

Incidence and risk factors of upper gastrointestinal bleeding in pediatric intensive care unit admitted patients

Saeedeh Haghbin, Department of pediatric, Division of pediatric intensive care , Faculty of medicine , Shiraz University of Medical sciences, Shiraz , Iran. Haghbins@sums.ac.ir

Ali Manafi Anari (*Corresponding author): Department of pediatric, Division of pediatric intensive care , Faculty of medicine , Iran University of Medical sciences, Tehran , Iran. amanafi55@yahoo.com

Zahra Serati, Department of pediatric, Division of pediatric intensive care , Faculty of medicine , Shiraz University of Medical sciences, Shiraz , Iran. zserati@yahoo.co.uk

Khashayar Aflaki, Department of pediatric, Division of pediatric intensive care , Faculty of medicine , Shiraz University of Medical sciences, Shiraz , Iran. aflakik@yahoo.com

Behzad Haghghi Aski, Department of pediatric, Division of pediatric intensive care , Faculty of medicine , Iran University of Medical sciences, Tehran , Iran.

haghghi_behzad@yahoo.com

Mohamad Reza Navaei far, Department of pediatric, Division of pediatric intensive care , Faculty of medicine , Mazandaran University of Medical sciences, Sari , Iran.dr.navaifar@gmail.com

Acknowledgements: The authors would like to thank Clinical Research of Namazee Hospital Center ,Shiraz University of Medical Sciences ,Shiraz,Iran

Received: 20 Dec 2015 Accepted: 24 Jan 2016

Abstract

Background and Objective: To assess the incidence and risk factors of upper gastrointestinal bleeding in children admitted to pediatric intensive care unit for more than 6 hrs.

Methods: We prospectively collected medical records of children between 1 month and 18 years old admitted to our 10 bed PICU of a tertiary care university hospital between December 1, 2014 and May 30, 2015. Demographic data, admission diagnosis and basic laboratory data were recorded. We defined upper gastrointestinal bleeding (UGI) as any evidence of blood in nasogastric aspirates, hematemesis and melena witnessed between minimum 6 hours to maximum 5 days after admission. We documented it and detected previously described factors for UGI bleeding such as mechanical ventilation, coagulopathy, organ failure, feeding, and drug prophylaxis. Finally data were used in a multivariate analysis.

Results: Of 157 medical records, 148 patients were eligible. The incidence of UGI bleeding was 34.45%. The most common indication for PICU admission was respiratory system dysfunction (32.2%). Mechanical ventilation, thrombocytopenia and prolonged PT and PTT were the significant factors in our study using univariate analysis and mechanical ventilation was the only significant risk factor using multivariate analysis

Conclusion: The incidence of UGI bleeding in PICU admitted patients is significant and mechanical ventilation is the most important risk factor for GI bleeding.

Keywords: Incidence, Risk factor, Upper gastrointestinal bleeding

Introduction

Gastrointestinal bleeding due to stress ulceration is one of the important complications in critically ill patients admitted to the intensive care unit, leading to significant morbidity and in some cases mortality (1). As previous studies indicate, in pediatric patients, the incidence of upper gastrointestinal (UGI) bleeding ranges from 10% to more than

50% in the first days of intensive care unit (ICU) stay (1-4). It is suggested that mechanical ventilation (MV) is one of the most significant risk factors of UGI bleeding in the ICU in adults and children (1,2,5-7). It seems that Coagulopathies, organ failure, thrombocytopenia and high PRISM are other important risk factors (2,6,8). On the other hand, enteral feeding is suggested as an independ-

ent protective factor and use of pharmacologic prophylaxis reduces UGI bleeding rates in mechanical ventilated patients (8,9). Some drugs such as ranitidine, omeprazole, pantoprazole have been used and compared in these studies, although they may not be cost effective and increase the incidence of ventilator associated pneumonia (1, 10,11).

There have been only few studies on the incidence and risk factors of UGI bleeding in ICU admitted patients and most focused on adult and newborn patients. So, this study was designed to assess the incidence and risk factors associated with UGI bleeding in PICU admitted children and to identify the patients at risk who may be benefited from the prophylaxis against UGI bleeding.

Methods

Patients

All patients admitted to the PICU of Namazi Hospital from December 1, 2014 to May 30, 2015 for longer than 6 hours were included in the study. They were between 1 month and 18 years old in age. Our hospital is a 10-bed tertiary care university center that covers almost south of Iran. The patients were categorized as 8 categories of diseases: respiratory, neurologic, cardiovascular, post-operative care, hematology/oncology, hepatic, renal and miscellaneous. We assessed the patients prospectively. The patients with the history of recent GI surgery, brain death and active bleeding from nose or throat were excluded from the study. As we had no excessive sampling or intervention in our patients so we did not have ethical problem.

Demographic data including patient characteristics, admission diagnosis and underlying disease as well as basic laboratory investigations including hemoglobin level, platelet count, prothrombin time (PT), partial thromboplastin time (PTT), blood urea nitrogen (BUN), creatinine (Cr), and liver function tests were recorded within 24 hours of admission and we repeated platelet count, PT and PTT in time of UGI bleeding if it would happen in future days. Of patients who had evidence of hematemesis, coffee ground gastric content, melena, or upper fresh GI bleeding were diagnosed as UGI.

