

Impact Of Endotracheal Tube Cuff Pressure **Monitoring On Micro Aspiration Of Gastric Contents**

Firouz Kamrani¹, Aram Feizi^{1*}, Hamid Rreza Khalkhali², Mohammed Amin Valizadeh³

¹ Department of Medical and Surgical, Faculty of Nursing and Midwifery, Urmia University of Medical Sciences, Urmia, Iran,

² Assistant Professor of Biostatistics Medical and Surgical Department, Faculty of Medical, Urmia University of Medical Sciences, Urmia, Iran

³Anesthesiologist, Fellowship of intensive care medicine, Department of Anesthesiology, Imam Khomeini Training Hospital, Urmia University of Medical Sciences, Urmia, Iran.

ABSTRACT

Background & Objective: Microaspiration is one of the common problems in endotracheal intubation in intensive care units (ICUs) associated with many complications such as pneumonia. This study aimed to identify and compare the effect of endotracheal tube (ETT) cuff pressure monitoring with manometer and palpation measurement on incidence of microaspiration in mechanically ventilated patients admitted to ICUs. Materials and Methods: This is a clinical trial study without randomization. 50 patients admitted to intensive care were selected through convenient sampling and divided into intervention and control groups of 25 individuals. ETT cuff was adjusted based on the researcher's executive protocol with a manometer in the intervention group and using palpation method in the control group. Three samples of lung secretions were taken through the ETT every 24 hours for three days from every patient. The samples were examined by measuring pepsin enzyme using ELISA technique in terms of microaspiration event. To summarize and analyze the data, descriptive and inferential statistics were imported into SPSS V21. Incidence rate and risk ratio of microaspiration were calculated in two methods of EFF cuff control. Results: Results showed that the incidence rate of microaspiration was 70 and 88 percent in the intervention and the control group, respectively. Average concentrations of pepsin was 20.24 ± 35.7ng per ml in the intervention group and 30.72 ± 43ng per ml (P value= 0.042) in the control group. The frequency of microaspiration occurrence was less in the intervention group compared to the control group (P value=0.040). Discussion & Conclusion: The results indicated that using manometer compared to palpation method had no effect on the incidence of microaspiration among patients undergoing endotracheal intubation; but, the use of a manometer to control the ETT cuff can decrease average concentrations of pepsin aspirated into the lungs and the frequency of microaspiration event.

Key Words: Microaspiration, Endotracheal Tube Cuff Pressure Control with Palpation Method, Endotracheal Tube Cuff Pressure Control with Manometer.

eIJPPR 2017; 7(2):43-49

HOW TO CITE THIS ARTICLE: Firouz Kamrani , Aram Feizi, Hamid Rreza Khalkhali, Mohammed Amin Valizadeh (2017). "Impact of endotracheal tube cuff pressure monitoring on micro aspiration of gastric contents", International Journal of Pharmaceutical and Phytopharmacological Research, 7(2), pp.43-49.

INTRODUCTION

Placement of an airway in critical patients is one of the most basic activities to maintain physiological stability [1]. Most of patients admitted to intensive units need respiratory support by a mechanical ventilation device. This requires providing an appropriate artificial airway, often with the use of an endotracheal tube (ETT) through the mouth [2]. Adjustment of ETT cuff pressure is one of the challenges of caring in ICU [3]. Appropriate pressure for ETT cuff has been recommended between 20 to 30 cm of water that is less than the capillary perfusion pressure and below 25 mm Hg in other studies [4-8]. If ETT cuff is filled excessively, it can cause tracheal wall damage [9],

E-mail: Aramfeizi@vahoo.com

Corresponding author: Aram Feizi

Address: Department of Nursing, Nursing and Midwifery school, Urmia university of Medical Sciences, Urmia, Iran.

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest . Received: 09 January 2017; Revised: 27 May 2017; Accepted: 24 June 2017

nerve damage [10], tracheal stenosis [11], tracheoesophageal fistula [12], hoarseness [13] and complications such as erosion, inflammation, softening the rings of cartilage, bleeding and infections [14]. In spite of using ETT with high volume and low pressure cuffs, the complications of cuff pressure have not diminished yet [7]. On the other hand, if the ETT cuff is not filled enough, it can cause lung secretions leak and microaspiration [15].

