

## Survey of h2-blocker antihistamines and proton pump inhibitors administration rate in patient admitted into the Intensive Care Unit (ICU) ward

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**Abstract: Background:** Stress ulcer disease (SU) is the injury and acute inflammation of the mucous tissue, which in hospitalized patients in the Intensive Care Unit(ICU) in early 72 hours in 100% of patients is common. For the prevention of stress ulcer H2 blockers commonly prescribed one of the drugs, proton pump inhibitors and antacids done. **Materials and Methods:** This study is a retrospective analysis 200 files of the archive of Sarab Imam Khomeini which according to required variables was evaluated and collected information was analyzed statistically. **Results:** Most patients were male and the average age of men and women were very close to each other causes of hospitalization mainly were GIB and respiratory diseases. The drugs used to reduce stomach acid is mainly Pantoprazole and the most therapist of ICU section were internal expert physicians had the Most therapist of ICU section. **Conclusion:** The results indicated that ICU physicians of Imam Khomeini hospital of Sarab prefer to use Pantoprazole to prevent digestion ulcers created with hospitalization.

[Dadashzadeh B, Issabeagloo E. **Survey of h2-blocker antihistamines and proton pump inhibitors administration rate in patient admitted into the Intensive Care Unit (ICU) ward.** *N Y Sci J* 2017;10(3):69-74]. ISSN 1554-0200 (print); ISSN 2375-723X (online). <http://www.sciencepub.net/newyork>. 10. doi:10.7537/marsnys100317.10.

**Keywords:** H2 blockers and proton pump inhibitors, peptic ulcer patients in Intensive Care Unit(ICU)

### 1. Introduction

Digestive disorders related to gastric acid is one of the postoperative disorders associated with increased pain and discomfort. The content of the gastric acid in patients undergoing surgery is pathological and responsible for digestive disorders such as heartburn and epigastric pain. Therefore, suppressing gastric acid in these patients is important (1-4). The highest peak of acidity of the stomach is after an overnight fast and at the time of arrival of the patient to the operating room for elective surgery (5-7). Upper gastrointestinal bleeding is among the known complications in critically ill patients which may lead to death (9-12). In definition, gastrointestinal bleeding includes bleeding from the proximal that can be classified as Variceal and non-Variceal complications. Variceal bleeding is one of the end-stage complications of liver diseases; and non-Variceal bleeding is associated with peptic ulcer disease. Non-Variceal bleeding is associated with hematochezia demonstrations (bloody vomiting) with or without Melena and hematochezia (13). Peptic ulcer disease is the most common cause of Upper Gastrointestinal Bleeding (UGIB). Stress-related mucosal damage diseases or stress ulcer is an acute inflammation damage of mucosal tissue caused by the reduction of visceral perfusion and impaired balance of body's natural physiological factors and the digestive tract (gastric acid and pepsin production (14) in diseases and imposed stresses. Stress ulcer involves

fundus area and gastric body. Deeper lesions can be extended to submucosa area and cause severe bleeding (15). Erosions usually emerge approximately 24 hours after the injury; however, severe bleedings usually occur 2 to 3 days after the injury (16). Critically-ill patients admitted to Intensive Care Unit (ICU) are exposed to minor injuries in gastrointestinal mucosa or acute wounds (17-18). Based on the studies, the presence of acid in the stomach lumen is very important in incidence of severe mucosal damage and bleeding (19-21). Blood loss in the digestive tract is one of the mortality causes in critically ill patients (22). Controlled secretion of acid and pH above 4 has a beneficial effect in the prevention of ulcers and bleeding, and bleeding is reduced from 15 to 5% by treatment and prophylaxis (23-26). In the estimations, the incidence of gastrointestinal bleeding and the development of gastric mucosal damage can be observed in critically ill patients after admission to the ICU (27). Stress-related mucosal bleeding during hospitalization is 50 to 77 percent (28). Studies have found that within 24 hours after admission to the ICU, approximately 75 to 100% of the cases had evidences of gastric-duodenal injury (29). SRMD in patients admitted to the ICU is prevalent up to 100% within the first 72 hours (30-31). Mechanical ventilation for more than 48 hours, burn more than 30%, coagulation disorders, cardiovascular and abdominal surgery, shock, trauma, sepsis, renal and hepatic failure, cytokines, anticoagulant drugs used by patients in ICU

