Optimizing Testing and Treatment for *Helicobacter pylori* Infection in Patients with Acutely Bleeding Gastroduodenal Ulcers: An Interventional Study

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**Abstract**

- **Objective:** To determine whether dissemination of inpatient practice guidelines for *Helicobacter pylori* management improves the testing and treatment rates of patients admitted with acute upper gastrointestinal (GI) bleeding from gastric or duodenal ulcers.
- **Design:** Prospective, non-randomized, interventional study.
- **Setting and patients:** 189 patients admitted to a single, urban academic medical center with a primary diagnosis of acute upper GI bleeding from gastric or duodenal ulcers between January 1998 and June 1999. The patients were managed by 18 gastroenterology physicians (12 staff, 6 private practice).
- **Outcome measures:** Rate and type of testing used for the diagnosis of *H. pylori* infection and the rate of initiation of appropriate anti-*H. pylori* therapy.
- **Interventions:** Outcomes were measured during a 6-month baseline period before dissemination of guidelines to gastroenterologists and during a 1-year period after dissemination of guidelines. In the year following dissemination, chart reminders and contacts by a physician opinion leader were used to increase physicians' adherence to the guidelines.
- **Results:** Testing for *H. pylori* increased from 78% in the baseline group (n = 58) to 88% in the postintervention group (n = 131) (P = 0.081). Testing for *H. pylori* using the rapid urease method increased from 27% in the baseline group to 51% in the postintervention group (P = 0.004). There was a highly significant increase in the rate of initiation of appropriate anti-*H. pylori* therapy (before hospital discharge) from 45% in the baseline group to 84% in the postintervention group (P < 0.001).
- **Conclusion:** *H. pylori* treatment can be markedly improved in patients admitted with acutely bleeding gastroduodenal ulcers by the active promotion of inpatient care guidelines.

Approximately 300,000 patients are hospitalized each year in the United States for treatment of upper gastrointestinal (GI) bleeding, resulting in more than $2.5 billion in health care costs [1,2]. Peptic ulcer hemorrhage is diagnosed in an estimated 50% of patients with severe upper GI bleeding who require hospitalization [3]. There is overwhelming evidence that the presence of *Helicobacter pylori* infection in the stomach is linked to peptic ulcer disease. In certain patient populations, *H. pylori* is the cause of 70% to 90% of gastric ulcers and 90% to 95% of duodenal ulcers not attributable to use of nonsteroidal anti-inflammatory drugs (NSAIDs) [4]. Eradication of *H. pylori* decreases the recurrence rate of peptic ulcer disease to less than 10%, compared to a recurrence rate of 70% in patients treated by acid suppression alone [4]. Moreover, prospective studies have shown that the treatment of *H. pylori* infection decreases the rate of recurrent peptic ulcer bleeding [5–7]. Because of these findings, testing for and treatment of *H. pylori* infection in peptic ulcer disease has become the standard of care [8].

The methods of testing for the presence of *H. pylori* infection are limited by their degree of invasiveness, cost, or sensitivity and specificity. The current accepted standard of care is to perform an esophagogastroduodenoscopy (EGD) in patients who present with acute upper gastrointestinal bleeding, both for diagnostic purposes and for possible endoscopic therapy of the bleeding lesion. Histopathologic analysis of gastric mucosal tissue obtained by EGD has a sensitivity between 95% and 100%, but the reliability of detecting *H. pylori* through this histologic method is dependent on the site, number, and size of the biopsy specimens gathered during the EGD procedure as well as the expertise of the pathologist in visualizing the bacteria [9,10]. In addition, this method is considered “minimally-invasive,” involves an upper endoscopy procedure during which the patient...
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receives intravenous conscious sedation [9,11], and is relatively costly and time consuming, requiring at least 3 to 5 working days for results to be obtained. This delay results in practical difficulties, as many patients are discharged from the hospital before the results are known. Alternative methods to histology are whole blood serology and urea breath testing, which are sensitive (estimated at > 95%) but time consuming (at least 3 to 5 working days) [12,13]. Use of proton pump inhibitors may cause false-negative urea breath tests [13], while a positive serologic result may not indicate current infection but may merely reflect past exposure that, in the absence of current infection, does not warrant specific treatment. The H. pylori finger-stick blood test for detecting H. pylori antibodies is another testing option, but its sensitivity has been reported to be significantly lower than either histology or standard whole blood serology [14].

