Upper Gastrointestinal Bleeding: One Center's Five Years Experience

Üst Gastrointestinal Sistem Kanaması: Tek Merkez Beş Yıllık Deneyim

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OBJECTIVES: Upper gastrointestinal bleeding (UGIB) is important for hospitalization. We investigated the etiologies and risk factors of 792 patients admitted to our hospital over five years.

METHODS: 792 patients admitted with hematemesis and/or melena were included in the study. Histories, examinations, laboratory tests, and endoscopic procedures were reported. Lesions that caused bleeding were determined, and they were identified based on Forrest classification. The specimens were evaluated in the pathology laboratory. The control group consisted of 713 patients without bleeding who had undergone gastroscopy for other complaints.

RESULTS: There were 550 male and 242 female subjects. The percentage of GI bleeding was 70% among patients ≥40 years. Helicobacter pylori positivity with CLO tests was observed in 163 patients. The most frequent lesions were duodenal ulcer, mucosal lesions, hiatal hernia, esophageal varices, stomach ulcer, stomach cancer, and portal hypertensive gastropathy. There was history of non-steroidal antiinflammatory drug (NSAID) use in 29.5%. The middle-aged group (54.2±15.8) presented with a higher frequency of bleeding due to NSAID. Duodenal ulcer and mucosal lesions were observed more commonly among smokers and middle-aged male patients. 44 patients had a history of alcohol, which correlated with mucosal lesions, esophageal varices and portal hypertensive gastropathy. 290 patients had a history of recurrent GI bleeding, which was associated with mucosal lesions, peptic ulcer and esophageal varices.

CONCLUSION: UGIB is still important for morbidity and mortality. The common use of endoscopy and the increase in experience enable treatments. However, age, comorbidities, and anti-thrombotic and NSAID use continue to increase risks.

Key words: Duodenal ulcer; risk factors; upper gastrointestinal bleeding.

Amaç: Üst gastrointestinal sistem (GİS) kanaması hastane yatışlarının önemli bir nedenidir. Biz hastanemize beş yılda hemate- mez ve melena ile başvuran hastalardaki etyoloji ve risk faktörlerini inceledik.


Anahtar sözcükler: Duodenal ülser; risk faktörleri; üst gastrointestinal sistem kanaması.

SUMMARY

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INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is a frequent cause of hospitalization, with an average incidence ranging from 50 to 150/100,000 patients. The incidence of UGIB is higher among patients of lower socioeconomic status and increases with age. Moreover, UGIB is 4-fold more frequent than lower GI bleeding and is twice as likely to occur in males compared to females. UGIB is an important contributor to hospital morbidity and mortality. The mortality rate which may be as high as approximately 10%, has been associated with patient’s presentation and age and comorbidities. The most important diagnostic tool in patients with UGIB is upper GI tract endoscopy. Gastroscopy is sensitive and specific in diagnosing lesions that cause UGIB. Treatment following diagnosis may lead to hemostasis, and recurrent bleeding can be prevented in many patients. UGIB requires immediate intervention. We investigated the etiology and risk factors for UGIB in 792 patients admitted to our hospital for UGIB between 2003 and 2008.

METHODS

The records of 792 patients admitted to our hospital between January 2003 and September 2008 with hematemesis and melena were retrospectively examined. Our study was performed in a restricted Turkish population all of whom were Caucasians. Hematemesis, melena, recurrent GI bleeding, and bleeding severity were determined based on the criteria of the American Society for Gastrointestinal Endoscopy. Data included the results of patients’ history, physical examinations, laboratory tests, and hemodynamic monitoring. The hemodynamic goals of treatment included a systolic blood pressure >100 mm Hg and a hematocrit >30%. Control group consisted of 713 patients without GIS bleeding, who had been evaluated by upper endoscopy for other complaints such as anemia or dyspepsia in the same interval. All patients provided informed consent prior to endoscopic procedures. All gastroscopic procedures were performed in our endoscopy unit, with lesions identified based on the Forrest classification and classified by etiology. Biopsies were examined by our hospital pathology department. Helicobacter pylori (Hp) was investigated with CLO test and histopathologically. Risk factors for UGIB included age, gender, presence of Helicobacter pylori, medication use (including NSAIDs and aspirin), previous GI bleeding, co-morbid conditions, and alcohol and tobacco use.

<table>
<thead>
<tr>
<th>Table 1. Features of patients and controls</th>
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<tr>
<td>GI bleeding (+) Group</td>
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<tr>
<td><strong>Age, years</strong></td>
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<td>≥40</td>
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<td>&lt;40</td>
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<td><strong>Gender</strong></td>
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<td>Male</td>
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<td>Female</td>
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<td><strong>Aspirin use</strong></td>
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<tr>
<td><strong>NSAID use</strong></td>
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<tr>
<td>-</td>
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<tr>
<td><strong>Alcohol use</strong></td>
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<td>+</td>
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<td>-</td>
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<tr>
<td><strong>Smoker</strong></td>
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<td>+</td>
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<td>-</td>
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<tr>
<td><strong>History of bleeding</strong></td>
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<td>+</td>
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<td>-</td>
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<td><strong>GIS operation</strong></td>
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Statistical analyses were performed using the NCSS 2007 program, with results compared using t-tests and chi-square tests. Odds ratios were used to identify risks, with statistical significance defined as a p value <0.05 with a 95% CI.