are among the risk factors for stress ulcer and SRMD (32-36). Visceral hypo perfusion is the important factor of SRMD development which, due to the activation of the nervous system and increased secretion of catecholamine, leads to hypovolemia (37-39). Food and drug administration approved Cimetidine in 1977, ranitidine in 1983, Famotidine in 1986, Lansoprazole in 1995, Omeprazole and Pantoprazole in 2000 and Esomeprazole in 2001 (41, 40). In order to prevent stress ulcers and mucosal damage, usually one of the histamine receptor antagonists (2), proton pump inhibitors, antacids and Sucralfate is prescribed (40-44). H2 blockers stimulate acid secretion from parietal cells by inhibiting histamine (45).

Proton pump inhibitors inhibit hydrogen, potassium and ATPase (39). Acid suppression treatment by H2 blockers, antacids and proton pump inhibitors reduce the incidence of bleeding (46-48). In recent years, proton pump inhibitors play a more important and more robust role than other drugs in this regard and has recently replaced H2 blocker (49-50).

Yang et al in their study in 2002 stated that proton pump inhibitors can replace H2-blockers in preventing gastrointestinal bleeding among patients in the ICU (51). Proton pump inhibitors are used to reduce the acidity of stomach contents before anesthesia (52-53). Several studies have shown the useful role of Omeprazole injections in the prevention of stress ulcers and gastrointestinal bleeding (50-55). A study by Levy et al, compared the efficacy of Omeprazole and ranitidine in patients with risk factors for stress-related bleeding, concluded that Omeprazole in patients in ICU is safer and more effective (56). Since in various studies, there is the possibility of using both blocker antihistamines and proton pump inhibitors in the management and prevention of stress-related mucosal disease (SRMD), or a stress ulcer (SU) in patients admitted to the intensive care unit, we decided in this study to evaluate the administration frequency of the two drug groups by expertise in Imam Khomeini hospital of Sarab city.

## 2. Material and Methods

The present study was a descriptive-analytical retrospective study conducted on patients hospitalized in ICU of Imam Khomeini hospital of Sarab during April 2015 to march 2016.

Regarding the previous studies and based on online sample size calculation formula, the sample size for this study was determined 180 that due to the possibility of exclusion of some patients in the study, the number of patients considered 200.

This study was carried out in a total duration of 12 months, examining the patients hospitalized in ICU

of Imam Khomeini hospital of Sarab. In this study, medical records of 200 patients admitted to the ICU, available at the archive of Imam Khomeini hospital of Sarab (April 2015 to March 2016) were investigated using a checklist provided including: date of admission, sex, age, visiting MD's expertise, medicines prescribed by doctors, underlying disease and social habits. Determining the mean or the frequency of each of the variables based on statistical methods, the difference between variables were analyzed and the population information obtained was analyzed by SPSS ver.19 software after collection and reported at the end.

## Limitations of the study

1. Limited number of beds due to lack of space in ICU of Imam Khomeini hospital of Sarab.

2. Limited number of patients hospitalized in ICU of Imam Khomeini hospital of Sarab.

3. Diversity and low number of physicians for patients in need of intensive care in ICU of Imam Khomeini hospital of Sarab.

## Ethical considerations

Given that the study was retrospective and during the study, the information of patients and doctors working in the ICU has been kept confidential, there have been no ethical issues.

## Statistical Analysis:

The collected data were analyzed by SPSS-19 statistical software. The collected data were expressed as percentage and mean  $\pm$  SD. Continuous (quantitative) variables were compared by Independent samples and Paired t test. Categorical (qualitative) variables were compared by contingency tables and Chi-square test or Fisher's exact test. P-value  $\leq 0.05$  was considered statistically significant.

## 3. Results

56% of patients were male and 44% were female. The mean age was  $62 \pm 19$  years for males and  $60 \pm 22$  years for females.

