Gastrointestinal Hemorrhage in Patients in a Respiratory Intensive Care Unit

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Significant gastrointestinal hemorrhage occurred in 20 percent (20) of the patients in a respiratory intensive care unit. Risk factors significantly associated with the development of gastrointestinal hemorrhage included (1) the principal respiratory diagnosis of adult respiratory distress syndrome; (2) increasing numbers of days on a ventilator, days in the respiratory intensive care unit, and total days of hospitalization; and (3) the development of thrombocytopenia. Factors not associated with an increased risk of gastrointestinal hemorrhage were the age and sex of the patient, the respiratory diagnosis of chronic obstructive pulmonary disease, and the use of therapy with either heparin or corticosteroids. Routine prophylactic administration of antacids was associated with a decreased incidence of hemorrhage. The mortality of bleeders was significantly greater than that of nonbleeders.

The association of gastrointestinal disease and, particularly, gastrointestinal hemorrhage with both acute and chronic pulmonary disease has long been recognized. The awareness of an association has increased in the last few years as patients with severe pulmonary disease are segregated into respiratory intensive care units. While reports of gastrointestinal hemorrhage in critically ill general medical, postsurgical, and burn patients are available, there are no published surveys of the incidence and course of gastrointestinal hemorrhage occurring in patients in a respiratory intensive care unit. Data concerning the risk factors associated with the development of gastrointestinal hemorrhage and the relationship of hemorrhage to commonly administered therapeutic agents (such as anticoagulant drugs, corticosteroids, and antacids) are lacking for the patient in the respiratory intensive care unit.

This study was undertaken to identify risk factors which contributed to gastrointestinal hemorrhage in patients, in the respiratory intensive care unit, in order to determine whether the underlying respiratory diagnosis or therapeutic agents used in the management of such patients may be contributing factors, and to evaluate the effect of prophylactic therapy with antacids on the incidence of gastrointestinal hemorrhage in these patients.

MATERIALS AND METHODS

A review of all patients who were admitted to the respiratory intensive care unit with a primary respiratory diagnosis during a one-year period from December 1974 to November 1975 was undertaken. Although there were 110 admissions to the unit, 12 patients were excluded because of a nonrespiratory diagnosis. The charts of the remaining 98 patients were extensively reviewed.

Statistical significance between two proportions was calculated by the z-test. The Student's t-test was used to determine statistical significance of two variables. A significant value for probability was P < 0.05.

Criteria for the diagnosis of gastrointestinal hemorrhage were (1) strongly hematemesis-positive or visually positive nasogastric aspirate, hematemesis, or melena; (2) a drop in the hemoglobin level greater than 1 gm/100 ml per 24 hours; and (3) confirmation of bleeding or the site of bleeding (or both) by endoscopic examination or autopsy when available. All patients fulfilled the first two criteria. Findings from autopsy or endoscopic results (or both) were available in 70 percent of the bleeding patients.

RESULTS

Twenty (20 percent) out of the 98 patients admitted to the respiratory intensive care unit fulfilled the criteria for gastrointestinal hemorrhage. The patients who bled had a mean drop in the hemoglobin level of 2.0 ± 0.3 gm/100 ml (± SE). They required 1.5 ± 0.5 units of blood in transfusion per episode of bleeding. Patients who bled had a mean age of 48...
years, and nonbleeders had a mean age of 51 years, a nonsignificant difference.

Although patients in the intensive care unit received multiple medications, three specific medications (corticosteroids, heparin, and antacids) were selected for particular scrutiny. A discussion of antacids will be considered later. Out of the 20 bleeders, 14 were receiving steroids, while 49 of the 78 nonbleeders were receiving steroids (difference not significant). Three of the 20 bleeders were receiving heparin, while 15 of the 78 nonbleeders were receiving this drug (difference not significant). There was no significant difference between the range of dosage or the frequency of use for corticosteroids and heparin in bleeding and nonbleeding patients.

Patients were categorized on the basis of their principal respiratory diagnosis (Fig 1). The diagnoses tabulated were chronic obstructive pulmonary disease, adult respiratory distress syndrome, asthma, primary restrictive disease, neurologic disease, pneumonia, pulmonary embolism, aspiration of gastric acid, bronchiectasis, drug overdose, and pulmonary edema. It can be seen that the largest number of patients in the unit carried the diagnosis of chronic obstructive pulmonary disease or the adult respiratory distress syndrome (Fig 1). Each group was then divided into bleeders or nonbleeders. Only four (9 percent) of the 44 patients with chronic obstructive pulmonary disease bled, while 11 (85 percent) of 13 patients with the adult respiratory distress syndrome bled. This was a highly significant difference (P < 0.01). There were no significant differences among the other diagnoses.

There were three significant differences in the time intervals (Fig 2) between bleeders and nonbleeders, i.e., the total number of days on a ventilator, the total number of days in the respiratory intensive care unit, and the total number of days of hospitalization. Bleeding patients required significantly longer support with the ventilator during their illness; they were in the intensive care unit more days, and their total stay in the hospital was longer.

In the group of 20 patients who bled (Fig 3), ten (50 percent) had more than one episode of bleeding during the same admission. Ten patients bled twice, and of these, three patients bled three times. The mean day in the unit on which the first episode of bleeding occurred was the third day, the mean

![Figure 1. Diagnosis of patients admitted to respiratory intensive care unit. COPD, Chronic obstructive pulmonary disease; ARDS, adult respiratory distress syndrome; RESTR DIS, restrictive disease; NEUR DIS, neurologic disease; PNEUM, pneumonia; and PE, pulmonary embolism.](image1)

![Figure 2. Differences in time intervals between bleeding and nonbleeding patients.](image2)

![Figure 3. Day of bleeding in respiratory intensive care unit.](image3)
day of the second bleed was the tenth day, and the mean day of the third bleed was the 24th day.