Microaspiration means crossing and leaking contents of the stomach, throat and mouth from around the ETT cuff to bronchial which is the common problem of all patients intubated in the intensive care [16] and causes several disorders such as atelectasis [17], pulmonary fibrosis diseases [18] and advanced pulmonary diseases [19]. Also, microaspiration of oropharyngeal contents and colonies of bacteria accumulated in the throat can cause lung infections such as ventilator-associated pneumonia [14], with a high morbidity and mortality in intensive care [6]. It is estimated that microaspiration occurs among 88 percent of intubated patients [16].

Various practices have been offered for prevention and decrease of microaspiration. To avoid the supine position, the end expiratory positive pressure of at least 5 cm of water, setting ETT cuff pressure based on provided patterns and decrease of the throat bacteria colony with suction and ventilation time reduction are some of the suggested practices [20, 21].

EFF cuff pressure is adjusted in different ways, including minimal leak technique, minimal occlusive volume, estimation or palpation method (palpation) and pressure control method using a manual or automatic manometer [22-24].

Nowadays, studies mostly suggest continuous control and automatic adjustment of ETT cuff pressure as the standard technique [22, 25], however, with respect to the clinical conditions in mechanically ventilated patients as well as due to the lack of access to existing equipment in ICU, there isn't yet clinical evidences and definite consensus to set the ETT cuff in ICU [22, 26, 27].

In most ICUs, measuring cuff pressure with a manometer is not common and it is adjusted by the use of an estimation method [22, 28]. Since ETT cuff adjustment is a technique preventing microaspiration, this study aimed to identify and compare the effect of ETT cuff pressure monitoring with manometer and palpation measurement on the incidence of microaspiration in mechanically ventilated patients admitted to ICU.

METHOD

This is a clinical trial study without randomization (simultaneous nonrandomized controls) and convenient

sampling was taken in 2016.Patients of general intensive cares in Urmia Imam Khomeini educational hospital were selected as the intervention group (adjusted ETT cuff with manometer) and patients of general intensive cares in Urmia Taleghani educational hospital were selected as the control group (adjusted ETT cuff with palpation). Patients who met the inclusion criteria were recruited consecutively since the start of sampling until the number of samples in each group reached up to 25 subjects. Participation criteria included: age between 18 to 80 years, being connected to the ventilator through an oral ETT for more than 72 hours, lack of weakened immune system diseases or not receiving drugs weakening the immune system, and the endotracheal tube with internal diameter of 8 and 8.5 mm in men and 7 and 7.5 mm in women.

Exclusion criteria included: patients' death during the study, removing the ETT in less than 72 hours, patients who began to suffer obvious aspiration and patients included in other studies during this research [16, 29]. ICU nurses set control group patients' ETT cuff by their finger as palpation once per shift. In the other group (intervention), patients were admitted on the basis of the researcher's executive protocol, ICU nurses with experience and previous training using a manometer (Mallinckrodt, Germany) pressure gauge fixed ETT cuff per shift (every 6 hours) on 25 cm of water and recorded cases altering ETT cuff such as suction, the patient's condition change and straining. ETT cuff was set back on 25 cm of water. EFF cuff pressure was measured in the supine position with a manometer and the pre-setting pressure was recorded in nursing report sheet.

Once ICU patients were placed ETT or entered ICU with ETT, three samples of secretions from the endotracheal tube were taken from patients every 24 hours for 3 days. Since immediate testing of individual samples wasn't possible in terms of laboratory techniques, the samples were sent immediately to the laboratory after collecting and were frozen at -20 $^{\circ}$ C.