We defined organ failure as following: renal-serum Cr level >2 times upper limit of normal for age or two-fold increase in baseline Cr or requiring dialysis; neurologic_ Glasgow Coma Scale <11 or acute change in mental status with a decrease in GCS >3 points from abnormal baseline; hepatic-total bilirubin >4mg/dl or serum alanine transaminase levels at least two times upper limit of normal

for age.

Coagulopathy was defined as the PT level >15, the PTT >50 or a platelet count <100000/mm³.

Routinely we started feeding for the patients as soon as possible if they had no contraindication such as shock, requiring high dose inotrope drugs, 6 hours after intubation or any generalized seizure; and administered pharmacologic prophylaxis (ranitidine or pantoprazole) for the patients who were NPO; although was prophylaxis discontinued after feeding starting.

All the patients were prospectively followed to determine the incidence and risk factors of UGI bleeding.

Statistical Analysis

All data were assessed by SPSS program. The incidence was defined as the number of patients with UGI bleeding per total number of the patients who were admitted in PICU for more than 6 hours and were included in the study. The demographic variables were compared between the patients with and without UGI bleeding by using chi-square test, Fisher's exact test where appropriate. The relative risk and 95% confidence interval of the significant factors were calculated. Multivariate analysis of various variables that could have been associated with UGI bleeding (p<0.05 in univariate analysis) was performed using logistic regression modeling. It identified independent risk factors.

Results

Over the 6-month period, there were 157 patients admitted to PICU for more than 6 hours. 9 patients were excluded from the study. 6 had active bleeding from nose or throat and the other 3 patients were excluded because of brain death. Therefore 148 patients were included in the study. There were 80 males (54.1%) and 68 females (45.9%). Frequencies of underlying diseases in our patients were as following: The most common system dysfunction was the respiratory system in 47 cases (32.2%), followed by neurologic system in 30 cases (20.5%), the post-operative patients were 14 (9.6%), the cardiovascular system dysfunction in 13 persons (8.9%), hematology/oncology in 11 cases (7.5%), renal in 8 patients (5.5%), hepatic in 5 cases (3.4%) and miscellaneous in 18 cases (12.3%).

Upper GI bleeding occurred in 51 cases (34.45%) of our 148 eligible patients. Forty had coffee ground materials in nasogastric aspirates, 8 had upper GI fresh bleeding and 2 had melena as the first sign of GI bleeding. Among these 51 patients, 28 cases (55%) developed UGI bleeding in first 48 hours of admission to PICU, 11 cases

Table 1. Risk factors of UGI bleeding by univariate analysis

Factor	UGI bleeding (n=51)	No GI bleeding (n=97)	p
Platelets<100000/mm ³ , n (%)	19 (38)	17 (18)	0.008
Prolonged PT (PT>15), n (%)	27 (55.5)	33 (35.5)	0.019
Prolonged PTT (PTT>60), n (%)	12 (24.5)	11 (11.7)	0.043
Mechanical Ventilation, n (%)	42 (84)	49 (52)	0.000

Table 2. Risk factors of UGI bleeding in PICU

Risk factor	p	Multivariate analysis
		Relative risk (95% CI)
Prolonged PT	0.431	4.54 (0.305-1.660)
Prolonged PTT	0.678	2.56 (0.256-2.428)
Platelet <100000/mm ³	0.103	6.58 (0.175-1.172)
Mechanical ventilation	0.003	11.88 (1.58-9.765) ^a

^a Mechanical ventilation is the only significant risk factor confirmed by multivariate analysis.

(21.6%) had UGI bleeding before PICU admission and 10 cases (19.6%) after 5 days of admission to PICU. Only for 2 patients (3.9%) UGI bleeding occurred between 2 to 5 days of admission. On the other hand, 33 patients (64.7%) developed UGI bleeding when they were under mechanical ventilation and 17 cases (33.3%) had this bleeding when they were not under mechanical ventilation. Only 1 patient had UGI bleeding after he had been weaned off from ventilator.

Among the different variables, significant factors associated with UGI bleeding using the univariate analysis were as following: platelet count<100000, prolonged PT and PTT, mechanical ventilation (Table 1). Mechanical ventilation was the only significant risk factor in our study, using multivariate analysis (Table 2). In this study feeding was not found to be as a protective factor which might result from the reason that we routinely administered prophylaxis in NPO patients and it was stopped when feeding started for the child.

Discussion

As reported in other studies, the prevalence of UGI bleeding in PICU admitted children is significant. It varied between 6.4% and more than 50% (1-4). We found that the prevalence of UGI bleeding in PICU admitted patients was 34.45% that is similar to the report of Nithiwathanapong et al (38.2%) and is lower than other studies like Cool et al (54.96%), Kuusela et al (53%) and Deerojanawong et al (51.8%) (1,2,7). This might result from that our study like the Nithiwathanapong's study was performed in the PICU admitted patients but the other above studies were in the mechanically ventilated patients in The ICU; although the Cook's study was in adults and Kuusela's was in neonates (2,6,7). In this study the mortality of the patients who had UGI bleeding was significantly

higher than that of those without UGI bleeding ($p<0.05$) that was in accordance with the previous reports (12, 13).

