Route selection for double balloon enteroscopy in patients with obscure gastrointestinal bleeding: Experience from a single center

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Background/aims: *This study was performed to clarify the best insertion route of double-balloon enteroscopy and to report the characteristics and proportions of small bowel pathologies detected by double-balloon enteroscopy in our patients with obscure gastrointestinal bleeding.* ***Materials and Methods:*** *Between January 2006 and December 2009, 75 patients with obscure gastrointestinal bleeding were enrolled into this study. The procedure was performed by oral route in 60 patients, anal route in 5 patients and both in 10 patients. Mean age of the patients was 50.8 years, and 57.3% of them were male. The main outcome measurements were total length of insertion, total time of double-balloon enteroscopy, diagnostic rates, anatomic location of the lesions, and final diagnosis of lesions detected.* ***Results:*** *Double-balloon enteroscopy was diagnostic in 75% of the patients. This rate was significantly higher in overt bleeding (91.7%). The source of bleeding could not be detected in 19 patients. Mean times of procedures were 119, 144 and 154 minutes for oral route, anal route and both, respectively. The mean insertion length was 310.65 cm (beyond the pylorus) for oral and 166.8 cm (beyond the ileocecal valve) for anal route. The most frequent pathologies were vascular malformations (n=20) and tumors (n=19). All malignant lesions were detected in the proximal part of the small intestine. Vascular malformations were distributed equally through the small intestine. Endoscopic treatment was performed in 30% of patients.* ***Conclusions:*** *Double-balloon enteroscopy is a safe and feasible examination for obscure gastrointestinal bleeding. Most lesions were localized in the proximal part of the small intestine. The oral route may be preferred as a first choice, if the imaging modalities including capsule endoscopy cannot detect the lesion.*

Key words: Obscure gastrointestinal bleeding, double balloon enteroscopy

Nedeni bilinmeyen kanamalarda çift balon enteroskopide yön seçimi: Tek merkezin deneyimi

Giriş ve Amaç: *Bu çalışmanın amacı, nedeni bilinmeyen kanamalarda çift balon enteroskopi için en uygun giriş yönünü belirlemek ve saptanan ince barsak patolojilerin özelliklerini değerlendirmektir.* ***Gereç ve Yöntem:*** *2006-2009 yılları arasında nedeni bilinmeyen kanama ile kliniğimize başvuran 75 hasta çalışmaya dahil edilmiştir. Çift balon enteroskopi ile ilgili veriler prospektif olarak değerlendirilmiştir. Çift balon enteroskopi, 60 hastada oral, 5 hastada anal ve 10 hastada her iki yönden yapılmıştır. Hastaların ortalama yaşı 50.8 yıl ve %57.3'ü erkek idi. Total giriş uzunluğu, total işlem süresi, tanı oranları, lezyonların anatomik lokalizasyonları ve son tanılar değerlendirilmiştir.* ***Bulgular:*** *Hastaların %75'inde tanı konulmuştur. Tanı oranı, aşikar kanaması olanlarda anlamlı olarak yüksekti (%91.7). Kanama nedeni 19 hastada saptanamadı. Ortalama işlem süresi, oral, anal ve her iki yön için sırasıyla; 119, 144 ve 154 dk idi. Ortalama giriş uzunluğu oral yol ile 310.65 cm (pilordan itibaren) ve anal yol ile 166.8 cm. (ileoçekal valvden itibaren) idi. En sık rastlanan patoloji vasküler malformasyonlar (n=20) ve tümörler (n=19) idi. Malign lezyonların hepsi proksimal ince bağırsak yerleşimliydi. Vasküler malformasyon tüm ince bağırsakta eşit dağılmakta idi. Hastaların %30'una endoskopik tedavi uygulandı.* ***Sonuç:*** *Çift balon enteroskopi, nedeni bilinmeyen kanamalarda güvenli uygulanabilir tanısal ve tedavi edici bir işlemdir. Lezyonların çoğu proksimal ince bağırsak yerleşimlidir. Kapsül endoskopi dahil görüntüleme metodlarının lezyon saptayamadığı durumlarda oral yol ilk tercih olabilir.*

Anahtar kelimeler: Nedeni bilinmeyen kanama, çift balon enteroskopi

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INTRODUCTION

There are many reasons for gastrointestinal system (GIS) bleeding. According to the new classification, GIS bleeding is classified as upper (proximal part of Treitz ligament), middle (between the Treitz ligament and ileocecal valve) and lower (distal part of ileocecal valve) (1,2). Obscure gastrointestinal bleeding (OGIB) is defined as persistent or recurrent bleeding from the GI tract after an initial negative endoscopic evaluation including colonoscopy and esophagogastroduodenoscopy (EGD).

Bleeding can be presented as occult (cannot be visualized) or overt (visualized as melena or hematochezia) (1). It is possible to detect the bleeding source from the small intestine with the technological progress in the last 10 years. The most important advantages of double balloon enteroscopy (DBE) over conventional endoscopy are endoscopic interventions like polypectomy, dilatation, and argon plasma coagulation (APC). The mean diagnostic ratio by DBE is 70% (3-6). On the other hand, it is difficult to perform anal and oral route in the session. It is sometimes very difficult to decide the first route of DBE.

This study was performed to clarify the best insertion route of DBE and to report the characteristics and proportions of small bowel pathologies detected by DBE in our patients with OGIB.

MATERIALS AND METHODS

The patients who were admitted to Yeditepe University Hospital because of OGIB between January 2006 and December 2009 were enrolled into this prospective case series study. This study was reviewed and approved by the local ethics committee. Informed consent was obtained from all patients.

