Significant Upper Gi – Bleeding In Critically III Patients

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Citation

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Abstract

Background: To evaluate risk factors for clinically important upper gastrointestinal bleeding in critically ill patients requiring mechanical ventilation.

Methods: In this prospective study, we determined the presence of clinically important gastrointestinal bleeding, evaluated relevant clinical, laboratory, and diagnostic criteria at four University-affiliated intensive care units in Tabriz, Iran. A total of 300 critically ill ICU patients were ventilated for at least 48 hours. Demographic data included patient characteristics and multiple organ dysfunction score. Each day in the ICU, physiologic measurements including multiple organ dysfunction score, feeding, and other drug variable were recorded. Data were analyzed by t-test and mann Whitney test.

Results: The significant risk factors for upper gastro intestinal bleeding were low platelet count, maximum serum creatinin, maximum pulmonary component multiple organ dysfunction score, maximum respiratory component multiple organ dysfunction score.

Conclusions: In critically ill ventilated patients, renal failure respiratory, cardiac dysfunction, and coagulopathy disorder were associated with an increased risk significant gastrointestinal bleeding whereas enteral nutrition and stress ulcer prophylaxis with ranitidine decreased gastrointestinal bleeding.

INTRODUCTION

Critically ill patients who are require mechanical ventilation are at increased risk for gastrointestinal bleeding from stress ulcer (1), and overt evidence of upper gastrointestinal bleeding is not uncommon in critically ill patients (2,3,4,5,6,7). Although hemorrhage from stress ulceration occurs in only 5-20% of patients in an ICU (8), there is evidence that routine prophylaxis decreases stress related gastro intestinal bleeding (9). We undertook this retrospective study to assess significant gastrointestinal bleeding in patients admitted to our intensive care units and determine risk factors in patients with multi organ dysfunction.

METHODS

Consecutive 300 patients who were hospitalized at four university-affiliated medical and surgical intensive care units and needed ventilation for more than 48 hours, were considered for study. Exclusion criteria were gastrointestinal bleeding in admission time, life expectancy lower than 72 hours and history of gastrointestinal surgery. Demographic data included patient characteristics, history and physical

exam, para clinic tests, nutrition, drugs, and prophylaxis. Clinically important upper gastrointestinal bleeding were defined as: spontaneous decreasing blood pressure> 20 mm hg at 24 hours after admission, increasing pulse rate 20 beats / minute and orthostatic blood pressure change, hemoglobin decreasing >= 2 gr/dl within 24 and need for blood transfusion within 24 hours after bleeding(3,14). Multiple organ dysfunction score assessment was defined as: respiratory system (defined Po2/Fio2 fraction> 300 = stage 0), cardiac system(pressure - adjusted heart rate <=10 = stage 0, stage 1 = 10.1 - 15, stage 2 = 15.1-20, stage 3 = 10.1 - 1020.1-30, stage 4>30), renal system(serum creatinine (mg/dl), stage0= 1, stage1=2.01-3.5, stage 3 = 3.51-5.00, stage4>5), hepatic system (serum billirubin (mg/dl), $stage0 \le 2$, stage1 = 2.1 - 6, stage2 = 6.1 - 12, stage3 = 12.1 - 24, stage4>24), hematologic system (platelet cell/ml3, stage0= 120000, stage1=81-120, stage 2=51-80, stage3=21-50, stage 4<=20), central nervous system(defined as Glasgow coma scale score)(10,11). Daily evaluation included significant upper GI bleeding symptoms as hematemesis, bloody aspiration in nasogastric tube, melena or hematochesis

,administration of heparin or warfarin, glucocorticoids, aspirine or another non steroidal anti inflammatory drugs, need for ventilation for at least 48 hours), using of enteral feeding, using of stress ulcer prophylaxis.

We analyzed variables with the Coxs regression model, compared them with students t-test and compared proportions with chi- square test. Variables were significantly associated (P<0.05) with clinically important bleeding.