As the other similar studies in adult and children, we found that the mechanical ventilation is the most significant risk factor for UGI bleeding in PICU admitted patients (1,4,6). It was identified in multivariate analysis. Mechanical ventilation causes decreased cardiac output and splanchnic hypoperfusion. This can result in gastric mucosal injury too(1,5). On the other hand increased production of pro-inflammatory mediators due to ventilator effect can cause mucosal injury of GI tract (1,5). In some studies coagulopathy is suggested as a significant risk factor (2-4, 6) but in this study it was observed only in univariate analysis and not in multivariate analysis that is similar to Nithiwathanapong's study (2). Organ failure and high PRISM, are the other suggested risk factors for UGI bleeding in a few studies (1); but we found no significant correlation between organ failure and UGI bleeding furthermore we did not check PRISM for the patients so that factor didn't analyzed in our study. Other factors such as feeding and drug prophylaxis are prescribed as protective factors in some studies (8,10,11,14-16) but in this study we did not find that; which might result from this reason that we routinely administered prophylaxis in NPO patients and it was stopped when feeding started for the child.

Conclusion

The incidence of UGI bleeding in PICU admitted patients is significant and mechanical ventilation is the most important risk factor for GI bleeding.

References

1. Deerojanawong J, Peongsujarit D, Vivatvakin B, Prapphal N. Incidence and risk factors of upper

- gastrointestinal bleeding in mechanically ventilated children. *Pediatric Critical Care Medicine*. 2009; 10(1):91-5.
2. Nithiwathanapong C, Reungrongrat S, Ukarapol N. Prevalence and risk factors of stress-induced gastrointestinal bleeding in critically ill children. *World Journal of Gastroenterology*. 2005; 11(43):6839.
 3. Lacroix J, Nadeau D, Laberge S, Gauthier M, Lapierre G, Farrell CA. Frequency of upper gastrointestinal bleeding in a pediatric intensive care unit. *Critical care medicine*. 1992;20(1):35-42.
 4. 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(4):933-8.
 5. Mutlu GM, Mutlu EA, Factor P. GI complications in patients receiving mechanical ventilation. *CHEST Journal*. 2001;119(4):1222-41.
 6. Cook DJ, Fuller HD, Guyatt GH, Marshall JC, Leasa D, Hall R, et al. Risk factors for gastrointestinal bleeding in critically ill patients. *New England journal of medicine*. 1994;330(6):377-81.
 7. Kuusela AL, Mäki M, Ruuska T, Laippala P. Stress-induced gastric findings in critically ill newborn infants: frequency and risk factors. *Intensive care medicine*. 2000;26(10):1501-6.
 8. Kuusela AL, Ruuska T, Karikoski R, Laippala P, Ikonen RS, Janas M, et al. A randomized, controlled study of prophylactic ranitidine in preventing stress-induced gastric mucosal lesions in neonatal intensive care unit patients. *Critical care medicine*. 1997;25(2):346-51.
 9. Darlong V, Jayalakhsmi T, Kaul H, Tandon R. Stress ulcer prophylaxis in patients on ventilator. *Tropical gastroenterology: official journal of the Digestive Diseases Foundation*. 2002;24(3):124-8.
 10. Kantorova I, Svoboda P, Scheer P, Doubek J, Rehorkova D, Bosakova H, et al. Stress ulcer prophylaxis in critically ill patients: a randomized controlled trial. *Hepato-gastroenterology*. 2003; 51(57):757-61.
 11. Lopriore E, Markhorst DG, Gemke RJ. Ventilator-associated pneumonia and upper airway colonisation with Gram negative bacilli: the role of stress ulcer prophylaxis in children. *Intensive care medicine*. 2002;28(6):763-7.
 12. Cook DJ, Griffith LE, Walter SD, Guyatt GH, Meade MO, Heyland DK, et al. The attributable mortality and length of intensive care unit stay of clinically important gastrointestinal bleeding in critically ill patients. *Critical care*. 2001;5(6):368.
 13. Osman D, Djibré M, Da Silva D, Goulenok C. Management by the intensivist of gastrointestinal bleeding in adults and children. *Ann Intensive Care*. 2012;2(1):46.
 14. Lasky MR, Metzler MH, Phillips JO. A prospective study of omeprazole suspension to prevent clinically significant gastrointestinal bleeding from stress ulcers in mechanically ventilated trauma patients. *Journal of Trauma and Acute Care Surgery*. 1998; 44(3):527-33.
 15. 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. *Critical care medicine*. 2002;30(6):S362-S4.
 16. Prakash S, Rai A, Gogia AR, Prakash S. Nosocomial pneumonia in mechanically ventilated patients receiving ranitidine or sucralfate as stress ulcer prophylaxis. *Indian Journal of Anaesthesia*. 2008;52(2):179.