Causes of hospitalization in ICU included respiratory diseases by 32%, neurological disease by 5-20%, cardiovascular diseases by 8.5%, and drug problems by 7% and malignancies by 6%. Respiratory diseases included COPD by 67.1%, pulmonary edema and pneumonia by 10.9%, asthma by 7.8% and tachypnea by 3.1%.

The frequency of types of malignancies in patients included hepatic malignancies by 16.6%, intestinal cancer by 50%, and gastric cancer by 16.6% and esophageal cancer by 16.6%.

The frequency of cardiovascular diseases in patients included cardiac arrhythmias by 70.5% and unstable angina by 29.4%.

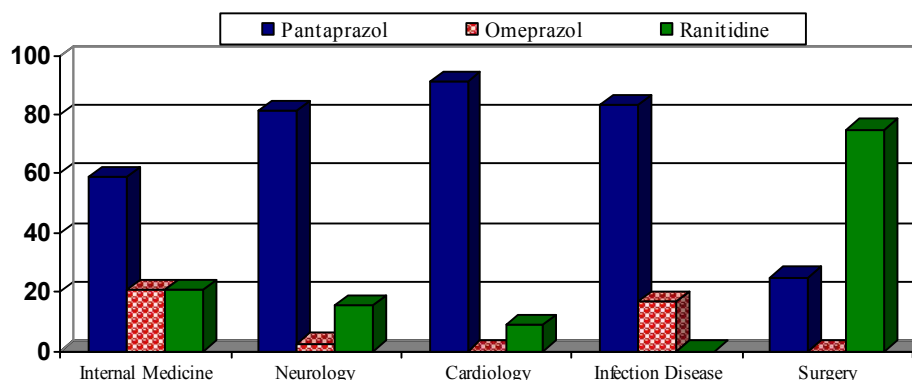


Figure 1: The frequency of gastric acid suppressor drugs prescribed by MDs in the ICU of Imam Khomeini Hospital of Sarab, based on expertise orientation

Types of medical problems causing hospitalization of patients included drug toxicity (50%) and medication errors (50%).

The frequency of neurological diseases included CVA (95.1%) and recurrent seizures (4.9%).

The frequency of other diseases leading to hospitalizations was GIB by 32.6%, the frequency of occurrence of loss of consciousness was 17.3%, the frequency of occurrence of sepsis was 13.8%, the frequency of occurrence of surgical bleeding was 13.4%, the frequency of occurrence of hypoglycemia was 11.5%, the frequency of occurrence of shock was 5.7%, the frequency of occurrence of bleeding in pregnancy was 3.8% and cirrhosis was 1.9%. 8.5% of patients were smokers and 2% narcotic addicts.

The frequency of acid suppressors administered included Pantoprazole by 65%, Omeprazole by 15.5% and ranitidine 19.5%.

#### 4. Discussions

This study is the first report on the prescription frequency of H<sub>2</sub> blockers and proton pump inhibitors in Imam Khomeini hospital of Sarab city. In this study, medical records of 200 patients admitted to the ICU of Imam Khomeini hospital of Sarab city was studied that the difference was not significant in terms of sex distribution. The mean ages of males and females are very close to each other. The most common causes of admission were GIB diseases (32.6%) and respiratory diseases (32%). Usage of drugs was Pantoprazole 65%, ranitidine 19.5% and Omeprazole 15.5%. In 2000, 1242 mortalities occurred in Iran due to lung cancer due to smoking (3). Smoking can be controlled and reduced using special publication and installation of posters promoting to quit smoking in order to informing people about the harms of smoking, and creating facilities for direct observation of those harms; so, the

incidence of respiratory diseases can be reduced which are the main reason of admission to ICU of ICU of Imam Khomeini hospital of Sarab city. Although no absolutely similar studies were found on general administration of these drugs at the national or international level, there are many studies in this field.