A reasonable alternative to these tests is the rapid urease test. The test is performed during the required EGD and involves the procurement of gastric mucosal tissue by endoscopic biopsy during the procedure. The biopsy specimens are then placed on a paper test strip that contains urea, a pH indicator and a buffer. Urease liberated from active H. pylori organisms will cause a rapid color change on the paper strip, with a final result available within 1 hour with the PyloriTek test system. This test is an inexpensive, sensitive, and quick way to determine if a patient with a peptic ulcer has a concurrent, active H. pylori infection [15]. The major limitation of the rapid urease test method is that its sensitivity can be affected by the use of proton pump inhibitors, the site and number of biopsy specimens, and the presence of fresh blood in the stomach.

Rates of testing and treatment of H. pylori infection have remained low, with studies showing poor adherence to the published National Institutes of Health Consensus Panel recommendations on the testing and treatment of H. pylori infection [8]. Using Medicare claims data to select patients hospitalized with a diagnosis of peptic ulcer disease, Offman and colleagues found that only 56% of these patients were actually tested for H. pylori infection and only 73% of patients testing positive were appropriately treated [16]. Importantly, Cooper et al examined data from both teaching and community hospitals to assess the rate of testing for and treatment of H. pylori infection in patients with bleeding peptic ulcers. This study found that only 28% of patients admitted with bleeding peptic ulcer were tested for H. pylori infection, and only 12.5% actually received therapy for the infection [17].

In the present study, we sought to determine whether the implementation of inpatient care guidelines at our institution would increase the rate of H. pylori testing (using the rapid urease method) and prompt the early initiation of appropriate anti-H. pylori treatment in patients presenting with acute peptic ulcer hemorrhage.

Methods

This prospective, nonrandomized, interventional study was conducted at a single urban academic medical institution from January 1998 to June 1999. Inpatient care guidelines relating to the management of patients with bleeding gastroduodenal ulcers were disseminated in written form to both staff and private gastroenterology physicians. Twelve full-time faculty members and 6 private physicians were involved in the study. The study period was divided into a 6-month baseline period prior to guideline dissemination and a 1-year postintervention period following guideline dissemination, during which the principal investigator and nurse care manager used interventions to increase guideline compliance.

Practice Guidelines

The guidelines were based on the NIH consensus conference on H. pylori in peptic ulcer disease [8]. The study guidelines advocated the use of the rapid urease test for all patients with endoscopically documented bleeding gastric or duodenal ulcers during their index EGD. Specifically, the study guidelines recommended that standard mucosal biopsies be obtained from the stomach for the rapid urease test (PyloriTek, Serim Research Corp., Elkhart, IN) in patients with bleeding gastroduodenal ulcers during the patients’ primary EGD. Although several rapid urease tests are commercially available, only one (PyloriTek) was used at our institution at the time of this study. The study guidelines recommended performing an EGD only if deemed medically necessary based on the patients’ acute gastrointestinal bleeding and did not recommend an EGD simply for the procurement of mucosal specimens for the rapid urease test.

In addition, these guidelines recommended prompt initiation of anti-H. pylori treatment, preferably prior to hospital discharge, for all patients found to be infected (by any method of H. pylori testing). The guidelines did not recommend empiric treatment for presumed H. pylori infection. Our standard anti-H. pylori treatment regimen consisted of triple therapy with a combination of amoxicillin, clarithromycin, and lan索razole for 14 days unless patients were allergic to specific medications.

