Gastrointestinal Bleeding in Stroke

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**Background and Purpose**
Patients with ischemic or hemorrhagic stroke are at risk for systemic complications. The reasons why gastrointestinal bleeding occurs after stroke are unknown and have intuitively been attributed to stress ulcers. No study to date has addressed causes of gastrointestinal hemorrhage in stroke.

**Methods**
Between 1976 and 1994, 17 patients identified from the Mayo Clinic medical record system as having gastrointestinal hemorrhage and ischemic stroke (n=14) or intracerebral hemorrhage (n=3) were reviewed for presentation, associated causes, and outcome. Results of the endoscopic procedures were compiled, and available gastric biopsies were reviewed.

**Results**
In 17 patients with gastrointestinal bleeding after stroke, sudden hematemesis, a decrease in hemoglobin level, or orthostatic hypotension was found as a presenting feature. One patient presented with massive hematemesis, exsanguination, and cardiac arrest. Endoscopic findings were available in 14 patients and included gastroesophageal erosions, hemorrhagic gastritis, and gastric ulcer. In one patient, an adenocarcinoma of the gastric cardia was found. Putative pathogenetic agents were found in 16 of 17 patients and included a long history of nonsteroidal anti-inflammatory drugs (n=6), acetylsalicylic acid (n=3), grossly prolonged anticoagulation (n=4), *Helicobacter pylori* (n=2), and corticosteroids (n=1).

**Conclusions**
Gastrointestinal bleeding after stroke is rarely severe and may not contribute significantly to mortality. Medication-induced gastrointestinal hemorrhage may be underappreciated in this setting. (Stroke. 1994;25:2146-2148.)

**Key Words**
• gastrointestinal hemorrhage • stress, psychological • stroke

**Systemic complications endanger patients with stroke; the most critical are aspiration pneumonia and sepsis.** After acute brain injury, stress ulcers may develop from vagal hyperactivity resulting in increased gastric acid secretion or from mucosal ischemia. Gastrointestinal bleeding may occur and may potentially be devastating in patients with stroke treated with anticoagulants.

The clinical relevance of gastrointestinal bleeding in major strokes is uncertain. When stress ulcers bleed, they may contribute to mortality rates in patients with large strokes, but whether prophylactic therapy with its enormous costs reduces time in the intensive-care unit, transfusion rates, or surgery is not known.

Scant data are available regarding gastrointestinal hemorrhage in head injury and subarachnoid hemorrhage. No study to date has addressed causes of gastrointestinal hemorrhage in stroke.

We report a review of gastrointestinal hemorrhage in 17 patients with stroke. We undertook this survey to determine the potential causes and to identify management strategies for prophylaxis.

**Subjects and Methods**
We reviewed the medical records of all patients with ischemic or hemorrhagic stroke who had a gastrointestinal hemorrhage as a complication during hospital stay in both Mayo Clinic-affiliated hospitals (Saint Marys Hospital and Methodist Hospital) from 1976 to 1994. We excluded patients with aneurysmal subarachnoid hemorrhage, patients with chronic alcohol abuse and liver cirrhosis, and patients with acute coagulopathies. A clinically significant gastrointestinal hemorrhage was diagnosed on the basis of hematemesis, a nasogastric return containing gross blood or coffee ground–like material, or melena. Results of the endoscopic procedures were compiled, and available gastric biopsies (K.P.B.) were reviewed in detail. Potential risk factors for a peptic ulcer or gastritis were recorded.

**Results**
We found 17 patients with a documented gastrointestinal hemorrhage. The mean age was 78 years (range, 63 to 96 years). In the study period, 16 612 patients with ischemic or hemorrhagic strokes were admitted to the hospital or developed in-hospital stroke; therefore, our study patients represent 0.1% of the total population. Of the 17 patients with gastrointestinal hemorrhage, 14 patients had a CT scan–documented ischemic stroke (lacuna [1 patient]; middle cerebral artery upper or lower division [7]; middle cerebral artery stem [3]; posterior cerebral artery territory [1]; and basilar artery territory [2]). An intracerebral hemorrhage was seen in 3 patients (putamen [1] and subdural localization [2]). The Glasgow coma sum scores on admission were 14 in 10 patients, 13 in 2 patients, and <8 in 5 patients.

Gastrointestinal hemorrhages presented in all patients within 2 weeks after admission. Among these 17 patients, 7 patients presented with hematemesis, 7 patients with melena, and 3 patients with a sudden decrease in hemoglobin level of >4 g/dL. Orthostatic hypotension (defined as a decrease of >20 mm Hg in the systolic blood pressure when measured sitting up) was noted in 2 patients. In 1 patient, massive hematemesis was followed by overt shock and cardiac arrest. In
none of the other patients was gastrointestinal bleeding life threatening at any point during the clinical course.

The endoscopic findings that were available in 14 patients are summarized in the Figure. Hemorrhagic gastritis, erosive gastritis, or gastric ulcers were found in 8 patients. In 1 patient, an adenocarcinoma of the gastric cardia was found. In another patient, a hiatal hernia was associated with mechanical erosion of fundic mucosa at the diaphragmatic esophageal hiatus, a lesion sometimes referred to as a "Cameron lesion." No endoscopic abnormalities were found in 4 patients. Endoscopy had not been performed in 3 patients with only minor hematemesis or hemorrhagic nasogastric return.