All samples of ETT secretions were prepared in morning shift and before feeding the stomach or intestine of the patient. Samples were taken in this manner that secretions were sucked at maximum duration of 6 seconds using the catheter number 14 (half-ml). Drop in arterial oxygen saturation and monitoring variations were noted during the suction. If any variation happened, the patient would be connected to the ventilator immediately. After the samples collected in each group reached 75 numbers, laboratory science professionals performed laboratory analysis using EIISA technique and according to the catalog kit (Human pepsin elisa kit) Manufactured by Co. ZellBio Gmbh Germany.

To analyze the data, descriptive and inferential statistics (Mann-Whitney test for independent samples and chisquare test to compare qualitative variables for both groups), calculating incidence, risk ratio and Fisher's exact test were used in SPSS V21.

RESULTS

The study included 50 patients hospitalized in the intensive care unit of Urmia University of Medical Sciences. The average age was 68.6 ± 14 and 59.08 ± 18 in the control and intervention group, respectively. In both groups, out of 25 patients,17 subjects were male and 8 of them were women (Table 1).

| Table 1. T | The demogra | aphic vai | riables the | subjects |
|------------|-------------|-----------|-------------|----------|
|------------|-------------|-----------|-------------|----------|

| | | | • |
|---|--|-----------------------------------|---------|
| Variable | Intervention group (25 subjects) | Control group (25 subjects) | P-value |
| Age(year), mean± Standard deviation, variation range | 18±08.59 (19 - 80) | 14±6.68 (24 - 80) | 06.0 |
| Body mass index(Kg per sqm) mean± Standard deviation, variation range | 84±2/93.24 (19 – 31) | 13.4±8.24 (18 – 36) | 96.0 |
| Height (cm), mean ± Standard deviation, variation range | 48.170±8 (152 – 184) | 7.52±7.168 (151 – 182) | 512.0 |
| Male gender (%) | (68) 17 | (68) 17 | 1 |
| History of lung disease(%) | (48) 12 | (56) 14 | 57.0 |
| Smoking(%) | (48) 12 | (40) 10 | 56.0 |
| History of gastroesophageal reflux (%) | (52) 13 | (48) 12 | 77.0 |

All the subjects had oral / nasogastric feeding tube.

The major cause of hospitalization of patients was lung problems in the control group and neurological problems in the intervention group. Analysis of ventilator-associated variables in the control and intervention groups showed that the average level of consciousness in GCS was 8.48 and 7.04, respectively (Table 2).

| Table 2. Ventilator-associated variables |
|--|
|--|

| Measured variables | | Control group | Intervention group | P-value |
|--|----|------------------|-----------------------|---------|
| Airway pressure* (mean± Standard deviation) | | 4.7±48.17 | 9.36±6.18 | 96.0 |
| ETT suction at 24hours, number (mean± Standard deviation) | | 8.10±1 | 48±1.9 | 095.0 |
| Consciousness level* (mean± Standard deviation) | | 8.48±1.8 | 9.04±1.7 | 011.0 |
| Airway pressure at the end of exhalation(PEEP), | *0 | (28) 7 | (24) 6 | 747.0 |
| number, (individual) (%) | *5 | (72) 18 | (76) 19 | |

* Cm of water ***** Glasgow Coma Standard (GCS)

The results also showed that 22 subjects in the control group (88%) and 19 patients (76%) of the intervention group have experienced microaspiration at least once during the study (Figure 1). Although controlling the ETT cuff with manometer has decreased the incidence risk of microaspiration compared to the palpation technique, it is not statistically significant (966 / 1-095 / 0 = CI, 86/0 = RR, 463 / 0 = P value).





Using Fisher's exact test, comparing the number of pepsin samples reported positive by the laboratory indicated that the number of positive pepsin samples in the intervention group had a statistically significant difference than the control group (Figure 2)(P-value=0.040). This implies that adjustment of the ETT cuff with manometer technique can be helpful in decrease of microaspiration incidence number than the case using palpation technique.



Fig. 2. Comparison of positive pepsin samples in studied groups

The mean scores of airway pepsin between the two groups were significantly different (P-value=0.042). The average scores of pepsin concentration were obtained as 20.24 ± 35.7 and 30.72 ± 43 in the intervention and control group, respectively. The study showed that the use of manometer to adjust ETT cuff can reduce concentration of the pepsin aspirated into the lungs of mechanically ventilated patients.