In a study by Prath et al in 2006 in California medical center on 36 healthy adults, examining the inhibitory effect of Omeprazole (20mg) and Pantoprazole (40mg) on gastric acid secretion, the results showed that the inhibitory effect of Pantoprazole was more than Omeprazole (57). In the studies by Mr. Dilek et al in the medical center of Turkey in 2003 on 90 patients, comparing the effectively of IV Pantoprazole and ranitidine in reducing gastric acidity, the first group (n=30) received salt solution 5mg, the second group (n=30) received Pantoprazole 40mg, and the third group (n=30) ranitidine 50mg injections. Pantoprazole was observed more effective in reducing gastric pH (58). Also, in the studies by Somberg et al at medical centers in Chicago in 2008 on 202 patients, Pantoprazole (40mg) and Cimetidine (300mg) were examined in critically ill patients at risk of stress-related mucosal disease. Their study confirmed that higher treatment was observed in Pantoprazole group (31).

The studies by Rahimi et al in 2013 in the medical center of Hamedan on 92 patients (68% of which were male), Pantoprazole 40mg every 12 hours and Ranitidine 50mg every 8 hours were administered to the patients and the results showed that Pantoprazole IV, compared with ranitidine, was more effective for prevention of gastrointestinal bleeding caused by stress ulcer (59). Overview of these studies shows that the results of these studies are in line with the performance of therapist personnel in Sarab hospital, where Pantoprazole is preferred as an

effective drug in reducing the pH and preventing gastrointestinal bleeding. At the meanwhile, more investigations indicated that some of the medical personnel in ICU had somehow different approach in treatment of ulcers induced by hospitalization in ICU, so that Omeprazole had a special position in their therapeutic protocol. In the study by Conrad et al in 2002 in the medical center of Shreveport, US, ranitidine 150mg was administered to 35 high-risk patients, and Omeprazole 40mg to 32 patients by mouth or through a nasogastric tube; 31% of those receiving ranitidine experienced gastrointestinal bleeding, which was observed in 6% of Omeprazole group (14).

The studies by Peghini et al in 1998 in the medical center of San Jose, US, on 12 volunteers under gastric pH monitoring, after 7 days of therapy with Omeprazole 20mg and ranitidine 150mg, showed that Omeprazole reduced the gastric pH from 48% to 31%, ranitidine reduced the gastric acidity by 5%, and acid suppression with Omeprazole was observed (60).

### Conclusion

This study evaluated the administration frequency of H<sub>2</sub> blockers and proton pump inhibitors in Imam Khomeini in Sarab, where parameters such as age, sex, physicians' expertise, prescribed medications, underlying disease, and social habits were investigated and it was concluded that respiratory diseases were the most common cause of hospitalization, and as for the social habits, 8.5% of hospitalized patients were smokers; and among the prescribed medications, use of Pantoprazole was significantly higher than ranitidine and Omeprazole. A study conducted in 2006 found that 59% of preventive methods performed by the medical residents have been wrong, that was reduced in significance level after educational intervention (61). This study showed that general surgeons are more willing to use ranitidine, which may be due to them in the course of the project and also have insufficient knowledge in the field of new drugs. Therefore, by improving the quality and quantity of human resources physically and educationally, the necessary conditions can be provided for high-quality services provided in the intensive care unit (62). In order to further enhancements in the intensive care unit, successful experiences can be shared with other hospitals by holding of joint conferences and group visits to successful hospitals.

