ORIGINAL ARTICLE

Risk Factors of Upper Gastrointestinal Tract Bleeding Caused by Stress Ulcer

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ABSTRACT During the period of December 1st 1997 until April 30th 1998, an observational study with cross sectional design was conducted at the Pediatric Intensive Care Unit (PICU). Risk factors of the occurrence of upper gastrointestinal tract bleeding (UGTB) on patients admitted to the PICU Medical School University of Indonesia / Ciptomangunkusumo Hospital were described analysed. Upper gastrointestinal tract bleeding was confirmed if there was evidence of brown or coffee ground material of the gastric fluid in the nasogastric or gastrotomy tube, hematemesis or melena, which was subsequently proved by benzidin test. The risk factors in this study was defined based on the risk factors found from prevous studies i.e. shock, sepsis, severe head injury, multiple complication, liver insufficiency, pneumonia, respiratory failure, intervention during treatment (operation >3 hours, ventilator, corticosteroid >3 days). From 26 patients with UGTB risk factors in this study, 19 persons (73%) developed UGTB. The proportion of UGTB was not different on the patient's characteristic (age, sex, nutritional status). UGTB found were bleeding through nasogastric tube (58%) and occult bleeding 37%, hematemesis only one person (1 1%).The majority of UGTB occurred on the 3rd day of hospitalization (84%) and after ventilator usage of >48 hours (58%). Patient who underwent >3 hours operations were craniotomies. All the patients who received >3 days of corticosteroid (4 persons) developed UGTB. **[Pediatr Indones 1999; 39:20-28]**

Introduction

Upper gastrointestinal tract (UGT) mucosa impairment developed in patients admitted to the pediatric intensive care unit (PICU) is categorized as an acute mucosal lesion which is usually called stress ulcer.[1-3] Upper gastrointestinal tract bleeding (UGTB) is

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one of the clinical manifestations seen in stress ulcer.[1] The clinical features of stress ulcer in UGT vary from gastritis to ulcer formation, with or without bleeding, and even to gastric perforation.[1,4] Since the majority of patients with stress ulcer are asymptomatic, it is often missed or not promptly diagnosed.[5] Stress ulcer is clinically diagnosed based on the occurrence of UGTB, because only 20% patients develop apparent or occult UGTB and 2-5% develop clinically significant UGTB.[6] Endoscopy is the most preferred examination in diagnosing stress ulcer which could discover almost all (75-90%) of the abnormality.[1,6,7]

Severe illness in children brings potential risk factors for the development of stress ulcer which manifests as UGTB, which may develop severe clinical manifestations, i.e. massive bleeding and perforation.[8,9] Improvement of the technology of treatment in PICU leads to more and more critically ill patients can be kept alive, so that stress ulcer becomes one of the problems in nursing.[10] Nababan et al in 1994[11] conducted a study in adults and found stress ulcer in 83.3% of severe cases which had *Acute Physiology and Chronic Evaluation III* (APACHE III) score of more than 50. There has not been any study regarding UGTB in children treated at PICU in Indonesia. Information on patient's characteristics and risk factors of UGTB are needed in order to have a better management and to give a more selective prophylaxis therapy, as well as a basis for more specific studies. The purpose of this study was to determine the incidence of UGTB, the characteristics of the patients, and the interventions that cause and the clinical manifestations of UGTB in patient at PICU.

Methods

This was a cross sectional study conducted at PICU of the Department of Child Health, Medical School, University of Indonesia / Cipto Mangunkusumo Hospital, Jakarta, during the period of December 1st 1997 - April 30th 1998. Study subjects were recruited based on history, clinical findings and laboratory examination. The criteria for inclusion were; (1) all patients aged 1 month to 18 years with the diagnosis of shock, sepsis/bacteremia, severe head injury, patients with multiple complications, liver insufficiency, and respiratory failure; (2) all patients who underwent operation lasting more than 3 hours or who used ventilator for more than 24 hours; (3) all patients who received corticosteroid for more than 3 days.

Patients with conditions that decreased the risk of UGTB (those who received continuous enteral feeding and antacid, receptor H2 antagonists, sucralfate therapy), or conditions that increased the risk of UGTB (those who received a non-steroid anti inflammation drugs such as aspirin, ibuprofen, indomethacin) were excluded from the study. The diagnosis of UGTB was clinically confirmed if there was evidence of brown or coffee ground material of the gastric fluid in the nasogastric or gastrostomy tube, hematemesis or melena.[4,12] In doubtful cases, a laboratory test using benzidin tablet

was done; a patient was diagnosed as UGTB if a blue color appeared on the filter paper on the benzidin test.[7,10] Data were presented descriptively; no attempt was made to analyze the data.