RESULTS

Of 300 patients admitted and studied in intensive care units (153 male, 147 female), 80 (26.7%) cases had clinically important gastrointestinal bleeding (42 had melena and coffee ground aspiration in nasogastric tube, 21 had only melena, 14 had melena and red aspiration, 3 had only red aspiration). 23.95 % had respiratory failure, 19.79 % had CNS problems and 16.79 % had cardiovascular dysfunction, 12.27 % had Sepsis.

Figure 1
Table 1: Risk factors in bleeder and non – bleeder groups

Variables	Bleeder(80)	Non bleeder(220)
MODS	7.1±3.9	5.9±3.2
Length of ventilation	19.8±18.5	7.5±5.6
Length of hospital stay	27.1±23.5	10.2±10.5

The significant risk factors for upper gastro intestinal bleeding were low platelet count, maximum serum creatinin, maximum pulmonary component multiple organ dysfunction score, maximum respiratory component multiple organ dysfunction score, maximum cardiac component multiple organ dysfunction score. 42.25% of patients had coagulopathy problem. Bleeding occurrence in 65% had been seen in the first 2 weeks after admission. Non bleeder group (220) were younger than bleeder group (80) but (55.7%) in non – bleeder group were female, had shorter stays in the intensive unit care (7.5±5.6 vs 19.8± 18.5,P = 0.001) and had lower MOD score(P=0.05). Significant differences were not seen between 2 groups about sex and age (P = 0.15).

Clinically important bleeding was associated with low platelet count (CI 95% = 4.44, P= 0.03), maximum serum creatinine (CI 95% = 6.87, P = 0.004), maximum pulmonary component (CI 95% = 1.08, P= 0.022), maximum cardiac

component (CI 95% = 1.05, P= 0.031), coagulopathy (P=0.03). Patients with high risk factors had high risk for bleeding, i.e positive relationship was seen between increasing risk factors and bleeding (P = 0.003).

DISCUSSION

We found that clinically important bleeding was associated with an increased risk, MODS score, length of ventilation, and length of hospitalization. Admitting diagnosis, ventilation length, bleeding status is important in our study. Other studies have estimated stress ulcer associated bleeding increased risk of ventilation and ICU stay, high morbidity and mortality rate. In our study, the incidence of clinically important gastrointestinal bleeding was 26.7%, But in Nithiwathanpong et al study $\binom{1}{20}$ its incidence was 43.5%, in Deborah et al (1) was 1.7%, in another Deorah (3) study was 1.5%, and in Pimentel et al study (8) was 0.17%. Therefore, the clinically important GI bleeding incidence vary in different studies but our result showed that bleeding in critically patients is not rare. Virtually all patients who are under the physiologic stress of an intensive care unit (ICU) are vulnerable to stress-related mucosal damage and ulceration (12). Current clinical opinion and available evidence suggests that the early appropriate referral of patients to ICU can significantly reduce early, and possibly late, mortality in the critically ill(13). This common event has high mortality and may be, prophylaxis can reduce risk factors and bleeding induced mortality. The current overview demonstrates that prophylaxis decreases clinically important bleeding (OR, 0.44; 95% CI, 0.22 to 0.88)(21). Although the bleeding episodes stops spontaneously in most of patients ($_{15}$), we found that 46 pateints (57.5%) had experienced stress ulcer bleeding episodes in first 6-10 days. Terdiman et al study showed that clinically important gastrointestinal bleeding occurred in 67 inpatients after a mean hospital length stay 14 ± 10 days (16), and Deborah et al observed the risk of bleeding to increased, 75% of events occurred in the first 2 weeks of ICU stay (19). Therefore, in different studies GI bleeding occur after 2 weeks of ICU admission. Prolonged mechanical ventilation and coagulopathy are the most important predictors of stress ulcer related bleeding. Critically ill patients with stress ulcer related bleeding should be managed in the acute setting just as patients presenting with upper gastrointestinal bleeding (14). In the Chaibou et al study, respiratory failure and coagulopathy were complications that attributed with gastrointestinal bleeding (17). A Canadian trial group found that risk factors for upper gastrointestinal bleeding were low