Frequency distribution of ETT cuff pressure in measured turns for three days in the intervention group revealed that in 47% of cases despite the ETT cuff set by the manometer, ETT cuff pressure didn't place in the normal range (20 to 30 cm of water).

Table 3. Frequency distribution of ETT cuff pressuremeasured in turns during three days in theintervention group subjects

| 8 1 9 | | | | |
|--|---|---------|--|--|
| | Number (%) | | | |
| | ETT cuff pressure below 20 cm of water | (22)65 | | |
| ETT cuff pressure in cm of water | ETT cuff pressure at appropriate level (20 to 30 cm of water) | (53)160 | | |
| | ETT cuff pressure over 30 cm of water | (25)75 | | |

DISCUSSION AND CONCLUSION

Microaspiration diagnosis is often overlooked until the pulmonary problem is revealed [30]. Many techniques including Technetium-99m [31], Blue Dye Test [32], Bile Acids [33] and pepsin [16, 34] are used to diagnose microaspiration of gastric and throat contents into the lungs among patients under mechanical ventilation with the endotracheal tube. But, some clinical or laboratory problems limit these methods. Technetium-99m is the golden and standard method to diagnose microaspiration; though, radiological radiation effects as well as transfer of patients to the radiology building is the most important limitation of this technique [31, 35]. In this study, microaspiration incidence rate was detected using pepsin enzyme. Pepsin can be found in tissues and many secretions such as pharyngeal mucosa, nasal sinus mucosa, saliva, secretions from the middle ear and above all gastric secretions [36, 37]. Pepsin as a sensitive and quantifiable indicator is utilized increasingly in the diagnosis of stomach contents microaspiration into the lungs, gastroesophageal reflux and related diseases [38, 39].

In addition, only in 52% of cases the ETT cuff pressure placed in the normal range (20-30 cm of water)despite the adjustment of ETT cuff. This may imply that in order to prevent side effects of increasing or decreasing cuff pressure less intervals may be needed to control it. This finding is pointed out by Mousavi [40] and Taslimi [41]. In the study conducted by Taslimi et al, despite the measurement of pressure cuff at 6-hour intervals, the pressure level was outside the normal range in 3.21% of cases.

In order to prevent microaspiration ETT cuff pressure should be modified following any case altering it. The cuff pressure varies at different times and under conditions such as patient movement, bed position , head extension, the patient's attempt to talk and other clinical conditions and doesn't guarantee prevention of microaspiration.

Moreover, the use of a manometer to set ETT cuff has no effect on the incidence of microaspiration compared to ETT cuff adjustment estimation method. In this study, the microaspiration incidence occurred frequently because of the high frequency of men in groups under the study. In Bohman's study [38] men's airway pepsin was more than women's.

Nseir et al (2011) adjusted ETT cuff using manometer as intermittently and continuously. Microaspiration incidence rate was 46 and 18 percent in intermittent and continuous groups, respectively [29]. Patients whose ETT cuff was set consistently suffered less microaspiration. factors can affect Various the incidence of microaspiration. Admitted patients' position is one of them. In the research conducted by Nseir et al [29], patients who had a contraindication for semi-sitting positions were excluded from the study. According to the guidelines published to prevent aspiration, the position is at least 30 degrees of patients' head [42, 43]. In the study conducted by Norma (2002), out of 14 positive pepsin samples, 13 cases (93%) occurred in patients who had a flat position [44].

The incidence of microaspiration was reported 88 % [16] in Norma's study, 70% in Gopalareddy's research [45] and 22% in Bohman and colleagues' study [38]. In the present study using a manometer to set the ETT cuff reduces the frequency of microaspiration incidence which is

consistent with Nseir's findings [29]. In Gopalareddy's research the rate of microaspiration incidence was reported 40% among patients with cuffed ETT, 94% in intubated patients without cuff and 62% in tracheostomised patients [45].