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### References

1. variations in admissions for acute myocardial Bhattacharyya T, Sarbapalli D, Pal R, Sarkar U, Kar S, Kundu KK, et al. Evaluating ranitidine, pantoprazole and placebo on gastric pH in elective surgery. *Saudi J Anaesth.* 2011 Jan;5(1):67-72.
2. Engelhardt T, Webster NR. Pulmonary aspiration of gastric contents in anaesthesia. *Br Anaesth.* 1999;83:453-60.
3. Warner MA, Warner ME, Weber JG. Clinical significance of pulmonary aspiration during the perioperative period. *Anesthesiology* 1993;78:56-62.
4. Olsson GL, Hallen B, Hambraeus-Jonzon K. Aspiration during anaesthesia: a computer-aided study of 185,358 anaesthetics. *Acta Anaesthesiol Scand* 1986;30:84-92.
5. Lunn, JN, Mushin, WW. Mortality associated with anaesthesia. *Anaesthesia* 1982 Aug;37(8):795-892.
6. Gon, S, Irie, Y, Takahashi, M. Effects of rabeprazole or famotidine during cardiac surgery on perioperative gastric and esophageal pH readings. *Jpn J Thorac Cardiovasc Surg.* 2006 Jul;54(7):278-84.
7. Escolano F, Castaño J, López R, Bisbe, E, Alcón A. Effects of omeprazole, ranitidine, famotidine and placebo on gastric secretion in patients undergoing elective surgery. *Br J Anaesth* 1992;69:404-6 failure *Nephrol Dial Transplant* (1998);13: 1189–1193.
8. Basso N, Bagarani M, Materia A, Fiorani S, Lunardi P and Speranza V. Cimetidine and antacid prophylaxis of acute upper gastrointestinal bleeding in high risk patients: controlled, randomized trial. *Am. J. Sur* (1981); 141: 339-41.
9. Smythe MA, Zarowitz BJ. Changing perspectives of stress gastritis prophylaxis. *Ann Pharmacother* 1994; 28 (9): 1073- 85.
10. Phillips JO, Olsen KM, Rebuck JA, Rangnekar NJ, Miedema, BW, Metzler MH. A randomized, pharmacokinetic and pharmacodynamic, cross-over study of duodenal or jejunal administration compared to nasogastric administration of omeprazole suspension in patients at risk for stress ulcers. *Am J Gastroenterol* 2001; 96 (2): 367- 72.
11. Martin LF, Booth FV, Karlstadt RG, Silverstein JH, Jacobs DM, Hampsey J, et al. Continuous intravenous cimetidine decreases stress-related upper gastrointestinal hemorrhage without promoting pneumonia. *Crit Care Med* 1993; 21 (1): 19- 30.
12. Gado AS, Ebeid BA, Abdelmohsen AM, Axon AT. Clinical outcome of acute upper gastrointestinal hemorrhage among patient admitted to a government hospital in Egypt. *Saudi Gastroenterol.* 2012;18(1):34-9.
13. Adufal H K, Naader SB, Darko R, et al. Upper gastrointestinal endoscopy at the Korle Bu teaching

