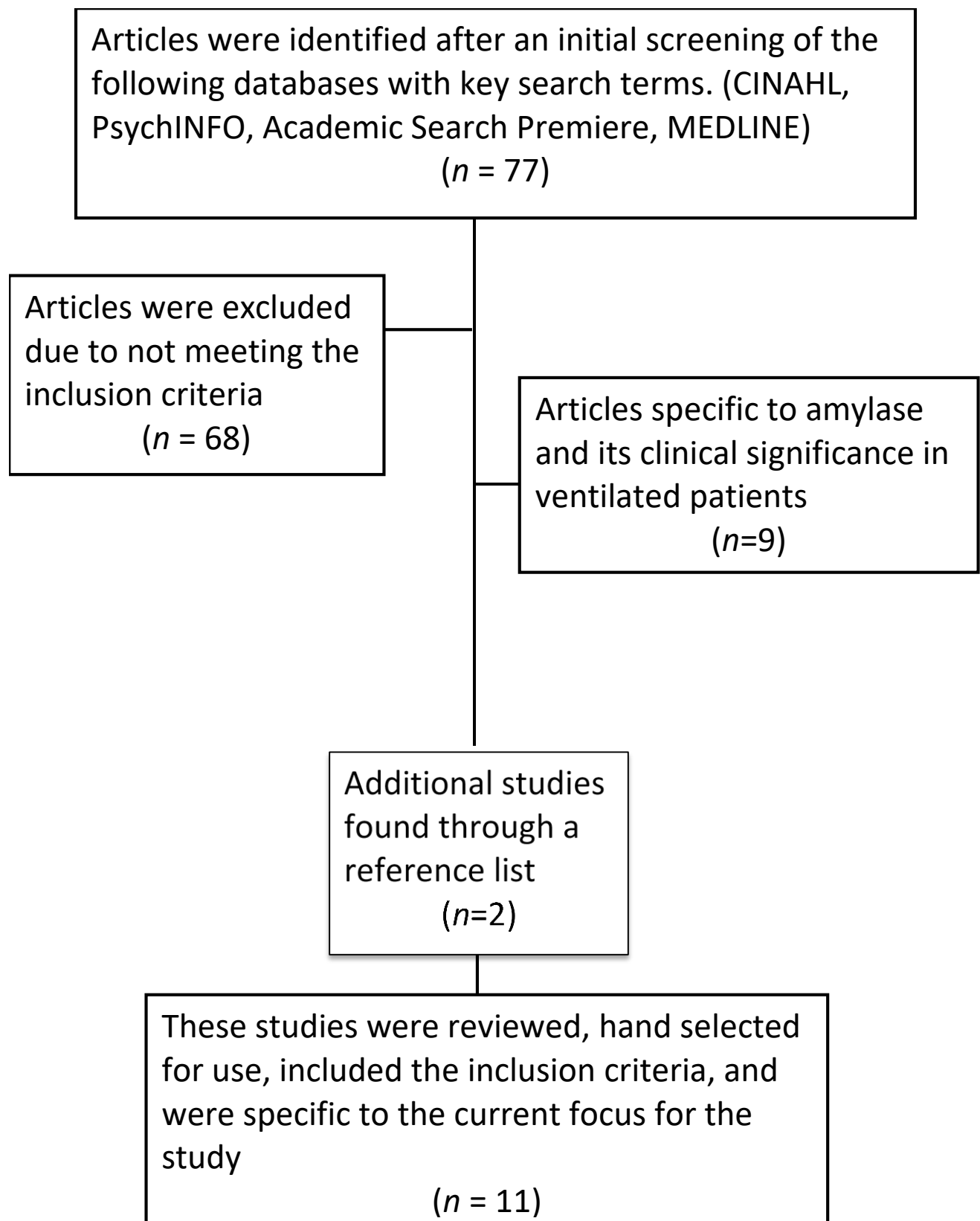
provided for researchers to continue the development of α -amylase as a biomarker for microaspiration.