The results showed that using manometer for adjustment of the ETT cuff is more effective than palpation method to reduce the concentration of pepsin aspirated into the lungs.

In Gopalareddy's study maximum amount of pepsin in three groups of juvenile (with cuff, without cuff and tracheostomy) respectively consisted of: 211.5 ± 174.9 , 216.9 ± 267.0 and 173.5 ± 200.4 ng per mL. There was no statistically significant difference between these values [45]. The sensitivity of the kit used in studies can be regarded as the reason of different grades of lungs secretions pepsin concentration. In a study by Middleton (2012), pepsin concentration was 24.72 and 8.10 ng per mL in oral and tracheal secretions, respectively [46].

Generally, factors affecting microaspiration can be divided as the following: patient tracheal tube, patient feeding tube, mechanical ventilation and the patient's condition. All the above factors should be controlled to prevent microaspiration in order to avoid microaspiration complications that ventilator-associated pneumonia is the most important. In this study, adjustment of ETT cuff was utilized as one of the methods lowering microaspiration and all the factors involved in development of microaspiration were homogenized.

ACKNOWLEDGMENTS

This article is the result of the research project approved by Urmia Medical Sciences University and a part of an intensive care nursing master thesis. Hereby, all employees and nurses of general intensive care unit of Imam Khomeini and Ayatollah Taleghani hospitals are thanked and honored.

REFERENCES

- [1] Jabre P, Combes X, Lapostolle F, Dhaouadi M, Ricard-Hibon A, Vivien B, et al. Etomidate versus ketamine for rapid sequence intubation in acutely ill patients: a multicentre randomised controlled trial. Lancet (London, England). 2009;374(9686):293-300.
- [2] Henderson J. Airway management in the adult. Miller's anesthesia 7th ed Philadelphia: Churchill Livingstone. 2010:1583.
- [3] Ono FC, Andrade APAd, Cardoso FPdF, Melo MdHOd, Souza RdN, Silva GHCd, et al. Cuff pressure analysis of intensive care unit patients with different inclinations of the head section of the bed.

Revista Brasileira de terapia intensiva. 2008;20(3):220-5.

- [4] Hoffman R, Parwani V, Kaban J, Dueffer H, Howell A, Sturmann K. 86: Comparison of Two Common Techniques for Inflating Endotracheal Tube Cuffs: Set Volume of Air Vs. Palpation of the Pilot Balloon. Annals of Emergency Medicine. 2006;48(4):27.
- [5] Nasiri E, Mohamadpoor R, Mortazavi Y, Khorrami M. A comparison change in endotracheal tube cuff pressure between air and Lidocaine and N2O with O2 cuff inflation during general anesthesia. Journal of Gorgan University of Medical Sciences. 2004;6(2):32-9.
- [6] Safdar N, Dezfulian C, Collard HR, Saint S. Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. Critical care medicine. 2005;33(10):2184-93.
- [7] Simmons K, Scanlan C. Airway management. Egan's Fundamentals of Respiratory Care 8th ed St Louis, MO: Mosby. 2003:653-704.
- [8] Diaz E, Rodríguez AH, Rello J. Ventilator-associated pneumonia: issues related to the artificial airway. Respiratory care. 2005;50(7):900-9.
- [9] Touzot-Jourde G, Stedman NL, Trim CM. The effects of two endotracheal tube cuff inflation pressures on liquid aspiration and tracheal wall damage in horses. Veterinary anaesthesia and analgesia. 2005;32(1):23-9.
- [10] Hoffman RJ, Parwani V, Hahn I-H. Experienced emergency medicine physicians cannot safely inflate or estimate endotracheal tube cuff pressure using standard techniques. The American journal of emergency medicine. 2006;24(2):139-43.
- [11] Terashima H, Sakurai T, Takahashi S, Saitoh M, Hirayama K. [Postintubation tracheal stenosis; problems associated with choice of management]. Kyobu geka The Japanese journal of thoracic surgery. 2002;55(10):837-42.
- [12] Pelc P, Prigogine T, Bisschop P, Jortay A. Tracheoesophageal fistula: case report and review of literature. Acta oto-rhino-laryngologica belgica. 2000;55(4):273-8.
- [13] Kriner EJ, Shafazand S, Colice GL. The endotracheal tube cuff-leak test as a predictor for postextubation stridor. Respiratory care. 2005;50(12):1632-8.
- [14] Irwin RS, Rippe JM. Irwin and Rippe's intensive care medicine: Lippincott Williams & Wilkins; 2008.
- [15] Coffin SE, Klompas M, Classen D, Arias KM, Podgorny K, Anderson DJ, et al. Strategies to prevent ventilator-associated pneumonia in acute care hospitals. Infection Control. 2008;29(S1):S31-S40.
- [16] Metheny NA, Clouse RE, Chang Y-H, Stewart BJ, Oliver DA, Kollef MH. Tracheobronchial aspiration

