Published in final edited form as:

Am J Crit Care. 2013 September ; 22(5): 408–411. doi:10.4037/ajcc2013546.

A Pilot Study of Pepsin in Tracheal and Oral Secretions

Marilyn Schallom, RN, MSN, CCRN, CCNS,

Critical Care Evidence Based Practice Clinical Nurse Specialist, Barnes-Jewish Hospital, St. Louis, MO

Sally M. Tricomi, M.Ed.,

Sr. Research Assistant Saint Louis University, St. Louis, MO

Yie-Hwa Chang, PhD, and

Associate Professor of Biochemistry and Molecular Biology, Saint Louis University, St. Louis, MO

Norma A. Metheny, RN, PhD

Professor of Nursing, Saint Louis University, St. Louis, MO

Abstract

Background—Because reflux of gastric juice into the oropharynx must precede its aspiration into the lungs, it is reasonable to hypothesize that the detection of pepsin (the major gastric enzyme in gastric juice) in oral secretions may provide a relatively non-invasive method to predict risk for aspiration.

Objective—The purpose of this pilot study was to describe the incidence of pepsin in oral and tracheal secretions collected concurrently from a sample of 50 mechanically ventilated, gastric-fed patients.

Methods—The study used an exploratory descriptive design with a convenience sample from four medical and surgical intensive care units. A single oral and tracheal secretion was collected concurrently from each patient (yielding a sample of 50 oral and 50 tracheal secretions). The tracheal secretions were obtained via the inline suction system with an attached sputum trap; oral secretions were obtained via a yankauer suction tip with an attached sputum trap. All specimens were assayed for pepsin by the Western Blot method.

Results—Oral secretions from ten patients (20%) were pepsin-positive while tracheal secretions from two patients (4%) were pepsin-positive. Both patients with pepsin-positive tracheal secretions also had pepsin-positive oral secretions. Pepsin was not found in the tracheal secretions from the remaining eight patients with pepsin-positive oral secretions.

Conclusions—Although reflux of gastric juice into the oropharynx must precede its aspiration into the lungs, individual reflux events do not necessarily lead to aspiration. Thus, it is reasonable that we found pepsin 5-times more often in oral secretions than in tracheal secretions.

Keywords

gastroesophageal reflux; aspiration; aspiration pneumonia

Aspiration of oral or gastric secretions is a leading cause of pneumonia and results in significant morbidity and mortality across a variety of settings.^{1–4} Witnessed large-volume aspirations are infrequent.⁵ Far more common in critically ill patients are repeated clinically silent aspirations of small-quantities of oral or gastric secretions (referred to as microaspirations). Several studies have indicated microaspirations occur frequently in gastric-fed patients.^{6–7} Clearly, gastroesophageal reflux precedes the aspiration of gastric contents. If episodes of gastroesophageal reflux could be detected before aspiration occurs,

nurses could implement interventions aimed at reducing reflux and subsequent aspiration. In turn, reduction of aspiration could lead to a lower rate of aspiration-related pneumonia in the critical care setting.

Background and Significance

Critically ill patients often have a decreased level of consciousness which impairs the gag reflex and leads to pooling of oral secretions in the posterior oropharynx. In patients with an endotracheal tube, a direct pathway is available for these secretions to enter the lungs.⁸ Aspiration events are reported in approximately 50–75% of patients with endotracheal tubes.⁹ Other risk factors for aspiration include emergent intubation, deeper sedation levels, neuromuscular diseases, and gastric distention.

Pepsin is used as a marker for aspiration in research because it is not normally found in the tracheobronchial tree or lungs; further, it remains detectable after aspiration and can be retrieved with minimally invasive procedures.¹⁰ The presence of pepsin in oral and/or tracheal secretions is also suggested as a biomarker for the detection of gastroesophageal reflux disease (GERD).^{11–14} Investigators found that pepsin in saliva and sputum correlated well with 24-hour esophageal pH monitoring in outpatients with known GERD symptoms.^{11–12} Other investigators have reported that pepsin in tracheal secretions is a reasonable marker for pulmonary aspiration in critically ill adult and pediatric patients.^{6,7,15–19} However, more information is needed to determine the relationship between pepsin-positive oral secretions and pepsin-positive tracheal secretions in gastric-fed, mechanically ventilated patients. The purpose of this pilot study was to describe the incidence of pepsin in oral and tracheal secretions collected concurrently from a sample of 50 mechanically ventilated, gastric-fed patients.