platelet count, maximum serum creatinin, maximum MOD score (maximum renal, hepatic, pulmonary)(18). Dysfunction of specific organs (pulmonary, hepatic, renal) and overall multiple organ dysfunction were associated with an increased risk of bleeding (19). Previously described factors for stress ulcer bleeding (mechanical ventilation, sepsis, acute respiratory distress syndrome, renal insufficiency, coagulopathy, thrombocytopenia, and intracranial pathology) were similarly in our study $\binom{1}{20}$.

The patients of the two treatment groups (each 16) were comparable with respect to diseases precipitating acute respiratory failure and risk factors of bleeding, e.g., renal failure, thrombopenia, coagulopathy, and anticoagulant treatment $\binom{1}{2}$. Laggner et al found that age, clinical evidence of shock, hepatic dysfunction and hemoglobin less than 8.0 g/dl (80 g/L) to be significant in prediction of risk of further hemorrhage(23) and, Supe et al study showed that significant risk factors for upper gastro intestinal bleeding were low platelet count, maximum serum creatinin, maximum pulmonary component multiple organ dysfunction score, maximum respiratory component multiple organ dysfunction score, maximum cardiac component multiple organ dysfunction score. We have similar results compared to other studies.

In summary, in our population of 300 patients ventilated for > 48 hours, it could be shown that clinically important gastrointestinal bleeding is associated with high MOD score, high duration of ventilation, and high length of ICU stay. Likely, it seems that bleeding can increase duration of above items.

References

- 1. Deborah Cook, Gordon Guyatt, John Marshall, David Leasa, Hugh Fuller, Richard Hall, Sharon Peters, Frank Rutledge, Lauren Griffith, Allan McLellan, Gordon Wood, Ann Kirby, Martin Tweeddale, Joe Pagliarello, Richard Johnston, for The Canadian Critical Care Trials, A Comparison of Sucralfate and Ranitidine for the Prevention of Upper Gastrointestinal Bleeding in Patients Requiring Mechanical Ventilation, The new England journal of medicine; 338:791-797.
- 2. Cochran EB, Phelps SJ, Tolley EA, Stidham GL, Prevalence of, and risk factors for, upper gastrointestinal tract bleeding in critically ill pediatric patients, Crit Care Med 1992; 20:1519-23.
- 3. Deborah J. Cook, Hugh D. Fuller, Gordon H. Guyatt, John C. Marshall, David Leasa, Richard Hall, Timothy L. Winton, Frank Rutledge, Thomas Todd, Peter Roy, Jacques Lacroix, Lauren Griffith, Andrew Willan, for The Canadian Critical Care Trials Group, Risk Factors for Gastrointestinal Bleeding in Critically Ill Patients, 1994; 330:377-381. 4. Maton PN. Review article: prevention of stress-related mucosal bleeding with proton-pump inhibitors. Aliment Pharmacol Ther. 2005 Dec;22 Suppl 3:45-52.