of gastric contents in critically ill tube-fed patients: frequency, outcomes, and risk factors. Critical care medicine. 2006;34(4):1007.

- [17] Gaszyńska E, Ratajczyk P, Wieczorek A, Szewczyk T, Gaszyński T. Comparison of Microaspiration Around Taperguard Tube Cuffs and Standard Tracheal Tubes in Obese Patients Subjected to Surgery Under General Anesthesia. Polish Journal of Surgery. 2014;86(3):107-10.
- [18] Lee JS, Song JW, Wolters PJ, Elicker BM, King T, Kim DS, et al. Bronchoalveolar lavage pepsin in acute exacerbation of idiopathic pulmonary fibrosis. European Respiratory Journal. 2012;39(2):352-8.
- [19] Sweet M, Patti M, Hoopes C, Hays S, Golden J. Gastro-oesophageal reflux and aspiration in patients with advanced lung disease. Thorax. 2009;64(2):167-73.
- [20] Blot SI, Poelaert J, Kollef M. How to avoid microaspiration? A key element for the prevention of ventilator-associated pneumonia in intubated ICU patients. BMC infectious diseases. 2014;14(1):119.
- [21]Bent S, Toschlog E. Reducing the Risk for Microaspiration and Postintubation Pulmonary Complications In the Surgical and Critical Care Settings. 2012.
- [22] Sole ML, Penoyer DA, Su X, Jimenez E, Kalita SJ, Poalillo E, et al. Assessment of endotracheal cuff pressure by continuous monitoring: a pilot study. American Journal of Critical Care. 2009;18(2):133-43.
- [23] Jordan P, Van Rooyen D, Venter D. Endotracheal tube cuff pressure management in adult critical care units. Southern African Journal of Critical Care. 2012;28(1):13-6.
- [24] Stewart SL, Seacrest J, Norwood BR, Zachary R. A comparison of endotracheal tube cuff pressures using estimation techniques and direct intracuff measurement. AANA journal. 2003;71(6):443-8.
- [25] Nseir S, Duguet A, Copin M-C, De Jonckheere J, Zhang M, Similowski T, et al. Continuous control of endotracheal cuff pressure and tracheal wall damage: a randomized controlled animal study. Critical care. 2007;11(5):1.
- [26] Rose L, Redl L. Minimal occlusive volume cuff inflation: A survey of current practice. Intensive and Critical Care Nursing. 2008;24(6):359-65.
- [27] Bolzan DW, Gomes WJ, Faresin SM, de Camargo Carvalho AC, De Paola ÂAV, Guizilini S. Volumetime curve: an alternative for endotracheal tube cuff management. Respiratory care. 2012;57(12):2039-44.
- [28] Jordan P, Rooyen D, Venter D. endotracheal tube cuff pressure management in the adult critical care units. SAJCC. 2012;28:6-13.