Methods

This was an exploratory descriptive study that used a convenience sample of 50 subjects. Inclusion criteria were: admission to one of four medical or surgical intensive care units at the clinical study site, age greater than 18 years, mechanical ventilation, and use of gastric tube feedings. The project was approved by the appropriate Institutional Review Board. Verbal assent for specimen obtainment was provided by the patient or a surrogate; patient participation was limited to one day. A single tracheal and oral secretion was collected from each patient between the hours of 0900–1000. Feeding method was not controlled; either bolus or continuous feedings were allowed. Bolus feedings initiated at 0800 were completed prior to data collection; continuous feedings were in progress during the 0900–1000 data collection period. Ventilation was administered via cuffed endotracheal or tracheostomy tube; none of the tubes had subglottic secretion suction. Oral secretions from the posterior oropharynx were obtained via a yankauer suction tip attached to a sputum trap. Tracheal secretions were suctioned via the inline suction system with an attached sputum trap. Saline, 1–2 ml, was used only to clear secretions from the suction tubing; no saline was instilled into the airway. Each sample was assigned a code number so that subject identification was not possible. The specimens were then placed on ice and delivered to a research laboratory within 60 minutes of collection. All specimens were assayed by Western Blot immunoassay by the same laboratory technician and confirmed by a biochemist. Demographic data were not obtained.

Results

Oral secretions from ten patients (20%) were pepsin-positive while tracheal secretions were pepsin-positive in two patients (4%). Both patients with pepsin-positive tracheal secretions

also had pepsin-positive oral secretions. The remaining eight patients with pepsin-positive oral secretions had pepsin-negative tracheal secretions.

Discussion

This preliminary study suggests that pepsin can be found more frequently in oral secretions than in tracheal secretions collected concurrently from critically ill, mechanically ventilated, gastric-fed patients. This is reasonable given that gastroesophageal reflux is a precursor to the aspiration of gastric contents. It is also reasonable to hypothesize that finding pepsin in oral secretions can serve as a marker for potential aspiration of gastric contents. This could be advantageous because obtaining oral secretions is easier, less stressful, and less invasive for the patient than is esophageal pH monitoring or obtaining tracheal secretions. It is not difficult to obtain sufficient oral secretions for pepsin analysis. For example, Sole et al reported that the mean 2-hour volume of suctioned oral secretions in 26 mechanically ventilated patients was 7.5 ml.²⁰

If patients at high-risk for aspiration could be identified by pepsin-positive oral secretions, preventive-interventions could be implemented. Among these could be head-of-bed elevation to 45 degrees,^{21–27} use of an intestinal feeding site,^{28–31} and use of subglottic secretion management.^{32–33} The impact of additional interventions to prevent reflux and aspiration in critically ill patients could be studied with concurrent pepsin assays on both oral and tracheal secretions. Possible areas of exploration include: comparison of the effect of endotracheal versus tracheostomy tubes on aspiration, use of small bowel feedings with concurrent gastric decompression versus no gastric decompression, and the amount of gastric residual volume that contributes significantly to reflux and aspiration. This research could lead to proven interventions to reduce gastric feeding reflux and subsequent aspiration that contribute to pneumonia and its associated morbidity and mortality. With advancement in assay techniques, bedside pepsin tests might eventually be developed to allow clinicians to quickly recognize reflux and aspiration events in critically ill patients.

This study has several limitations. No demographic or clinical data were obtained to describe the patient population; therefore, it was not possible to describe risk factors for either gastroesophageal reflux or aspiration. Among the most significant missing data were gastric residual volume, sedation level, and degree of head-of-bed elevation. Also, the timing of mouth care was not controlled prior to the collection of oral secretions; thus, the results may have been negatively impacted.

Conclusion

Although reflux of gastric juice into the oropharynx must precede its aspiration into the lungs, individual reflux events do not necessarily lead to aspiration. Thus, it is reasonable that we found pepsin five-times more often in oral secretions than in tracheal secretions. More study is needed to determine if there is a quantifiable relationship between pepsin-positive oral secretions and pepsin-positive tracheal secretions. If such a relationship can be established, pepsin in secretions obtained less invasively via oral suctioning could be used as the marker for potential aspiration. More study is also needed to determine risk factors associated with dually pepsin-positive oral and tracheal secretions as well as interventions aimed at reducing reflux and aspiration.