RESULTS

The baseline demographic and clinical factors of the 792 patients who underwent endoscopy because of UGIB are shown in Table 1. Also shown are the same parameters in a control group of 713 patients who underwent gastroscopic examination for other reasons, including anemia or dyspepsia.

Bleeders was significantly older than nonbleeders (52.30±15.70 years vs. 45.26±15.04 years, p=0.0001). Bleeders tended to be male and ≥40 years of age, with a history of aspirin and NSAID use. In addition, bleeding was 7.5-fold more frequent in patients with bleeding history than patient without a history of GI bleeding; and 2.6-fold more frequent in patients who had undergone a previous upper GI system operation. Multivariate analysis showed that older age, male gender, aspirin and NSAID use, and history of bleeding or GI surgery were risk factors for UGIB (Table 2).

We observed no correlation between Hp positivity and GI bleeding (Table 3).

Pathological endoscopic diagnosis in patients with UGIB are shown in Table 4.

We investigated the lesions according to Forrest classifications in 163 patients who had bled from gastric or duodenal ulcer. There was 1 patient in Forrest Ib and there were 18 patients in Forrest Ia, 8 patients in Forrest IIb, 11 patients in Forrest IIc and 25 patients in Forrest III. Sclerotherapy was performed using adrenalin injection in Forest Ib and Forest Ila patient groups.
DISCUSSION

UGIB is a frequently encountered emergency situation, with various etiologies, that affects patient mortality and morbidity. Hematemesis, melena, or hematochezia are the most commonly experienced clinical findings in GI bleeding. GI bleeding varies by age and gender. We found that most of our patients with UGIB were male, accounting for almost 70% of the total. Bleeding was also associated with increased age, in as much as 77% of our patients were ≥40 years old, in agreement with previous results.

Our patients admitted for GI bleeding and the control group was investigated endoscopically for anemia or dyspepsia. We tried to make these two groups randomly from consecutive patients. For ethical reasons we did not make a healthy control group without any risk factors. This may be a limitation of our study.

The most common cause of UGIB is the presence of duodenal ulcers, which are more frequent than gastric ulcers in such patients. We found that duodenal ulcers were 3-fold times more common than were gastric ulcers. Hemorrhaging of duodenal ulcers is caused by erosion of an underlying artery, with the severity of the hemorrhage being dependent on the size and diameter of the affected artery. Thus, posterior duodenal ulcers resulting from erosion of the gastroduodenal artery cause serious bleeding.

Duodenal ulcers are associated with Hp infection, which disrupts the mucous barrier and has a direct inflammatory effect on the gastric and duodenal mucosa. The presence of Hp in patients with duodenal ulcers can be shown both by the CLO test and carbon urea breath test and by pathological examination. Using the CLO test, we found that 368 patients (46.4%) were Hp-positive, with 163 (54.2%) of such patients being histopathologically positive. The sensitivity of CLO-test to detect Hp is low and shows a wide difference with the material used. The gold standard test is histopathological evaluation. However, we observed no correlation between Hp positivity and GI bleeding.

Aspirin and other NSAIDs are major causes of UGIB worldwide. It has been estimated that more than 30 million people throughout the world consume NSAIDs daily, and many studies have shown that these drugs have toxic effects on the GI mucosa. NSAIDs are used primarily by patients with musculoskeletal system diseases. These drugs have GI-related side effects, including dyspepsia, peptic ulcers, hemorrhage, and even death. NSAIDs affect cyclooxygenase-1, resulting in impairment of the mucosal defenses to acid. NSAID disturbs prostaglandin synthesis and causes a decrease in mucus and bicarbonate secretion through topical damage. In addition, such drugs inhibit mucosal proliferation by decreasing mucosal blood flow, thus causing erosions, ulcerations, and bleeding in the gastric mucosa. We found that NSAID use continues to be a significant risk factor for GI bleeding in elderly patients. For example, we found that 234 patients (29.5%) with UGIB had a history of NSAID use, including 157 (67%) males and 77 (33%) females. The middle-aged group of patients (54.2±15.8 years of age) presented with a higher frequency of bleeding caused by NSAID use. Holvoet et al. reported that patients with GI bleeding from erosive lesions associated with NSAID ingestion were older than patients who did not use NSAIDs. Cyclooxygenase-2 (COX-2) inhibitors, which are extensively used because of anti-inflammatory and analgesic properties, show decreased GI toxicity. Although different types of NSAID have been associated with various bleeding risks, no anti-inflammatory drug, including selective COX-2 inhibitors, is completely safe for the GIS. Furthermore, use of injurious medicine concomitantly, the combination of COX-2 inhibitors or non-selective NSAIDs with low-dose aspirin, non-aspirin antiplatelet agents, or warfarin increased the risk of GI bleeding.