Upper gastrointestinal biopsy specimens had been taken in only 3 patients. Two of these showed Helicobacter pylori-associated gastritis; histological evidence of ulceration was present in one of these. The third case revealed near-normal mucosa with focal erosion that was felt to represent mechanical trauma to the gastric fundus at the diaphragmatic esophageal hiatus in a patient with hiatal herniation.

Thus, review of history and histology revealed possible risk factors for upper gastrointestinal hemorrhage in all except 1 patient: long-term use of nonsteroidal anti-inflammatory drugs (NSAID) (dose, ≥75 mg/d) (6 of 17), grossly prolonged anticoagulation (4 of 17), aspirin (dose, 325 to 975 mg/d) (3 of 17), corticosteroids (1 of 17), and biopsy-proven H. pylori (2 of 17).

None of the patients required mechanical ventilation. No patients were treated with prophylactic antacids or histamine H2-receptor antagonists. After gastrointestinal bleeding, 7 patients required a blood transfusion, all patients were treated with cimetidine, and repeat hemorrhage did not occur. Emergency surgery was not needed.

**Discussion**

The pathogenesis of upper gastrointestinal bleeding after stroke is unclear; intuitively it has been connected with "stress.” Erosive or hemorrhagic gastritis was a frequent endoscopic finding in our patients with gastrointestinal bleeding after stroke. However, the cause of these changes may not be simply "stress,” since alternative explanations for the hemorrhage were present in nearly all cases. Our findings suggest a strong association with previous long-term NSAID and aspirin use; however, without a control group a causal relation is not established. The significance of H. pylori in 2 of 3 patients is not clear, since H. pylori would be expected to be relatively common in the elderly population.

One rationale for analyzing gastrointestinal hemorrhage after stroke is to determine whether high-risk patients can be identified and whether potentially costly prophylactic treatment is indicated. Previous studies conducted in neurosurgical populations or critically ill patients found that no specific risk factor could be identified, although there was an increased incidence in patients on mechanical ventilators and, not unexpectedly, in patients with a coexisting coagulopathy. Our patient population, therefore, may not represent the full spectrum of gastrointestinal bleeding with stroke because the majority of patients were not mechanically ventilated.

Stress-related gastric lesions generally occur in multiple sites. They may be confined to the mucosa (erosions) or extend into submucosa or beyond (ulcers). The pathophysiology of stress-related damage is not well understood. Experimental models have shown that stress activates the hypothalamus, resulting in cholinergic stimulation to the stomach. Substances such as acetylcholine, histamine, and endogenous throtropin-releasing hormone may also increase the vulnerability of the mucosa. In addition, it has been stated that stress-related lesions in the gastric mucosa cannot be distinguished from medication-induced lesions. Since at least one mechanism by which NSAIDs cause gastric erosion/ulceration is by inhibition of prostaglandins, a similar mechanism in stress is possible.

We documented a potential trigger other than stress for upper gastrointestinal hemorrhage in the majority of our patients. This suggests that stress from acute brain injury may in fact be quite infrequent or perhaps may act as an additive risk factor in patients with other predispositions for upper gastrointestinal hemorrhage. The endoscopic and histological similarities between stress gastritis and NSAID-associated gastritis make it difficult to distinguish these two processes. We did not recognize any cases of endoscopically diagnosed erosive or hemorrhagic gastritis in the absence of prior NSAID use. The presence of NSAID use in a large proportion of our patients is of interest, since they are all established. The significance of H. pylori in 2 of 3 sampled patients is not clear, since they are well-established causes of gastric ulcers and erosions. A recent cross-sectional study found erosive gastritis in about 50% of patients who used NSAIDs. The significance of H. pylori in 2 of 3 patients is not clear because so few patients underwent biopsy. H. pylori would be expected to be relatively common in the elderly, thus stroke-prone, population. The association between Helicobacter jejuni and gastric ulcers has been demonstrated in many studies, and risk of infection increases with age.

In the vast majority of our patients gastrointestinal hemorrhage did not produce a life-threatening situation. Mild hematemesis, melena, and sudden decrease in hemoglobin were important presenting signs, and treatment with H2-receptor antagonist and a single blood transfusion resolved this complication. Fortunately, massive bleeding was uncommon and was not observed in patients with ischemic stroke on heparin.
during hospitalization. In patients who presented with clinical signs of gastrointestinal bleeding, upper endoscopy was often helpful because in most patients localization of the hemorrhage to the stomach could be realized by the finding of fresh blood with a demonstrable lesion. An exposed vessel on the posterior wall of the duodenum or on the lesser curve of the stomach, typically associated with high risk of rebleeding, was absent and reinforces conservative management.

It should be pointed out that in this study, patients with very minor gastrointestinal hemorrhages may have been missed. Most patients in our series had fairly significant hemorrhages that resulted in endoscopic investigations. The true frequency of gastrointestinal hemorrhage in stroke therefore remains unknown.

However, the very low incidence of significant gastrointestinal bleeding requiring blood transfusion in our retrospective series precludes indiscriminate use of prophylactic therapy. In stroke, prophylactic treatment with agents that reduce gastric acidity, known to effectively reduce gastric bleeding, may be tailored toward patients with a history of peptic ulcer disease or use of aspirin, NSAIDS, or corticosteroids.

References

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