Acknowledgments

This project was supported by the National Institute of Nursing Research, grant no. R21NR011228

References

1. Safdar N, Dezfulian C, Collard HR, Saint S. Clinical and economic consequences of ventilator-associated pneumonia: A systematic review. *Critical Care Medicine*. 2005; 33:2184–93. [PubMed: 16215368]
2. Melsen WG, Rovers MM, Koeman M, Bonten MJ. Estimating the attributable mortality of ventilator-associated pneumonia from randomized prevention studies. *Critical Care Medicine*. 2011; 39:2736–42. [PubMed: 21765351]
3. Bekaert M, Timsit JF, Vansteelandt S, et al. Attributable mortality of ventilator-associated pneumonia: A reappraisal using causal analysis. *American Journal of Respiratory & Critical Care Medicine*. 2011; 184:1133–39. [PubMed: 21852541]
4. Shigemitsu H, Afshar K. Aspiration pneumonias: Under-diagnosed and under-treated. *Current Opinion in Pulmonary Medicine*. 2007; 13:192–8. [PubMed: 17414126]
5. Elpern EH, Stutz L, Peterson S, et al. Outcomes associated with enteral tube feedings in a medical intensive care unit. *American Journal of Critical Care*. 2004; 13:221–7. [PubMed: 15149056]
6. Metheny NA, Clouse RE, Chang YH, et al. Tracheobronchial aspiration of gastric contents in critically ill tube-fed patients: Frequency, outcomes, and risk factors. *Critical Care Medicine*. 2006; 34:1007–15. [PubMed: 16484901]
7. Gopalareddy V, He Z, Soundar S, et al. Assessment of the prevalence of microaspiration by gastric pepsin in the airway of ventilated children. *Acta Paediatrica*. 2008; 97:55–60. [PubMed: 18076720]
8. Cason CL, Tyner T, Saunders S, Broome L. Nurses' implementation of guidelines for ventilator-associated pneumonia from the Centers for Disease Control and Prevention. *American Journal of Critical Care*. 2007; 16:28–36. [PubMed: 17192524]
9. DeLegge MH. Aspiration pneumonia: Incidence, mortality, and at-risk populations. *Journal of Parenteral & Enteral Nutrition*. 2002; 26:S19–24. [PubMed: 12405619]
10. Farrell S, McMaster C, Gibson D, et al. Pepsin in bronchoalveolar lavage fluid: A specific and sensitive method of diagnosing gastro-oesophageal reflux-related pulmonary aspiration. *Journal of Pediatric Surgery*. 2006; 41:289–93. [PubMed: 16481237]
11. Potluri S, Friedenber F, Parkman HP, et al. Comparison of a salivary/sputum pepsin assay with 24-hour esophageal pH monitoring for detection of gastric reflux into the proximal esophagus, oropharynx, and lung. *Digestive Diseases & Sciences*. 2003; 48:1813–17. [PubMed: 14561007]
12. Kim TH, Lee KJ, Yeo M, et al. Pepsin detection in the sputum/saliva for the diagnosis of gastroesophageal reflux disease in patients with clinically suspected atypical gastroesophageal reflux disease symptoms. *Digestion*. 2008; 77:201–6. [PubMed: 18617742]
13. Knight J, Lively MO, Johnston N, et al. Sensitive pepsin immunoassay for detection of laryngopharyngeal reflux. *Laryngoscope*. 2005; 115:1473–78. [PubMed: 16094128]
14. Samuels TL, Johnston N. Pepsin as a marker of extraesophageal reflux. *Annals of Otolaryngology & Laryngology*. 2010; 119:203–8.
15. Farhath S, Aghai ZH, Nakhla T, et al. Pepsin, a reliable marker of gastric aspiration, is frequently detected in tracheal aspirates from premature ventilated neonates: relationship with feeding and methylxanthine therapy. *Journal of Pediatric Gastroenterology & Nutrition*. 2006; 43:336–41. [PubMed: 16954956]
16. Ward C, Forrest IA, Brownlee IA, et al. Pepsin like activity in bronchoalveolar lavage fluid is suggestive of gastric aspiration in lung allografts. *Thorax*. 2005; 60:872–4. [PubMed: 16055614]
17. Metheny NA, Chang YH, Ye JS, et al. Pepsin as a marker for pulmonary aspiration. *American Journal of Critical Care*. 2002; 11:150–4. [PubMed: 11888127]
18. Metheny NA, Dahms TE, Chang YH, et al. Detection of pepsin in tracheal secretions after forced small-volume aspirations of gastric juice. *Journal of Parenteral & Enteral Nutrition*. 2004; 28:79–84. [PubMed: 15080601]
19. Krishnan U, Mitchell JD, Messina I, et al. Assay of tracheal pepsin as a marker of reflux aspiration. *Journal of Pediatric Gastroenterology & Nutrition*. 2002; 35:303–8. [PubMed: 12352517]
20. Sole ML, Penoyer DA, Bennett M, et al. Oropharyngeal secretion volume in intubated patients: The importance of oral suctioning. *American Journal of Critical Care*. 2011; 20:141–5.