Aspirin is a leading agent in primary and secondary protection from cardiovascular diseases. Even at low doses (75-300 mg), however, aspirin may cause GI bleeding. There was no meaningful difference in the amount of bleeding between patients taking 75 mg or 300 mg aspirin, and no differences in GI toxicity profiles between patients taking enteric-coated and conventional aspirin. However, a meta-analysis of 31 clinical studies that included 192,000 patients showed that GI bleeding was significantly
less frequent in patients taking less than 100 mg/day aspirin than in those taking more than 200 mg/day (1.56% vs. 2.29%, p<0.001).\cite{29,30} It has been shown that the incidence of hemorrhage increases in the first two months of aspirin treatment, followed by a stable period for up to six months, with a continued but decreasing risk thereafter.\cite{29} We found that 7.8% of the UGIB group used aspirin regularly, a significantly higher percentage than in the control group.

Before the widespread use of fiberoptic endoscopy, it was not possible to determine the location of UGIB, but increased use of endoscopy and experience have led to better diagnosis and treatment of GI lesions. GI mucosal lesions such as gastritis, duodenitis, and gastroduodenal erosions are frequently related to the use of NSAIDs and presence of Hp. Often, the eradication of Hp and discontinuation of NSAIDs reverse mucosal lesions.\cite{2} We found that mucosal lesions occurred most frequently in patients with a history of GI bleeding, particularly in those who used NSAIDs. Moreover, in agreement with previous findings, we observed that NSAIDs frequently caused GI bleeding in multiple regions. NSAIDs were found to be responsible for 29.5% of all cases of UGIBs. Furthermore, the side-effects of NSAIDs are not homogeneous, being dependent on molecular structure and dosage. Although COX-2 inhibitors have been reported to decrease the GI bleeding risk;\cite{22,23} other studies have found no significant differences in the frequency of GI hemorrhage between patients using COX-2 inhibitors and other NSAIDs.\cite{24} Esophageal varicose bleedings constitute only 5-10% of all UGIBs, but may lead to more serious hemorrhage. Esophageal varices were detected during diagnosis in 60% of patients with decompensated liver disease and in 30% of patients with compensated disease. The risk of bleeding has been associated with the size and number of varices, the condition of the liver, and alcohol use.\cite{2} We found that bleeding was attributable to esophageal varices in 12.5% of patients, but in 20% of patients with a history of alcohol use. In patients with portal hypertension (other than varices), bleedings caused by portal gastropathy may be observed. We found that 7% of bleeders had portal hypertensive gastropathy and 12.9% showed esophageal varices.

Alcohol can injure different areas of the upper GI tract in various ways. Even a single incident of intense alcohol use may cause mucosal inflammation and hemorrhage. As heavy alcohol intake independently increases risk, the incidence of UGIB is highest among persons who are both heavy drinkers and users of aspirin or ibuprofen.\cite{3,31-33} We found that only 5.6% of our patients with UGIB had a history of alcohol consumption. Smoking has also been reported to be a risk factor for GI bleeding;\cite{3,32,34,35} although some studies have found no such association.\cite{21} We did not find any association between smoking and UGIB.

A history of previous duodenal ulcer and bleeding has also been linked with both upper GI bleeding.\cite{28,34,35} We found that 290 patients (36.6%, p=0.0001) had experienced previous GI bleeding.

140 patients had cardioesophageal sphincter insufficiency. Similarly 75 patients had hiatal hernia. Although these lesions are known not to lead bleeding per se these were the pathological findings in our patient group. These subjects might have bled before hospital admission, so no bleeding was observed at the time of endoscopic evaluation. Another reason for bleeding may also be plausible. We did not write our other diagnostic procedures and final diagnose here in this paper for the subjects who had colonoscopy or enteroscopic evaluation.

Patients with active arterial bleeding, nonbleeding visible vessel or adherent clot needs aggressive therapy with adrenalin, alcohol or sclerosan injection, electrocoagulation, heater probe coagulation or endoclips.\cite{36-38} We performed sclerotherapy for active bleeding patients. All patients received high dose intra venous proton pomp inhibitors and transfusion when needed. None of our patients needed emergency surgery.

**CONCLUSION**

Despite advances in medicine and technology, UGIB is still an important cause of admission to emergency departments. Increased use of and experience with endoscopy have made it easier to diagnose and
treat such lesions. We found that age ≥40 years, male gender, use of antithrombolytics and NSAIDs, alcohol consumption, and previous GI system operation or bleeding were significant risk factors for UGIB.

REFERENCES

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