SUMMARY

More research is needed to associate α -amylase as a primary biomarker for assessing for aspiration and look at risks for pulmonary complications, such as VAP. There is not enough education in the field of nursing on this topic to create a standard competency. More information on the universal diagnostic ranges of α -amylase need to be investigated further. Financial stability, regulated training, and suitability of gathering samples are potential barriers to a prospective life changing implementation. Though these barriers can seem vastly inaccessible for individuals in healthcare research, the outcomes can outweigh these factors.

APENDIX A

FIGURE I: PRISMA FLOW CHART



APENDIX B

TABLE I: TABLE OF EVIDENCE

Study	Purpose	Sample Size	Study Design	Methodology and Instruments	Findings and Conclusions	Comments/Limitations
Abu-Hasan M, Elmallah M, Neal D, Brookes, J. Salivary amylase level in a bronchoalveolar fluid as a marker of chronic pulmonary aspiration in children. <i>Pediatr Aller Imm Pul.</i> 2014;27(3), 115-119.	Explore the use of salivary amylase in bronchoalveolar lavage (BAL) fluid as a diagnostic tool for chronic pulmonary aspiration (CPA) in children	64 children with chronic respiratory illness requiring bronchoscopy were included.	A retrospective review of BAL amylase and medical records.	<p>Amylase in BAL fluid was measured by a functional assay using photometric techniques. Analysis of variance, Student's <i>t</i>-test, logistic regression analysis, and correlation analysis was utilized to assess statistical significance.</p> <p>Patient clinical and demographic variables were analyzed using multiple regression analysis to determine any impact on BAL amylase.</p>	<p>When the high and low-risk groups were combined, a significant difference ($p=.03$) (higher amylase levels of 1,722 vs. 307 IU/L) was noted compared to the remaining group.</p> <p>BAL amylase was significantly higher in the following groups: positive BAL gram stains (1,857 vs. 479 IU/L; $p=0.014$), in positive BAL cultures (1,632 vs. 84 IU/L; $p=0.049$), and in positive BAL oral flora cultures (1,803 vs. 270 IU/L; $p=0.004$).</p>	<p>Variability in amylase levels existed among groups, potentially due to equipment contamination with upper airway secretions and/or acute aspiration during the bronchoscopy.</p> <p>It is impractical to fully generalize results of children to adults due to differing variables (i.e., young age and inevitable aspiration).</p> <p>Standardization of and collection of urea levels are suggested in the BAL collection process to reduce variability.</p>
Bai C, Liu J, Song Y. Amylase in bronchoalveolar lavage fluid: a new marker of pulmonary aspiration. <i>Critical Care Med.</i> 2013;41(3), 916-917.	To discuss the findings of Weiss et al. (2013) exploring the impact of α -amylase as a predictor of aspiration.	280 mechanically ventilated patients from five medical centers were included. Of these	This study provided an overview of Weiss et al. (2013) and the retrospective study design utilized.	The correlation between BAL amylase concentration, BAL microbial culture results, and pre-intubation aspiration risk factors were assessed.	<p>A strong association existed between BAL amylase and risk factors for aspiration.</p> <p>With a BAL amylase concentration cutoff of < 125 IU/L, the sensitivity was 70% for predicting bacterial pneumonia (negative predictive value of 85%).</p>	<p>No, a "gold standard" exists for diagnosis of bacterial pneumonia. Due to the evolving nature of BAL amylase, several measurements should be done rather than one. BAL amylase collection requires training (requiring time and financial resources).</p>

