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Prophylactic injection therapy is necessary for Forrest type 2b duodenal ulcers

Forrest tip 2b duodenal ülserlerde profilaktik enjeksiyon tedavisi gereklidir

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BACKGROUND

We aimed to assess the effect of prophylactic injection therapy during the index gastroscopy on upper gastrointestinal bleeding due to Forrest type 2b duodenal ulcer.

METHODS

The patients who were admitted with upper gastrointestinal bleeding and who underwent emergency gastroscopy between January 2004 and January 2011 were recruited to the study retrospectively. Among those, the patients with Forrest type 2b duodenal ulcer were selected and divided into two groups. The patients in Group 1 had only diagnostic gastroscopy, whereas those in Group 2 had prophylactic injection therapy during the index gastroscopy.

RESULTS

Eighty-seven patients were included in the study. There were 41 patients in Group 1 and 46 patients in Group 2. There was a significant difference in the incidence of rebleeding (26.8% versus 6.5%, p=0.017). The mortality rate was similar in the two groups (9.7% versus 2.1%, p=0.184).

CONCLUSION

We recommend prophylactic injection therapy in patients with upper gastrointestinal bleeding who have Forrest type 2b duodenal ulcer.

Key Words: Gastrointestinal bleeding; Forrest classification; rebleeding; mortality; injection therapy.

AMAÇ

Bu çalışmada Forrest tip 2b duodenal ülserlerde ilk endoskopi işlemi esnasında yapılan profilaktik enjeksiyon tedavisinin ülserin tekrar kanama oranı üzerine etkisinin belirlenmesi amaçlandı.

GEREÇ VE YÖNTEM

Çalışmaya hastanemizde 2004-2011 yılları arasında üst gastrointestinal sistem kanaması nedeniyle yapılan acil endoskopilerinde Forrest tip 2b duodenal ülser belirlenmiş hastalar alındı. Olgular rastgele olmayan iki gruba ayrıldı. Birinci gruba yalnızca tanısal endoskopi yapılan hastalar ve ikinci gruba tanısal endoskopiye ek olarak profilaktik enjeksiyon tedavisi yapılan hastalar alındı. Çalışmadaki birincil sonuç ölçütleri yeniden kanama ve ölüm oranı idi.

BULGULAR

Çalışmaya 87 hasta alındı. Bunlardan 41'i birinci, 46'sı ikinci grupta idi. Tekrar kanama oranı açısından her iki grup arasında anlamlı fark saptanırken (%26,8 ve %6,5, p=0,017), ölüm oranı açısından iki grup arasında istatistiksel anlam taşıyan bir farklılık gözlenmedi (%9,5 ve %2,1, p>0,05).

SONUÇ

Yeniden kanama riskini anlamlı düzeyde azalttığı için, Forrest tip 2b duodenal ülserlerde profilaktik enjeksiyon tedavisi uygulanmalıdır.

Anahtar Sözcükler: Sindirim sistemi kanaması; Forrest sınıflaması; yeniden kanama; ölüm; enjeksiyon tedavisi.

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In spite of widely available effective therapeutic agents such as proton pump inhibitors and increasing rates of *Helicobacter pylori* eradication, complications of peptic ulcer disease are still among the most common problems that clinicians face in the emergency setting.[1] If the patients with esophageal varices are excluded, duodenal ulcer is the leading cause of upper gastrointestinal bleeding (UGIB), which is associated with significant morbidity and mortality.[2]

Gastroscopy not only establishes the diagnosis in most patients with UGIB but also leads the clinician to assess the proper treatment option on an individual basis.[3] In addition, endoscopic findings form the major component of various scoring systems used for stratification of the patients with UGIB.[4] Forrest classification, one of the most popular scoring systems, depends solely on endoscopic findings and divides the patients with UGIB into three categories (Table 1).[3] Forrest classification serves as a useful tool to estimate the rebleeding rate, which is considered to be the major determinant for prognosis in patients with bleeding duodenal ulcer.[3,4]

Whereas therapeutic endoscopy for Forrest type 1 lesions and prophylactic endoscopic treatment for Forrest type 2a lesions are widely accepted as the standard care in patients with UGIB, the necessity of prophylactic endoscopic treatment for Forrest type 2b lesions remains controversial.[5,6] In this respect, we conducted a retrospective study to assess the efficacy of prophylactic endoscopic treatment with injection therapy in patients with Forrest type 2b bleeding duodenal ulcer. The study showed that prophylactic injection therapy during the index gastroscopy for such lesions results in a significant reduction in the rebleeding rate.