21. Bassi GL, Torres A. Ventilator-associated pneumonia: role of positioning. *Current Opinion in Critical Care*. 2011; 17:57–63. [PubMed: 21169827]
22. Torres A, Serra-Batlles J, Ros E, et al. Pulmonary aspiration of gastric contents in patients receiving mechanical ventilation: the effect of body position. *Annals of Internal Medicine*. 1992; 116:540–3. [PubMed: 1543307]
23. Kollef MH. Ventilator-associated pneumonia: A multivariate analysis. *Journal of the American Medical Association*. 1993; 270:1965–70. [PubMed: 8411554]
24. Drakulovic MB, Torres A, Bauer TT, et al. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomized trial. *The Lancet*. 1999; 354:1851–8.
25. Keeley L. Reducing the risk of ventilator-acquired pneumonia through head of bed elevation. *Nursing in Critical Care*. 2007; 12:287–94. [PubMed: 17983363]
26. Metheny NA, Davis-Jackson J, Stewart BJ. Effectiveness of an aspiration risk-reduction protocol. *Nursing Research*. 2010; 59:18–25. [PubMed: 20010041]
27. Alexiou VG, Ierodiakonou V, Dimopoulos G, Falagas ME. Impact of patient position on the incidence of ventilator-associated pneumonia: A meta-analysis of randomized controlled trials. *Journal of Critical Care*. 2009; 24:515–22. [PubMed: 19327314]
28. Heyland DK, Drover JW, MacDonald S, et al. Effect of postpyloric feeding on gastroesophageal regurgitation and pulmonary microaspiration: Results of a randomized controlled trial. *Critical Care Medicine*. 2001; 29:1495–1501. [PubMed: 11505114]
29. Montecalvo MA, Steger KA, Farber HW, et al. Nutritional outcome and pneumonia in critical care patients randomized to gastric versus jejunal tube feedings. The Critical Care Research Team. *Critical Care Medicine*. 1992; 20:1377–87. [PubMed: 1395657]
30. Hsu CW, Sun SF, Lin SL, et al. Duodenal versus gastric feeding in medical intensive care unit patients: A prospective, randomized, clinical study. *Critical Care Medicine*. 2009; 37:1866–72. [PubMed: 19384225]
31. Metheny NA, Stewart BJ, McClave SA. Relationship between feeding tube site and respiratory outcomes. *Journal of Parenteral and Enteral Nutrition*. 2011; 35:346–55. [PubMed: 21527596]
32. Dezfulian C, Shojania K, Collard HR, et al. Subglottic secretion drainage for preventing ventilator-associated pneumonia: a meta-analysis. *The American Journal of Medicine*. 2005; 118:11–18. [PubMed: 15639202]
33. Leasure AR, Stirlen J, Lu SH. Prevention of ventilator-associated pneumonia through aspiration of subglottic secretions: A systematic review and meta-analysis. *Dimensions of Critical Care Nursing*. 2012; 31:102–117. [PubMed: 22333720]

Summary of Key Points

- Gastric-fed, mechanically ventilated patients are at-risk for gastric reflux and subsequent aspiration of gastric contents into the lung.
- Gastric reflux can be detected by finding pepsin in oral secretions; aspiration can be detected by finding pepsin in tracheal secretions. Because reflux of gastric juice into the oropharynx must precede its aspiration into the lungs, it is reasonable to hypothesize that testing for pepsin in oral secretions could be a relatively non-invasive method to predict risk for aspiration.
- In this study of gastric-fed, mechanically ventilated ICU patients, pepsin was found five times more frequently in oral secretions than in tracheal secretions.
- The relationship between pepsin-positive oral secretions and aspiration requires more investigation.