Study	Purpose	Sample Size	Study Design	Methodology and Instruments	Findings and Conclusions	Comments/Limitations
		patients, 296 BAL samples were collected.				A standardization of collection mechanisms for BAL amylase (collection volume and location) is recommended.
Bain B.C, Clarke P.D, Davies A, Levin G.E, Lamber H.P. Aspiration in seriously ill patients: A study of amylase in bronchial secretions. Journal of Clinical Pathology, 1981;34, 803-805.	To explore the increased levels of amylase activity in the bronchial secretions in patients in the ICU.	21 patients with moderate to severe chest infections were obtained by transtracheal aspiration.	Exploratory/observational Quantitative	ES was collected either immediately before or during the TTA procedure in alert patients, but pharyngeal suction specimens were used in some of the seriously ill patients. Specimens were stored at + 4°C for a variable period of up to three weeks before estimation of the amylase activities. Sera taken at the time of the procedure were stored at - 20°C for similar periods before analysis. The specimens were diluted and homogenized with dithiothreitol.	In seriously ill patients the mean TTA amylase activity was 50 000 IU/L while in the less ill patients it was 1565 IU/L (p < 0 0005). The mean ES amylase activity was 206 000 IU/L. The mean serum amylase activity was 260 IU/L. Although TTA is a valuable diagnostic method in difficult pulmonary infections, contamination by oropharyngeal flora is not uncommon and will cause difficulties of interpretation. The second findings serve as a reminder of the frequency and importance of aspiration in seriously ill patients.	The reproducibility of this method for estimating amylase in sputum and tracheal aspirate is poor, partly due to the lack of homogeneity of the samples, and partly to the difficulty of pipetting viscous material, with a coefficient of variability of 27% on nine paired samples. The seriously ill patients (6/21) had all undergone pharyngeal suction and nasogastric intubation as routine nursing procedures in the ICU; these procedures could have yielded to the high levels of amylase activity found in TTA samples. Compared to the fifteen who were not given the same treatments.
Dewavrin F, Zerimech F, Boyer A, et al. Accuracy	The purpose of this study was to determine the	1055 tracheal aspirates,	Retrospective analysis of prospectively	Pepsin was quantitatively measured in all tracheal aspirates during a 48-h period. All tracheal	Mean α -amylase level, and percent of tracheal aspirates positive for α -amylase were	The use of α -amylase as a diagnostic tool for microaspiration is

Study	Purpose	Sample Size	Study Design	Methodology and Instruments	Findings and Conclusions	Comments/Limitations
of α -amylase in diagnosing microaspiration in intubated critically ill patients. <i>Plos One</i> . 2014;9(3), e90851.	accuracy of α -amylase in diagnosing microaspiration in critically ill patients.	collected from 109 patients.	collected data.	aspirates were frozen and later tested for α -amylase. Microaspiration was defined as the presence of at least one positive tracheal aspirate for pepsin (>200 ng/mL). Abundant microaspiration was defined as the presence of pepsin at a significant level in >74% of tracheal aspirates.	significantly higher in patients with microaspiration, and in patients with abundant microaspiration compared with those with no microaspiration; and similar in patients with microaspiration compared with those with abundant microaspiration. α -amylase and pepsin were significantly correlated ($R^2=0.305$, $p=0.001$).	moderate. It was found to be less conclusive when compared to pepsin and often inaccurate. Weaknesses include the sample size at a single institution, markers for microaspiration were not measured during the whole period of mechanical ventilation, and while the definition of microaspiration as the presence of pepsin at a significant level is likely correct, this only applies to aspiration of gastric contents. This could have altered the accuracy of the assessment. The cut-off of 1688 IU/L might have artificially strengthened the results.
Filloux B, Bedel A, Nseir S. Tracheal amylase dosage as a marker for microaspiration: a pilot study. <i>Minerva Anesthesiol</i> . 2013;79(9), 1003-1010.	Assess the ability to use α -amylase as a diagnostic tool in quantifying microaspiration of oral secretions.	($n=26$) intubated high-risk patients yielded 277 paired oral/tracheal specimens. 12 ($n=12$) non-ventilated patients	Prospective study	Twenty-six patients were intubated for at least 48 hours with a subglottic suction ETT, were considered high risk of microaspiration. Twelve non-ventilated patients that required a bronchoscopy made up the low-risk control group. Tracheal (T) amylase was compared between the groups. In the intubated group, a series of oral (O), subglottic (Sg) and tracheal (T) suction samples	Tracheal amylase was lower in the control group than the intubated group (191 [10–917] Vs .6661 [2774–19,358] IU/L, $p < 0.001$). Amylase gradually increased from tracheal (6661 [2774–19,358] IU/L), to subglottic (130,750 [55,257–157,717] IU/L), to oral samples (307,606 [200,725–461,300] IU/L),	Amylase is a simple, stable, and inexpensive enzyme to measure, and gives reproducible results. Beyond the crude quantitative assessment of tracheal amylase, the tracheal/oral amylase ratio may enable quantification of microaspiration.