Interventions

Patients admitted with a primary diagnosis of upper GI bleeding were identified prospectively by a nurse case manager (JAG) through a daily (weekday) search of the hospital admission and emergency department admission records. All patients with upper GI bleeding due to a gastroduodenal ulcer were followed on a daily basis by the nurse case manager until hospital discharge. Data on NSAID use, endoscopic findings, method of testing for H. pylori, treatment of peptic ulcer disease, length of hospital stay, and follow-up plans were prospectively collected by the nurse case manager using
men, were tested for the presence of had a history of NSAID use prior to admission (line group (64%) and 76 (58%) in the postintervention group, and 131 (42%) of these had gastric of 311 patients were admitted with upper GI bleeding in the 58 (43%) of these had gastric and/or duodenal ulcers. A total of 447 patients were admitted with a primary diagnosis of upper GI bleeding during the study period. Of these, 136 patients were admitted during the baseline period, and 58 (43%) of these had gastric and/or duodenal ulcers. A total of 311 patients were admitted with upper GI bleeding in the postintervention group, and 131 (42%) of these had gastric and/or duodenal ulcers. Thirty-seven patients in the baseline group were successfully contacted and questioned about completion of prescribed treatment. Thirty-seven of these 39 patients (95%) successfully completed the full course of treatment.

In the baseline group, 3 patients (5%) were treated empirically for H. pylori infection compared to 5 patients (4%) in the postintervention group. There were no significant differences between the 2 study groups in mortality from upper GI bleeding or 30-day readmission rate for recurrent bleeding. The mortality rate was 0% in the baseline group and 1% (1 death due to metastatic cancer) in the postintervention group (Figure 1). Anti-H. pylori therapy was initiated before hospital discharge significantly more frequently following the intervention (84% baseline versus 45% postintervention; \( P < 0.001 \)) (Figure 2). Thirty-nine of the 46 patients who tested positive and received anti-H. pylori treatment in the postintervention group were successfully contacted and questioned about completion of prescribed treatment. Thirty-seven of these 39 patients (95%) successfully completed the full course of treatment.

Discussion

All patients presenting with acutely bleeding gastric or duodenal ulcers should be promptly tested for H. pylori infection and receive appropriate treatment if infection is present. However, the literature shows that there is poor adherence to these recommendations [17]. There have been many studies on the management of various aspects of H. pylori infection, but few studies have examined ways in which physician behavior can be positively modified. The major objectives of the guidelines in our study were to advocate the use of the rapid urease test to quickly determine the H. pylori status of patients and to promptly initiate appropriate treatment in those found to be infected. Both of these objectives were met in a statistically significant manner. Our study demonstrated that there was a significant increase in the use of the recommended rapid urease

Table 1. Patient Demographics

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<thead>
<tr>
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<th>Baseline Group (n = 58)</th>
<th>Postintervention Group (n = 131)</th>
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<tbody>
<tr>
<td>Men, n (%)</td>
<td>31 (53.4)</td>
<td>70 (53.4)</td>
</tr>
<tr>
<td>Mean age (range), yr</td>
<td>63.5 (20–89)</td>
<td>67.4 (17–95)</td>
</tr>
<tr>
<td>Taking NSAIDs, n (%)</td>
<td>37 (64)</td>
<td>76 (58)</td>
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NSAIDs = nonsteroidal anti-inflammatory drugs.
test method ($P = 0.004$) and, more importantly, a highly significant increase in the initiation of anti-\textit{H. pylori} treatment before the patient was discharged from the hospital (84\% versus 45\%; $P < 0.001$).

The importance of beginning \textit{H. pylori} treatment before hospital discharge was documented in a study by Roll et al, in which less than half of the patients with peptic ulcer disease and a positive test for \textit{H. pylori} infection received appropriate treatment. These investigators were unable to identify the reason for this low treatment rate, but of the 223 tests performed to detect \textit{H. pylori} infection, 56\% utilized histology, while the rapid urease test accounted for only 33\% [18]. The authors did not specifically examine whether better results would have been obtained if more physicians had used the rapid urease test, but this may be a possibility given the results of our study.