- hospital, Accra, Ghana. *Ghana Med J*, 2007;41:12-16.
14. Conrad SA (2002). Acute upper gastrointestinal bleeding in critically ill patients: Causes and treatment modalities. *Crit Care Med* 30: S365-368.
  15. Cook, DJ. Stress ulcer prophylaxis. Gastrointestinal bleeding and nosocomial pneumonia. Best evidence hypothesis. *Scand J Gastroenterology* 1995; 30: 48-56.
  16. Tamir Ben-menachem, Ronald Fogel, Rakesh V, et al. Prophylaxis for stress-related gastric hemorrhage in the medical intensive care unit. A randomized, control single blind study: *Ann Intern Med* 1994; 121: 568-75.
  17. Fennerty, MB. Pathophysiology of the upper gastrointestinal tract in the critically ill patient: rationale for the therapeutic benefits of acid suppression. *Crit Care Med* 2002;30 (6 Suppl): S351-5.
  18. Nava F, Stengrub J. Stress ulcer: is routine prophylaxis necessary *Gastroenterology* 1995; 90:708-13.
  19. Kamada T, Sato N, Kawano S, Fusamoto H, Abe H. Gastric mucosal hemodynamics after thermal or head injury. A clinical application of reflectance spectrophotometry. *Gastroenterology*. 1982 Sep;83(3):535-40.
  20. Yasue N, Guth PH. Role of exogenous acid and retransfusion in hemorrhagic shock-induced gastric lesions in the rat. *Gastroenterology* 1988; 94 (5 Pt 1): 1135-43.
  21. Zinner MJ, Zuidema GD, Smith PL, Mignosa M. The prevention of upper gastrointestinal tract bleeding in patients in an intensive care unit. *Surg Gynecol Obstet* 1981; 153 (2): 214-20.
  22. Zuckerman GR and Shuman R. Therapeutic goals and treatment options for prevention of stress ulcer syndrome. *Am. J. Med.* (1987); 83: 29-35.
  23. JBS Haldane. gastrointestinal prophylaxis, in: Paul L. Marino the Icu book, 2st ed, Williams & Wilkins 1998: 94105.
  24. Kenneth Waxman M.D, F.A.C.S. Acute abdominal complication in the intensive care unite, In: shoemaker ayres grenvik Holbrook textbook of critical care, 4th ed, W.B. Saunders company 2000: 160311.
  25. Howard M. Stress ulcers, In: Howard M. SPIRO clinical gastroenterology, 4th ed, McGrawHill 1993:3224.
  26. Loren Laine. Acute and Chronic Gastrointestinal Bleeding, In: Sleisenger & Fordran's gastrointestinal and liver disease. 6th ed, Saunders 1998: 211 2.
  27. Czaja AJ, McAlhany JC, Andes WA, Pruitt BA Jr. Acute gastric disease after cutaneous thermal injury. *Arch Surg* 1975; 110 (5): 600- 5.
  28. Sesler JM. Stress-related mucosal disease in the intensive care unit: an update on prophylaxis. *AACN adv. Crit. Care* (2007); 18: 119.
  29. Constantin VD, Paun S, Ciofoaia VV, Budu V, Socea B. Multimodal management of upper gastrointestinal bleeding caused by stress gastropathy. *J Gastrointestin Liver Dis* 2009;18(3):279- 84.
  30. Marrone GC, Silen W. Pathogenesis, diagnosis and treatment of acute gastric mucosal lesions. *Clin Gastroenterol* 1984; 13(2):635-50.
  31. Somberg L, Morris Jr, Fantus R., et al. Intermittent intravenous pantoprazole and continuous cimetidine infusion: effect on gastric pH control in critically ill patients at risk of developing stress-related mucosal disease. *J Trauma* 2008; 64(5):1202-10.
  32. Wyllie P, Iraci S. Stress Ulcer. In: *Textbook of Adult Emergency Medicine*, Philadelphia; Churchill Livingston 2000:2427.
  33. George F, David A Peura. Stress Ulcer. In: *clinical practice of Gastroenterology*, Current Medicine 1999: 2817.
  34. Tryba M, Cook D. Current guidelines on stress ulcer prophylaxis. *Drugs* 1997;54:581-596.
  35. Hamishehkar H, Beigmohammadi MT, Abdollahi M, Ahmadi A, Mahmoodpour A, Mirjalili MR, Abrishami R, Khoshayand MR, Eslami K. Identification of enhanced cytokine generation following sepsis. Dream of magic bullet for mortality prediction and therapeutic evaluation. *DARU J. Pharm. Sci.* (2010);18: 155-162.
  36. Cook DJ, Fuller HD, Guyatt GH., Marshall JC, Leasa D, Hall R, Winton TL, Rutledge F, Todd TJ, Roy P, et al. Canadian Critical Care Trials Group. Risk factors for gastrointestinal bleeding in critically ill patients. *N Engl J Med* 1994;330(6):377-381.
  37. Mutlu GM, Mutlu EA and Factor P. GI Complications in patients receivin mechanical ventilation. *Chest*. 2001 Apr;119(4):1222-41.
  38. Martindale RG. Contemporary strategies for the prevention of stress-related mucosal bleeding. *Am J Health Syst Pharm*. 2005 May 15;62(10 Suppl 2): S11-7.
  39. Spirt MJ, Stanley S. Update on stress ulcer prophylaxis in critically ill patients. *Crit Care Nurse* 2006;26(1):18-20, 22-28.
  40. Lucas CE, Sugawa, C, Riddle J, Rector F, Rosenberg B, Walt AJ. Natural history and surgical dilemma of "stress"gastric bleeding. *Arch Surg* 1971;102 (4): 266- 73.
  41. ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis. ASHP Commission on Therapeutics and approved by the ASHP Board of Directors on November 14, 1998. *Am J Health Syst Pharm*, 1999; 56:347-379.
  42. Grube RR, May DB. Stress ulcer prophylaxis in hospitalized patients not in intensive care units. *Am J Health-Syst Pharm*. 2007;64:1396-1400.