Study	Purpose	Sample Size	Study Design	Methodology and Instruments	Findings and Conclusions	Comments/Limitations
		that required a bronchoscopy yielded 12 paired specimens (the control group).		were collected and T/O, T/Sg, Sg/O amylase ratios were determined.	resulting in a median 5.5% T/O ratio. This study indicated that T/O amylase ratio could be used towards quantifying microaspiration of oral secretions in mechanically ventilated patients.	Limitations include contamination of the tracheal secretions with oral secretions during the bronchoscopy, the use of an open tracheal suctioning system, and the study's limited collection centers and subject number.
Jaillette, E., Brunin, G., Girault, C., Zerimech, F., Chiche, A., Behal, H., Chiche, A., . . . Nseir, S. (2017). Impact of tapered-cuff tracheal tube on micro-aspiration of gastric contents in intubated critically ill patients: A multicenter cluster-randomized cross-over controlled trial study protocol for a randomized controlled trial. <i>Intensive Care Medicine</i> , 43, 1562-1571.	The aim of this study was to determine the influence of the shape of tracheal cuff on abundant microaspiration of gastric contents in critically ill patients.	A total of 326 patients were enrolled in the ten participating ICUs (162 in the PVC tapered-cuff group and 164 in the standard-cuff group)	Clustered randomized controlled trial	In ten different French ICU's patients who were older than 18 that were intubated, had at least 48 hours of mechanical ventilation, weren't pregnant, could receive enteral feedings, and screened positive for 72 hours and over intubation were eligible for the study.	A total of 326 medical patients were randomized in the 10 participating ICUs. Pepsin and salivary amylase were quantitatively measured in 2739 tracheal aspirates coming from 303 patients. Amylase levels >1685 IU/L in >30% of tracheal aspirates per patient were defined as an abundant amount. No tracheal secretions were present in 23 patients. The median number of tracheal aspirates per patient in which pepsin and salivary amylase were measured was similar in the two groups.	Tapered-cuff tracheal tube was not superior to standard-cuff tracheal tube in reducing microaspiration of gastric contents. The results suggested that tapered-cuff tracheal tube should not be used to prevent microaspiration or VAP in ICU patients.
Nandapalan, V., McIlwain, J. C., & Hamilton, J. A	The aim of this study was to evaluate	15 patients ventilated via a fresh	Descriptive Study	Tracheobronchial secretions were obtained from the patients on the first, second, and third days.	Six out of the fifteen patients showed very high levels of amylase activity in their	All but one of the patients developed a form of a chest infection.