- [29] Nseir S, Zerimech F, Fournier Cm, Lubret Rm, Ramon P, Durocher A, et al. Continuous control of tracheal cuff pressure and microaspiration of gastric contents in critically ill patients. American journal of respiratory and critical care medicine. 2011;184(9):1041-7.
- [30] Amantéa SL, Piva JP, Sanches PR, Palombini BC. Oropharyngeal aspiration in pediatric patients with endotracheal intubation*. Pediatric Critical Care Medicine. 2004;5(2):152-6.
- [31] Heyland DK, Drover JW, MacDonald S, Novak F, Lam M. Effect of postpyloric feeding on gastroesophageal regurgitation and pulmonary microaspiration: results of a randomized controlled trial. Critical care medicine. 2001;29(8):1495-501.
- [32] Beuret P, Philippon B, Fabre X, Kaaki M. Effect of tracheal suctioning on aspiration past the tracheal tube cuff in mechanically ventilated patients. Annals of intensive care. 2012;2(1):45.
- [33] Wu Y-C, Hsu P-K, Su K-C, Liu L-Y, Tsai C-C, Tsai S-H, et al. Bile acid aspiration in suspected ventilator-associated pneumonia. CHEST Journal. 2009;136(1):118-24.
- [34] Nseir S, Zerimech F, De Jonckheere J, Alves I, Balduyck M, Durocher A. Impact of polyurethane on variations in tracheal cuff pressure in critically ill patients: a prospective observational study. Intensive care medicine. 2010;36(7):1156-63.
- [35] Nseir S, Zerimech F, Jaillette E, Artru F, Balduyck M. Microaspiration in intubated critically ill patients: diagnosis and prevention. Infectious Disorders-Drug Targets (Formerly Current Drug Targets-Infectious Disorders). 2011;11(4):413-23.
- [36] Sole ML, Conrad J, Bennett M, Middleton A, Hay K, Ash-worth S, et al. Pepsin and amylase in oral and tracheal secretions: a pilot study. American Journal of Critical Care. 2014;23(4):334-8.
- [37] Krishnan U, Mitchell JD, Messina I, Day AS, Bohane TD. Assay of tracheal pepsin as a marker of reflux aspiration. Journal of pediatric gastroenterology and nutrition. 2002;35(3):303-8.
- [38] Bohman JK, Kor DJ, Kashyap R, Gajic O, Festic E, He Z, et al. Airway pepsin levels in otherwise healthy surgical patients receiving general anesthesia with endotracheal intubation. CHEST Journal. 2013;143(5):1407-13.
- [39] Samuels TL, Johnston N. Pepsin as a causal agent of inflammation during nonacidic reflux. Otolaryngology--Head and Neck Surgery. 2009;141(5):559-63.
- [40] Mousavi Saj, Niakan Lahiji M, Akhovatian F, Moradi Moghadam O, Valizade Hassanlouei Ma. An

Investigation of endotracheal Tube cuff Pressure. 2. 2009;17(83):43-8.

- [41] Taslimi L, Ghanbari A, Kazemnezhad Leili E. Study of endotracheal tube cuff pressure and time of measurement among intensive care units patients. Holistic Nursing And Midwifery Journal. 2016;26(2):29-37.
- [42] Tablan O, Anderson L, Besser R, Bridges C, Hajjeh R. CDC; Healthcare Infection Control Practices Advisory Committee. Guidelines for preventing health-care-associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. MMWR Recomm Rep. 2004;53(RR-3):1-36.
- [43] McClave SA, DeMeo MT, DeLegge MH, DiSario JA, Heyland DK, Maloney JP, et al. North American summit on aspiration in the critically ill patient: consensus statement. Journal of Parenteral and Enteral Nutrition. 2002;26(6 suppl):S80-S5.
- [44] Metheny NA, Chang Y-H, Ye JS, Edwards SJ, Defer J, Dahms TE, et al. Pepsin as a marker for pulmonary aspiration. American Journal of Critical Care. 2002;11(2):150-4.
- [45] Gopalareddy V, He Z, Soundar S, Bolling L, Shah M, Penfil S, et al. Assessment of the prevalence of microaspiration by gastric pepsin in the airway of ventilated children. Acta paediatrica. 2008;97(1):55-60.
- [46] Middleton A. Pepsin and salivary amylase: Biomarkers of microaspiration in oral and tracheal secretions of intubated patiebys: University of Central Florida Orlando, Florida; 2012.

49