The initiation of anti-\textit{H. pylori} treatment prior to hospital discharge has a number of potential advantages. First, it eliminates the possibility that a known infected patient will not receive appropriate treatment due to lack of follow-up care that may result if the patient fails to show up for follow-up appointments or the patient’s primary care physician overlooks test results reported after hospital discharge. Moreover, initiating treatment during hospitalization has the potential to significantly reduce the time and effort entailed in contacting infected patients after hospital discharge to initiate anti-\textit{H. pylori} treatment. A second advantage is that patients’ concerns regarding the cost and side effects of treatment can be addressed before discharge (eg, medication assistance programs can be used in those unable to afford the cost of treatment), and an opportunity is provided for patient education regarding the importance of treatment compliance. Theoretically, this has the potential to increase patient compliance with the treatment regimen.

As more data accumulate supporting the early discharge of selected patients (within 1 to 2 days) with “low-risk” upper GI bleeding [1,19], a method that allows for the rapid screening of patients for \textit{H. pylori} infection will assume even greater importance. Some investigators have advocated prompt patient discharge from the emergency department depending upon the results of upper endoscopy performed in the emergency department, without hospital admission [20].

Although gaining physician compliance with consensus guidelines can be challenging, some methods of implementation have been shown to be effective, including using a respected physician in the role of an opinion leader [21] as well as academic detailing involving lecturing and chart reminders [22]. In the present study, we successfully employed both of these methods. The principal investigator served as the opinion leader and, with the help of a nurse care manager, provided the education and reminders required. Our present study supports the effectiveness of these methods in promoting positive physician behavior.

Since the inception of this study, data have accumulated on the variable sensitivity of the rapid urease test method in patients with acutely bleeding gastroduodenal or peptic ulcers. Lower rates of sensitivity of 40\% to 75\% have been noted for the detection of \textit{H. pylori} infection in the setting of a bleeding peptic ulcer [23–26]. Although a precise mechanism for the decrease in sensitivity has not been elucidated, the presence of fresh blood in the stomach at the time of

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**Figure 1.** Testing methods for \textit{H. pylori} in the baseline and postintervention groups. NS = nonsignificant. *$P = 0.004$; †$P < 0.001$.

**Figure 2.** Initiation of anti-\textit{H. pylori} therapy prior to hospital discharge in the baseline and postintervention groups.
biopsy may be a major factor [26]. Nonetheless, authorities in this area have continued to recommend the use of the rapid urease test for initial endoscopic screening, as many patients will not have fresh blood in the stomach at the time of EGD. Laine et al have recommended that additional biopsies should be obtained at the initial endoscopy, saved, and subsequently sent for histologic evaluation if the rapid urease test result is negative [12]. We agree with this recommendation. Given the importance of initiating H. pylori therapy in the setting of a bleeding peptic ulcer, this so-called method of dual testing appears to be prudent.

The present study has some limitations. First, there is no true control group; instead a historical control group was used that consisted of patients admitted before the guidelines and interventions were instituted. This group was demographically well matched with the postintervention group (Table 1), and the same gastroenterologists and physicians were responsible for managing the patients in both study groups. Second, this study was carried out at a single urban academic institution with a principal investigator and/or nurse care manager continuously reviewing and contacting physicians. Thus, the results may not be generalizable to all practice or patient settings in which this degree of intervention is not possible. Further studies evaluating the influence of specific interventions such as chart/verbal reminders and lectures on physician behavior with regards to treatment of peptic ulcer disease, both in academic and community settings, need to be performed to confirm the efficacy of these techniques. Last, since the interventional phase of the study was conducted for only a 12-month period, the long-term influence and impact of these guidelines on physician practice remains unclear.

In conclusion, this study demonstrates that guidelines for inpatient care can positively and significantly influence the rate of testing for and treatment of H. pylori infection associated with an acutely bleeding peptic ulcer. Future outcome studies are needed to examine the effectiveness of dual testing for H. pylori infection and its influence on the rapidity of treatment and on patient compliance with treatment. In this way, the benefits of H. pylori eradication in this common and potentially life-threatening disease can be extended to patients who may otherwise go untreated.

References


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