Results

Thirty patients with UGTB were recorded at the PICU during the period of December 1, 1997- April 30, 1998. Four of them were excluded from the study because they were already out of the PICU by the second day of treatment. From the 26 subjects who fulfilled the study criteria, 19 patients (73%) developed UGTB either macroscopically or microscopically and 7 (27%) did not develop UGTB.

1. Subject characteristics

The age of the subjects of this study ranged from 2 months to 12 year. The proportion who developed UGTB was almost the same at each age group. The number of boys was the same as girls and the proportion who developed UGTB was also almost similar between boys (77%) and girls (69%). The majority of patients (58%) belonged to the undernourished group and the proportion who developed UGTB was also similar between the undernourished and the well-nourished group. All of the 3 patients with severe malnutrition developed UGTB

2. Risk factors

Table 1 depicts the occurrence of UGTB as related to the underlying disease and intervention. Of the 14 patients with severe-illness, 3 (21%) did not develop UGTB and 9 patients (79%) develop UGTB. Table 1 shows that the total number of the subjects was 33 because 7 of subjects were counted twice based risk factors and intervention.

The association between intervention and the occurrence of UGTB can be seen in Table 2. There were 19 patients who received intervention, all of those received corticosteroid developed UGTB, 7 patients of those who used ventilator developed UGTB and 4 patients of who under operation >3 hours developed UGTB.

The clinical manifestations of patients with UGTB were depicted in Table 3. It shows that most of UGTB presented with bleeding via naso-gastric tube. Only one patient developed UGTB that was clinically significant and required blood transfusion. The time in which UGTB occurred is depicted in Table 4. The majority (84%) of patients who developed UGTB had the bleeding on day 3 of hospitalization.Most of patients who used ventilator (58%) developed UGTB after 48 hours of intervention and only 1 person developed UGTB on the 24th hour of intervention (Table 5). There were 6 patients who had undergone surgery, i.e., 5 had craniotomy, and 1 had laparotomy. Four of the 5

patients who had undergone craniotomy developed UGTB and the only one patients who had undergone laparotomy did not develop UGTB. See Table 6.

Table 1. Distribution of UGTB based on risk factors

Risk factors	UGTB (+)	UGTB (-)	Total
	n	n	n
Shock	3	_	3
Sepsis	1	_	1
Head injury	1	_	1
Liver insuffisiency	1	_	1
Pneumonia	1	1	2
Respiratory stress	3	1	4
Multiple complication	1	1	2
With intervention	15	4	19
Total	26	7	33

Table 2. Distribution of UGTB based on intervention

Intervention	UGTB (+)	UGTB (-)	Total
	n	n	
Operation >3 hours	4	2	6
Ventilator >24 hours	7	2	9
Corticosteroid>3 days	4	-	4
Without intervention	11	3	14
Total	26	7	33

Table 3. Distribution of UGTB clinical manifestations

UGTB	n
Melena/hematemesis	1
Bleeding through nasogastric tube	11
Occult bleeding	7
Total	19

Table 4. Distribution of UGTB occurrence based on day hospitalization at the PICU

UGTB	Total
	n
1st day hospitalization	3
3rd day hospitalization	16
Total	19

Table 5. Distribution of the occurrence of UGTB based on the use ventilator

Duration of ventilator usage	UGTB
	n
24 hours	1
>24 hours-48 hours	2
>48 hours	4
Total	7

Table 6. Distribution of UGTB occurrence based on type of operation

Type of operation	UGTB (+)	UGTB (-)	Total
	n	n	n
Craniotomy	4	1	5
Laparotomy	-	1	1
Total	4	2	6

Discussion

This study has some limitations, which is centered on the number of the subjects which was too small, so that no statistical analysis could be performed and no firm conclusion could be drawn. However, with the limited information we still be able to have some idea on the phenomena which have not been investigated in Indonesia concerning UGTB in infants and children admitted to pediatric intensive care unit. Furthermore the results found in our series could not be readily compared to other results published in the literature, since some of the criteria and definitions were not similar.