The relationship of thrombocytopenia to gastrointestinal bleeding was evaluated for the bleeding and nonbleeding patients. Thrombocytopenia was defined as a platelet count of less than 100,000/cu mm. In the group of 20 patients who bled, 12 (60 percent) were thrombocytopenic at the time of bleeding, while only two (3 percent) out of the 78 nonbleeders were thrombocytopenic at any point in their stay in the intensive care unit. This was a highly significant relationship (P < 0.001). The relationships of other measurements of clotting, such as the prothrombin time, partial thromboplastin time, and fibrinogen level, were not studied.

In the group of bleeding patients who were thrombocytopenic (Fig 4), the mean platelet count at the time of bleeding was 62,000/cu mm, with the range being 24,000/cu mm to 90,000/cu mm. Three of the four patients with chronic obstructive pulmonary disease and with gastrointestinal bleeding were thrombocytopenic at the time of the bleeding, while six out of 11 patients with the adult respiratory distress syndrome who bled were thrombocytopenic.

The results from administration of antacids are shown in Figure 5. In the group of 20 bleeding patients, four patients received no antacids, either prophylactically or therapeutically. Two of the patients who received no antacids had multiple episodes of bleeding. Fourteen patients received therapeutic administration of antacids after the onset of bleeding. Eight of these had no further episodes of bleeding. Only two patients who bled had received prophylactic therapy with antacids, while 41 out of 78 patients who did not bleed had received prophylactic therapy with antacids. This was a highly significant difference (P < 0.01).

Seventeen (22 percent) of the 78 nonbleeders died, while 13 (65 percent) of the 20 bleeders died. Reports from autopsies in 11 patients demonstrated diffuse multiple areas of ulceration in the upper gastrointestinal tract in all cases.

**DISCUSSION**

Gastrointestinal hemorrhage is recognized as a significant and frequent complication in critically ill patients. No previous data have dealt with risk factors for the development of gastrointestinal hemorrhage in patients in a respiratory intensive care unit or with the influence of therapeutic agents on the course of the bleeding.

Our results indicate that the diagnosis of the adult respiratory distress syndrome is a significant risk factor for the development of gastrointestinal hemorrhage. Past reports primarily have associated the diagnosis of chronic obstructive pulmonary disease with gastrointestinal hemorrhage. While our data confirm that patients with chronic obstructive pulmonary disease did have gastrointestinal hemorrhage, it was not as significant a risk factor for the development of hemorrhage as was the diagnosis of the adult respiratory distress syndrome.

Thrombocytopenia was seen in the majority of bleeding patients. While Atik and Matini have...
described qualitative defects in the platelets of patients with gastrointestinal hemorrhage, previous identification of thrombocytopenia as a risk factor for gastrointestinal hemorrhage in the setting of an intensive care unit has not been made.

It is known that patients with the adult respiratory distress syndrome frequently develop thrombocytopenia during the course of their illness; the etiology of the thrombocytopenia remains unclear.12,13 Six (55 percent) of the 11 patients with the adult respiratory distress syndrome who bled were thrombocytopenic at the time of bleeding, but three (75 percent) of the four patients with chronic obstructive pulmonary disease were also thrombocytopenic at the time of bleeding. It would appear that thrombocytopenia is a risk factor for the development of gastrointestinal hemorrhage, regardless of the respiratory diagnosis.

Numerous studies, both in the clinical setting of the critically ill patient and in the experimental animal model,14,15 have implicated the usage of corticosteroids as a contributing factor in the cause of gastrointestinal hemorrhage. This supposition remains to be documented. Our results indicate that therapy with corticosteroids was not significantly associated with the development of gastrointestinal hemorrhage. This finding corresponds to more recent experimental and clinical reports which would indicate that therapy with steroids actually may be beneficial in reducing the incidence of gastrointestinal hemorrhage in critically ill patients.16

The efficacy of prophylactic therapy with antacids remains unproven, but experimental evidence would appear to confirm a protective role for these agents.4 Our data indicate a decreased incidence of hemorrhage in patients who receive prophylactic therapy with antacids. The need for a randomized well-controlled study of the influence of prophylactic administration of antacids is apparent.

Patients who developed gastrointestinal hemorrhage in our intensive care unit were more seriously ill than the nonbleeding patients, as delineated by more days on a ventilator, more days in the intensive care unit, and more days in the hospital than for nonbleeders. The mortality of patients who had gastrointestinal hemorrhage was also significantly greater; 65 percent (13) of the bleeders died, while only 22 percent (17) of the nonbleeders died. It would appear that (1) the identification of patients with a high probability of developing gastrointestinal hemorrhage and (2) subsequent prophylactic administration of antacids might reduce the morbidity and mortality in this subset of patients. The final answer rests in a prospective study.

In conclusion, significant gastrointestinal hemorrhage occurred in 20 percent (20) of the patients hospitalized in our respiratory intensive care unit in a one-year period. The diagnosis of the adult respiratory distress syndrome, a prolonged hospitalization, and thrombocytopenia were contributing factors in the development of gastrointestinal hemorrhage. From this study, it appears that the prophylactic administration of antacids decreased the incidence of gastrointestinal hemorrhage.

REFERENCES