- 5. Maton Pn. Review article: prevention of stress. related mucosal bleeding with proton . pump inhibitors, Aliment Pharmacol Ther . 2005; 3:45-52
- 6. Metz DC, Preventing the gastrointestinal consequences of stress-related mucosal disease, Curr Med Res Opin 2005;
- 7. ER Gonzalez, Pathophysiologic changes in the critically ill patient: risk factors for ulceration and altered drug metabolism, DICP, The Annals of Pharmacotherapy:1990 11: 5-7.
- 8. Pimentel M, Roberts DE, Bernstein CN, Hoppensack M, Duerksen DR, Clinically significant gastrointestinal bleeding in critically ill patients in an era of prophylaxis. Am J Gastroenterol 2000; 95:2801-6.
- 9. Ohmann C, Thon K, Hengels KJ, Imhof M, Incidence and pattern of peptic ulcer bleeding in a defined geographical area. DUSUK Study Group. Scand J Gastroenterol 1992; 27:571-81.
- 10. Schuster DP, Rowley H, Feinstein S, McGue MK, Zuckerman GR. Prospective evaluation of the risk of upper gastrointestinal bleeding after admission to a medical intensive care unit. Am J Med. 1984 Apr;76(4):623-30. 11. John C marshall, Deborah J. Cook, Nicolas V. Christou,
- Gordon R. Bernard, Charles L. Sprung, William Sibbald, Multiple organ dysfunction scorre: a reliable descriptor of a complex clinical outcome, crit care 1995;23:10.
- 12. Yang YX, Lewis JD, Prevention and treatment of stress ulcers in critically ill patients. Semin Gastrointest Dis. 2003 Jan;14(1):11-9.
- 13. BRIAN H. CUTHBERTSON and NIGEL R. WEBSTER, The role of the intensive care unit in the management of the critically ill surgical patient, .R.Coll.Surg.Edinb., 44, October 1999, 294-300 14. Deborah J Cook, Lauren E Griffith, Stephen D Walter,
- Gordon H Guyatt, Maureen O Meade, Daren K Heyland, Ann Kirby, Michael Tryba, and for the Canadian Critical Care Trials Group, The attributable mortality and length of intensive care unit stay of clinically important gastrointestinal bleeding in critically ill patients, Crit Care.
- 2001; 5(6): 368-375.
- 15. Al-Akeely MH, Alam MK, Al-Salamah SM, Abdu MA, Al-Teimi IN, Mohammed AA, Initial factors predicting rebleeding and death in bleeding peptic ulcer disease. Saudi Med J 2004; 25:642-7.
- 16. Terdiman JP, Ostroff JW. Gastrointestinal bleeding in the hospitalized patient: a case-control study to assess risk factors, causes, and outcome. Am J Med. 1998 Apr;104(4):349-54.
- 17. Chaïbou M, Tucci M, Dugas MA, Farrell CA, Proulx F, Lacroix J, Clinically significant upper gastrointestinal bleeding acquired in a pediatric intensive care unit: a prospective study. Pediatrics 1998; 102:933-8.
- 18. Cook D, Heyland D, Griffith L, Cook R, Marshall J, Pagliarello J. Risk factors for clinically important upper gastrointestinal bleeding in patients requiring mechanical ventilation. Canadian Critical Care Trials Group. Crit Care Med. 1999 Dec;27(12):2812-7.
- 19. Deborah cook, Daren Heyland, Lauren Griffith, Richard Cook, John Marshall, Joe Pagliarello, Risk factors for clinically important upper gastrointestinal bleeding in patients requiring mechanical bleeding ventilation, Crit Care Med 1999, 27:12.
- 20. Nithiwathanapong C, Reungrongrat S, Ukarapol N. Prevalence and risk factors of stress-induced gastrointestinal bleeding in critically ill children. World J Gastroenterol. 2005 Nov 21;11(43):6839-42.
- 21. D. J. Cook, B. K. Reeve, G. H. Guyatt, D. K. Heyland, L. E. Griffith, L. Buckingham and M. Tryba, Stress ulcer

prophylaxis in critically ill patients. Resolving discordant meta-analyses, JAMA 1996;275:4.
22. Laggner AN, Lenz K, Base W, Druml W, Schneeweiss

B, Grimm G, Prevention of upper gastrointestinal bleeding

in long-term ventilated patients. Sucralfate versus ranitidine, Am J Med 1989; 86:81-4.
23. Supe AN, Soonawala PF, Mathur SK, Samsi AB, Prognostic markers in upper gastrointestinal hemorrhage, Indian J Gastroenterol 1989; 8:233-6.

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