In this study, 73% of the 26 subjects developed UGTB either macroscopically or microscopically. This high proportion of UGTB incidence in this study was due to the fact that all of the patients involved in this study already had risk factors. The highest incidence of UGTB in children was 25%. Other authors, with certain differences in definitions, reported the incidence of 6.4%.[4,13]

Based on characteristics of our patients, the occurrence of UGTB was almost the same at every group and this result was nearly the same as that obtained by Cochran et al[4] where there was no significant difference between certain age group. Lacroix et al[13] reported that the probability of UGTB occurrence increased with the decreasing age. Other study based on the patients treated at the PICU due to respiratory problem reported that there was no difference in age between those who developed UGTB and those who did not.[14] In this study, the sex ratio was 1 : 1 (13 females and 13 males). The sexual proportion of those who developed UGTB was almost similar, as has been reported before.[4,14,15]

The nutritional status in the majority of the study subject was undernourished. It could be caused by disease severity of the disease or insufficient intake. In patients with severe malnutrition, the epithelial cells of the gastrointestinal mucosa become thinner and the control mechanism of gastric acid excretion decreases so that gastric hyperacidity as well as impairment of digestive enzymes occur.[16] All of our study subjects developed UGTB. It has not known whether nutritional status could affect UGTB because no studies have been perform before.

The patients involved in this study were patients who had risk factors for UGTB which were determined based on the studies previously.[4,13] It occurred that all patients who had risk factors developed UGTB, except pneumonia, respiratory failure, and multiple complication. On the other hand, all of the 3 cases with (hypovolemic) shock developed UGTB. These results were different from that obtained by Fusamoto et al[17] who reported that the incidence of UGTB in patients with shock was 8.9% with a mortality rate of 33.3%. It was also reported that septic shock caused UGTB more frequently compared to hemorrhagic shock.

Patients who received intervention during hospitalization were mostly patients who clinically have had risk factors for UGTB, i.e. patients with respiratory failure would also be using a ventilator so that the number of subjects became 19 and those who developed UGTB were 79%. Only one of the patients who used ventilator did not develop UGTB; this was probably because the patients already had risk factors such as gastric hyperacidity, which was in accordance with the known pathogenesis. This condition would be worsened by the use of a ventilator. The use of a ventilator may indirectly increases the incidence of UGTB, one of which is through ischemia of the gastric mucosa.[18] Upper gastrointestinal tract bleeding was found in only 20% of the patients on ventilator, this may be due to the fact that the patients involved in the study had already received antacid.[14]

All patients who received corticosteroid developed UGTB, this was different from statement made by Euler[3] who said that UGTB complications caused by corticosteroid, in contrast to in adults, rarely happened in children, and that the incidence of UGTB caused by corticosteroid was only 12%.[16] Harris et al[14] reported that corticosteroid was found to be effective in decreasing the incidence of UGTB. The high incidence of UGTB in this study was probably due to the severity of the illness in most patients studied, and because all patients suffered from encephalitis which involved more than one pathogenesis.

Four of 6 patients who had undergone an operation more than 3 hours developed UGTB; this was in accordance with Cochran et al[4] where an operation of more than 3 hours was a risk factor of UGTB.

Only one patient had UGTB that was clinically significant with a decrease in hemoglobin of more than 2 g/dl during hospitalization, requiring blood transfusion administration.[15] According to previous studies, the incidence of massive UGTB was low, i.e. less then 10% and only 2% in other studies.[4,18] The majority of UGTB that occurred was not clinically significant , i.e. bleeding through nasogastric tube in 11 patients and occult bleeding in 7 patients. Previous studies reported that more than 50% of the patients experienced occult bleeding and clinically apparent bleeding (UGTB through nasogastric tube).

Eighty four percent of UGTB in our series occurred on the 3rd day of intervention during hospitalization. This was agreed with the result of endoscopic examination which showed that erosion of the gastric mucosa usually occurred on the 72nd hour of hospitalization.[19] This was supported by a study done by Lacroix [13] which stated that most of UGTB occurred on the 72nd hour of hospitalization. Four of 7 patients developed UGTB after 48 hours usage of a ventilator, this was the same as that reported by Cook et al[15] which state that UGTB occurred more often after a ventilator usage of more then 48 hours.

Four of the patients who underwent craniotomy with the duration of operation of more then 3 hours developed UGTB. This was the same as the report of Cochran et al[4] where patients who underwent craniotomy of more than 3 hours developed UGTB more frequently compared with those who underwent other operations with the same duration.

To sum up, our study showed that 73% of the patients who had been determined to have risk factors developed UGTB. It seemed that the characteristics of patients who developed UGTB were not different from those who did not developed UGTB. Most of UGTB were bleeding that can be seen clinically and occult bleeding. UGTB generally occurred on the third day of hospitalization, and it seems that the bleeding was related to ventilator use of more than 48 hours, duration of surgery of more than 3 hours, and corticosteroid use of more than 3 days. We suggest to conduct a case control study with sufficient sample size so that more precise prevalence and the role of risk

factors could be determined. While awaiting for the results of such study, it is rational to recommend to administer prophylaxis for UGTB to high risk patients.

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