MATERIALS AND METHODS

The study was designed as a retrospective analysis, and was started after receiving approval of the local review board. Medical records of the patients who admitted for UGIB to the emergency department and who underwent an immediate gastroscopy between January 2004 and January 2011 were reviewed. Inclusion criterion was the presence of Forrest type 2b duodenal ulcer located at the posterior wall of the bulbus on endoscopic examination.

Group 1 was the control group, and included patients who underwent only diagnostic gastroscopy, whereas Group 2 was the prophylactic treatment group, and included those who received endoscopic injection therapy in the same session. All of the endoscopic procedures were performed by attending endoscopists experienced in both diagnostic and therapeutic endoscopy, and the standard equipment used for gastroscopy was Fujinon EVE 2200. A 1/10000 epinephrine solution was used for prophylactic injection therapy. Two millimeters of the solution was injected to each quadrant around the duodenal ulcer by an endoscopic needle.

Table 1. Forrest classification for upper gastrointestinal bleeding

Forrest classification		Rebleeding
Type 1	Active bleeding	
	1a Spurting hemorrhage	90-100%
	1b Oozing hemorrhage	80-85%
Type 2	Signs of recent bleeding	
	2a Non-bleeding visible vessel	40-50%
	2b Adherent clot on lesion	20-30%
	2c Hematin-covered lesion	5%
Type 3	Lesion without bleeding (flat spot, clean base)	≤3%

All of the patients were observed with hemodynamic monitoring, and were started routinely on intravenous fluids and parenteral form of proton pump inhibitors (pantoprazole, 80 mg/day). Blood transfusion was considered for patients with a hemoglobin level <7 g/dl and for those with systemic comorbidities and a hemoglobin level less than 10 g/dl. In the event of the development of the following findings during the follow-up period, an immediate re-gastroscopy was carried out: 1. Deterioration in hemodynamic parameters (hypotension, tachycardia, oligoanuria); 2. Progressive decrease in hemoglobin levels; and 3. Hematemesis and bright red bleeding per rectum. The patients with rebleeding were managed preferentially by therapeutic gastroscopy. Immediate re-gastroscopy was avoided in patients without clinical signs of rebleeding. The patients were discharged at the end of a 24-hour period without hemodynamic alteration or a decrease of >2 g/dl in hemoglobin levels.

All of the patients were asked to return for follow-up gastroscopy after a six-week period with medical treatment by proton pump inhibitor (esomeprazole, 40 mg/day, peroral). Since the CLO test is not reliable in patients with UGIB, the test was not carried out, and a combined antibiotherapy with clarithromycin (1000 mg/day, peroral) and amoxicillin (2000 mg/day, peroral) for *H. pylori* eradication was prescribed on a routine basis as well.[4]

Exclusion criteria were: 1. Hemodynamic instability on admission; 2. Serious systemic comorbidities; 3. Use of anticoagulant or antithrombotic agents; 4. Lesions categorized as other than Forrest 2b; 5. Concomitant gastric lesions or multiple duodenal ulcers on endoscopy; 6. Failure to complete the endoscopic examination due to patient intolerability or technical problems; 7. No return for follow-up endoscopy after

Table 2. The results and comparison of outcome measures

Outcome measure	Group 1 (n=41)	Group 2 (n=46)	*p*
Rebleeding	26.8% (11/41)	6.5% (3/46)	0.017
The length of hospital (h)	100.9±54.8 (36-264)	65.2±35.6 (36-192)	0.004
Mortality	9.7% (4/41)	2.1% (1/46)	0.184

the six-week period.

The primary outcome measure was the rate of rebleeding. Secondary outcome measures were the length of hospital stay and mortality rate.