Study	Purpose	Sample Size	Study Design	Methodology and Instruments	Findings and Conclusions	Comments/Limitations
study of alpha-amylase activity in tracheobronchial secretions of seriously ill patients with tracheostomies. <i>Journal of Laryngology and Otolaryngology</i> , 1995; 109, 640-643.	salivary aspiration in seriously ill patients with tracheostomies and to see whether there was any correlation with subsequent development of chest infection. The presence of amylase in tracheobronchial secretion was used as an indicator of tracheobronchial contamination by saliva.	tracheostomy and all had Shiley tracheostomy tubes. Patients had no clinical or radiological evidence of lung disorder at the time of the study.		<p>Samples from the trach tube were collected via a sputum trap and a sample of saliva was gathered from each patient routinely. The specimens were sent to the lab to assess for alpha-amylase.</p> <p>Alpha-amylase activity in the samples was analyzed by the blocked substrate maltoheptaose method at 37°C. The presence of amylase in tracheobronchial secretion was used as an indicator of tracheobronchial contamination by saliva above and below the cuff. Chest xray changes, bronch findings, and partial pressure changes across alveolar membranes were looked at.</p> <p>The control was the alpha-amylase in tracheobronchial secretions of patients who had normal lungs.</p>	<p>tracheobronchial secretions and these levels increased from Day 1 to Day 3.</p> <p>Bacteriological culture of the sputum during the time of chest infection revealed that of the eight patients who had anaerobic organisms, five had clear evidence of aspiration. Three patients grew aerobic organisms and in three patients there was some growth of a mixed flora in the sputum but there was no significant pathological count.</p>	<p>Of the patients studied; six were able to be confirmed infection from a salivary aspiration.</p> <p>Patients 1,2,3,4 and 5 had an increase in the percentage ratio of tracheobronchial amylase to salivary amylase. As well as, in the absolute amylase levels in the tracheobronchial on Day 3. It is likely that contamination of the trachea is beyond the cuff which could have led to chest infections amongst the patients. Since the chest infections are not always associated with salivary aspiration, the reason for severe chest infection in patients 7 and 13.</p>
Sole, M.L., Conrad, J., Bennett, M., Middleton, A., Hay, K., Ashworth, S., Devendra, I.M Pepsin and Amylase in oral and tracheal secretions: A pilot study. <i>American</i>	To assess the presence of pepsin and amylase in paired oral-tracheal secretions of adult patients being treated with	10 men and 3 women with a median age of 56 years. Majority were intubated with a subglottic suction	Descriptive Design Study	In this descriptive study, samples of oral and tracheal secretions were obtained from adult patients at baseline and again within 4 hours when a need for endotracheal suctioning was assessed. Assays of pepsin and amylase were processed in a specialty diagnostic laboratory.	Pepsin was present in oral secretions of 9 patients (69%), and in tracheal specimens of 7 patients (54%) at one or both sampling times. Amylase was detected in all patients' oral secretions and in tracheal secretions of 5 patients (38%) at one or both sampling times. Pepsin was	Micro-aspiration of oral and gastric secretions does occur frequently.

Study	Purpose	Sample Size	Study Design	Methodology and Instruments	Findings and Conclusions	Comments/Limitations
<i>Journal of Critical Care</i> , 23(4), 334–338.	mechanical ventilation.	endotracheal tube (69%); and 85% were receiving enteral feedings with the majority (67%) gastric.			more commonly detected than was amylase.	
Samanta S, Poddar B, Azim A, Singh RK, Gurjar M, Baronia AK. Significance of mini bronchoalveolar lavage fluid amylase level in ventilator-associated pneumonia. <i>Critical Care Med.</i> 2018;46(1),71-78.	Assess if α -amylase in mini-BAL specimens can be indicative of VAP in intubated patients with high clinical suspicion.	151 patients.	Prospective single-centered observational study.	Mini-BAL samples were collected within 72 hours of endotracheal intubation. Samples were sent for α -amylase level assay and quantitative culture. VAP was confirmed with mini-BAL microbial cultures of greater than or equal to 10 cfu/mL, and patients were divided into VAP and no VAP groups. Pre- and post-intubation risk factors for aspiration were assessed.	Presence of VAP 64.9% ($n=98$) of the 151 patients. Median mini-BAL amylase levels in VAP group were 287 IU/L and no VAP group 94 IU/L, ($p < 0.001$). Median amylase level in patients with 0, 1, 2, and 3 pre-intubation risk factors respectively were 65 U/L, 200 IU/L, 867 IU/L, and 3453 U/L ($p < 0.001$). Median amylase in patients with 1 and 2 post intubation risk factors were 472 IU/L and 731 IU/L ($p < 0.001$). Patients with VAP have higher mini-BAL amylase levels than non-VAP and amylase levels increase with the number of risk factors.	Limitations include the lack of a gold standard of diagnosis for aspiration, a single measurement of amylase may not reflect the actual clinical situation, oral care and endotracheal suctioning may increase the risk of aspiration, and the small sample size needs to be expanded to further validate α -amylase as a diagnostic tool.
Qu G-P, Fang X-Q, Xu Y-P. Predictive	Investigates correlations of	147 elderly ventilated	Retrospective analysis of	Tracheal aspirates were collected from elderly patients within two	α -amylase level increased with the amount of risk	α -amylase can serve as a predictive tool for VAP.