43. Pisegna JR (2002). Pharmacology of acid suppression in the hospital setting: Focus on proton pump inhibition. *Crit Care Med* 30: S356–361.
44. Cook D, Guyatt, G, Marshall J, et al. (1998) A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. Canadian critical care trials group. *N Engl J Med* 338:791–797.
45. Stollman N, Metz DC. Pathophysiology and prophylaxis of stress ulcer in intensive care unit patients. *J Crit Care* 2005;20(1):35–45.
46. Priebe HJ and Skillman JJ. Methods of prophylaxis in stress ulcer disease. *World J. Surg.* (1981);5: 223-9.
47. Geus WP. Are there indications for intravenous acid-inhibition in the prevention and treatment of upper GI bleeding *Scand J Gastroenterol* 2000; 232 Suppl:10-20.
48. Shuman RB, Schuster DP and Zuckerman GR. Prophylactic therapy for stress ulcer bleeding: a reappraisal. *Ann. Internal Med.* (1987); 106: 562-9.
49. Lugo RA, Harrison AM, Cash J, Sweeley J, Vernon DD. Pharmacokinetics and pharmacodynamics of ranitidine in critically ill children, *Crit Care Med* 2001;29(4):75964.
50. Laterre PF, Horsmans Y. Intravenous omeprazole in critically ill patients: a randomized, crossover study comparing 40 with 80 mg plus 8 mg/hour on intragastric PH. *Crit Care Med* 2001 Oct;29(10):1931-5.
51. Jung R, MacLaren R. Proton-pump inhibitors for stress ulcer prophylaxis in critically ill patients. *Ann Pharmacother* 2002; 36 (12): 1929- 37.
52. Prakash A, Faulds D. Rabeprazole. *Drugs* 1998; 55:261-7.
53. Roberts RB, Shirley MA. Reducing the risk of acid aspiration during caesarean section. *Anesth Analg.* 1974;53:859-68.
54. Keshavarz AA, Rahimi A. The effect of two different doses of Omeprazole on gastric PH in ICU patients. *Iranian Journal of Medical Science* 2004; 29(1):40-42.
55. Steinberg KP. Stress-related mucosal disease in the critically ill patient: risk factors and strategies to prevent stress-related bleeding in the intensive care unit, *Crit Care Med* 2002; 30(6 suppl), S 362-4.
56. Levy MJ, Seelig CB, Robinson NJ, Ranney JE. Comparison of omeprazole and ranitidine for stress ulcer prophylaxis. *Dig Dis Sci* 1997;42(6):1255–1259.
57. Prath A, Visaya S. (2006) Inhibition of Pentagastrin Stimulated Gastric Acid Secretion by Pantoprazole and Omeprazole in Healthy Adults, *Digestive Diseases and Sciences.* 51: 123-131.
58. Dilek, M.E., Alparslan, T.V., Beyhan, K.A., Pinar, S.A., Zafer, P.A. The effect of intravenous pantoprazole and Ranitidine for improving preoperative gastric fluid properties in adults undergoing elective surgery. *Anesth Analg.* (2003), 97: 1360-3. endoscopy at the Korle Bu teaching hospital, Accra, Ghana. *Ghana Me J* 2007. 41, 12-6.
59. Farshid, Rahimi Bashar., Alireza, Rastgouyaghgi., Saadat, Torabian., Mohammad Reza, Hajiesmaeili., Alireza, Sedaghat., Shahram, Seifi., Mahdis, Solhjo. Prevention of Stress Related Mucosal Disease with Intermittent Intravenous Pantoprazole and Ranitidine in Critically Ill Patients. *J Pharm Care* 2013. 1(3), 81-84.
60. Peghini, PL., Katz, PO., Castell, DO. Ranitidine controls nocturnal gastric acid breakthrough on omeprazole: a controlled study in normal subjects. *Gastroenterology* 1998. 115(6), 1335-9.
61. Liberman JD, Whelan CT. Brief report: Reducing inappropriate usage of stress ulcer prophylaxis among internal medicine residents. A practice-based educational intervention. *J Gen Intern Med* 2006;21(5):498-500.
62. Jadidi R, Norouzi A, Moshiri E. The relationship between physical and human resources in the Intensive Care Units and patients mortality rate in Hospitals of Markazi Province's:2007. *Journal of Arak University of Medical Sciences.* 2009;12(2):29-38.

3/9/2017