The Statistical Package for the Social Sciences (SPSS) 10.1 for Windows was used for statistical analysis. The comparison between the groups was made by Mann-Whitney U and Fisher's exact test. Descriptive statistics were expressed as mean value and standard deviation. A *p* value less than 0.05 was considered to be statistically significant.

RESULTS

Totally, 1148 patients were recruited for the study. Eighty-seven patients with Forrest 2b duodenal ulcer found at gastroscopy were included in the study. There were 41 patients in Group 1 and 46 patients in Group 2. The mean age and female-to-male ratio in Groups 1 and 2 were 43.7±28.2 (19-83) and 39.6±18.4 (21-73) and 0.5 (14/27) and 0.9 (21/25), respectively.

The success rate at re-gastroscopy in Group 1 and 2 was 70% (7/10) and 66% (2/3), respectively. One patient in Group 1 underwent immediate surgical treatment without an attempt for a re-gastroscopy because of subconsciousness. The patients in whom re-gastroscopy failed underwent emergency surgery.

The results and comparison of outcome measures are shown in Table 2. The sole cause of mortality in both groups was rebleeding.

DISCUSSION

Rebleeding in patients with UGIB has several clinical consequences. It strongly correlates with mortality, and is usually the major cause of death.[3] Rebleeding also has a significant impact on morbidity. It apparently diminishes the physiological compensation mechanism that has already been insulted, which may be of paramount importance in patients with limited physiological reserve due to systemic comorbidities.[7] Moreover, it also increases the need for blood transfusion as well as the amount of blood transfusion.[8] Finally, rebleeding results in a prolonged length of hospital stay, and thus causes a significant increase in costs.[9]

The rebleeding rate after diagnostic gastroscopy in patients with Forrest type 2b duodenal ulcer in the present study is consistent with the estimated rate in the literature [26.5% and 20-30%].[10,11] Nevertheless, many endoscopists advocate using only the diagnostic feature of endoscopy or the "wait-and-see" strategy in this setting in order to avoid manipulation of the lesion that has already stopped bleeding and has been covered by an adherent clot.[11] In addition, they rely on the availability of highly effective acid-reducing agents and the fact that most such lesions that rebleed can readily be treated by a second endoscopic intervention.[11]

On the other hand, the present study showed that the incidence of rebleeding (26.8% *vs.* 6.5%, p=0.017) significantly reduced in patients with UGIB due to Forrest type 2b duodenal ulcer who received prophylactic injection therapy during the index gastroscopy when compared to those who underwent only diagnostic gastroscopy. Moreover, this could be readily done using a safe, relatively simple, and cost-effective method like injection therapy, which has a complication rate of less than 0.1%.[5] The reduction in the incidence of rebleeding also minimizes the need for re-gastroscopy, which leads to additional anxiety and fear of death for the patient. In addition, in the case of re-gastroscopy, the endoscopist has to deal with an upper grade lesion, and thus, there is a decrease in success rate and increase in complication rate. Likewise, the success rate at re-gastroscopy was found to be 66-70% in Group 2 in the present study, whereas it was 100% in the index gastroscopy. Finally, there was also a significant difference in the length of hospital stay between the groups, which means it is possible to gain cost-effectivity using a method with a negligible increase in costs. A recent meta-analysis also reported similar results.[12]

We failed to show a statistical difference between the mortality rates of the groups (9.7% *vs.* 2.1%, p=0.184) in spite of the significant difference between the rebleeding rates. Whereas this disparity is somewhat surprising, it also supports the fact that the mortality rate in patients with UGIB remains unchanged regardless of emerging treatment modalities.[2]

The major limitation of the present study is its retrospective, non-randomized nature. Furthermore, the decision to carry out prophylactic injection therapy in patients with Forrest type 2b duodenal ulcer used to

be made arbitrarily because strong evidence for such a procedure was lacking until recently. However, after analysis of our own experience in 2011, we were encouraged by the increasing data and began performing prophylactic injection therapy in patients with Forrest type 2b duodenal ulcer on a routine basis.

In conclusion, we recommend prophylactic injection therapy in patients with UGIB who have Forrest type 2b duodenal ulcer, as it significantly reduces the incidence of rebleeding and associated morbidity. In other words, it seems rational to adopt the "nip it in the bud" policy rather than the "wait-and-see" policy.

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