Study	Purpose	Sample Size	Study Design	Methodology and Instruments	Findings and Conclusions	Comments/Limitations
<p>value of α-amylase in tracheal aspirates for ventilator-associated pneumonia in elderly patients. <i>Clin Respir J.</i> 2018;12(4),1685-1692.</p>	<p>α-amylase in tracheal aspirates and aspiration risks with incidence of ventilator-associated pneumonia (VAP) in elderly patients undergoing mechanical ventilation.</p> <p>Examines clinical value of α-amylase for predicting VAP.</p>	<p>patients grouped based on the presence of VAP.</p>	<p>prospectively collected data.</p>	<p>weeks of tracheal intubation and α-amylase was assessed.</p> <p>Patients were placed in groups based on VAP diagnosis. Relationships between α-amylase and aspiration risks were assessed before intubation and VAP.</p>	<p>factors for aspiration in place prior to intubation.</p> <p>α-amylase level was significantly higher in the VAP group than in the non-VAP group.</p> <p>Logistic multivariate analysis revealed the following risk factors for VAP: having ≥ 3 risk factors before intubation, Glasgow scores of < 8, the absence of continuous aspiration of subglottic secretion, and a tracheal aspirate α-amylase level of $> 4,681.5$ IU/L.</p>	<p>Regardless of the occurrence of VAP, tracheal aspirate α-amylase level increased with the increase in the number of risk factors for aspiration before intubation; tracheal aspirate α-amylase level was significantly higher in VAP patients than in non-VAP patients, wherein the higher the number of times the tracheal aspirate α-amylase value exceeded 4681.5 IU/L, the higher the possibility of VAP was.</p> <p>α-amylase could work as a predictor of aspiration and VAP.</p>

Study	Purpose	Sample Size	Study Design	Methodology and Instruments	Findings and Conclusions	Comments/Limitations
<p>Weiss, C. H., Moazed, F., & Wunderink, R. G. Bronchoalveolar lavage fluid amylase is elevated in patients with a high risk of aspiration. <i>American Journal of Respiratory and Critical Care Medicine</i>, 2011; 183, A3915.</p>	<p>To determine whether amylase only produced in the salivary glands and gastrointestinal tract found in bronchoalveolar lavage fluid is associated with an increased risk of aspiration.</p>	<p>591 patients in an ICU</p>	<p>Retrospective Study</p>	<p>Nonbronchoscopic or bronchoscopic specimens were collected within 72 hours of endotracheal intubation. Collection of the data was done blinded and aspiration risk factors were included. Significance was determined by the Wilcoxon rank-sum tests. Data was presented as interquartile range.</p>	<p>Data from 93 patients of the 591 were analyzed. Median BAL amylase was higher in patients with at least one aspiration risk factor compared to zero (264 units/L. vs 70 IU/L, <0.001 p). Median amylase increased as the number of aspiration risk factors increased. Median amylase was higher in patients with a positive BALF Gram stain, and higher in patients with a positive culture for bacteria, normal flora, or yeast compared to a negative culture (25.15 IU/L[94 IU/L-832 IU/L] vs.63 IU/L [22 IU/L], p<0.001). There was no difference in BAL amylase patients with a new/progressive pulmonary infiltrate vs. unchanged/improving infiltrate.</p>	<p>Aspiration of oropharyngeal or gastric contents into the respiratory tract needs additional study. The diagnosis for aspiration was rather difficult due to the criteria of aspiration. Therefore, it was difficult to have statistical evidence from one etiology of aspiration.</p> <p>High levels of amylase in bronchoalveolar lavage fluid (BALF) fluids are associated with both increased risk of aspiration and evidence of microbial infection. Amylase may be useful tool for diagnosis aspiration.</p>

BAL, bronchoalveolar lavage; EBP, Evidence Based Practice; ES, Expectorated sputum ICU, intensive care unit; VAP, ventilator associated pneumonia

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