Data associated with the DBE procedure were collected prospectively. In the beginning of the study, medical history and clinical characteristics of all patients were collected by the same physician (U-A). Drug history was obtained from all patients (especially warfarin, clopidogrel, acetylsalicylic acid, non-steroid anti-inflammatory drugs).

All patients underwent EGD and colonoscopy. DBE was performed by oral and/or anal route in patients for whom conventional methods could not detect a source for bleeding (7). All patients underwent abdominal computed tomography (CT), and two patients underwent small bowel enteroclysis before DBE.

Inclusion Criteria:

(a) Patients with occult or overt OGIB in whom the bleeding site could not be shown by conventional methods.

Exclusion Criteria:

(a) Hemodynamic instability.

(b) Comorbidity (hemodialysis patients because of chronic renal failure, congestive heart failure, new onset acute ischemic heart disease).

(c) Cardiopulmonary disease.

(d) Complaints not related to OGIB (abdominal pain, diarrhea, inflammatory bowel disease) without signs of intestinal obstruction.

(e) History of abdominal surgery.

All patients underwent DBE after 12-hour fasting. Additionally, patients who underwent anal route DBE used standard colon lavage solution the day before. In patients with active bleeding, oral intake was prohibited.

Propofol and midazolam were used for sedation during the procedure. Intravenous propofol was given at a dose of 1 mg/kg and midazolam as 2-4 mg. If necessary, propofol was provided repeatedly.

Double Balloon Enteroscopy Technique

Double balloon enteroscopy (DBE) was performed with FUJIFILM high-resolution enteroscopy device (EN450-P5/20, Fujinon Inc., Saitama, Japan). The enteroscope provides a working length of 200 cm and has an outer diameter of 8.5 mm. The length of the flexible tube over the device is 140 cm with an outer diameter of 12 mm. The working channel of the device is 2.2 mm. The procedure was performed with a latex controlled balloon system (PB-10) that could inflate and deflate on the tip of the device and flexible tube as described before (8). We used P-tube (additional flexible tube from mouth to esophagus) to decrease complications in some patients (high-risk patients for respiratory complications and mucosal bleeding [aspirin- and Coumadin-using]) (9).

The procedure was performed either by oral or anal route, depending on the likely location of the pathology due to patient history and physical examination. If a diagnosis was not obtained with the primary access route, the alternative route was used. If both the oral and anal routes were performed, Indian ink was used to mark the farthest point, to check full enteroscopy. Advancement of the

instrument was measured by counting the number of full 40 cm advancement sequences carried out after the reference point established by initial full-length insertion of the endoscope (10). All biopsy specimens at DBE were reviewed by histology.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) 15.0 (SPSS Inc., Chicago, IL) was used for statistical analysis. Pearson correlation test, chi-square and Student-t test were performed. A p value less than 0.05 was accepted as statistically significant.

RESULTS

During the study period, of 188 patients who underwent DBE, 75 patients were enrolled into this study according to the inclusion and exclusion criteria. The mean age of patients was 50.8 years (16-80 years), and 57.3% of patients (n=43) were male (Table 1). Thirty-two of the patients had overt bleeding (n=50). The procedure was performed by oral route in 60 (80%) patients, anal route in 5 (6.7%) patients and both in 10 (13.3%) patients. Total enteroscopy was performed in 8% (6/75) of the patients. Mean times of DBE were 119, 144 and 154 minutes for oral route, anal route and both, respectively (Table 1). There was no statistically significant difference between mean time between oral and anal route (p<0.05). The entire

small bowel was completely explored in 2 patients by oral route. Retrograde route was not used to examine any small intestines, if the lesion was reached. The mean insertion length was 310.65 cm (beyond the pylorus) for oral and 166.8 cm (beyond the ileocecal valve) for anal route (Table 1).

Intravenous propofol and midazolam were used to achieve sedation. Before the procedure, mean oxygen saturation, systolic blood pressure, and heart rate of patients were 95±3%, 120±25 mmHg, and 87±20 /min, respectively. During the procedure, mean oxygen saturation decreased significantly (from 95±3% to 83±5%) (p<0.005). There was no anesthesia-related complication and no need for intubation.

Generally, the DBE procedure was well tolerated by most patients. The only observed complications were mild acute pancreatitis in 10 patients (13%) and broken tooth in 1 patient (1.5%). No other complication was observed. The only observed side effects were abdominal pain in 10 patients (13%) and sore throat in 20 patients (26%).

In 19 patients (25.3%), the bleeding source could not be shown. The ratio of detecting a source of bleeding was significantly higher in patients with overt than occult bleeding (91.7% vs 76.2%; p=0.029). The macroscopic appearances of the lesions detected in patients by DBE were as follows: vascular malformation, 35.7% (n=20); ulcer, 30.7% (n=17); polypoid lesion, 21.4% (n=12); polyp, 7.1% (n=4); nodular image, 3.6% (n=2); and Meckel diverticulum, 1.8% (n=1) (Figures 1, 2).

Table 1. Demographic characteristics of patients and technical features of double balloon enteroscopies

	Patients (n=56)
Mean age±SD, years	50.8±16.2
Gender (n, %)	
Male	43 (57.3)
Female	32 (42.7)
Route of DBE	
Oral	60 (80)
Anal	5 (6.7)
Both	10 (13.3)
Mean±SD of total time of DBE, min	
Oral	119±26
Anal	144±32
Both	154±25
Mean±SD of total length of insertion	
Oral	310.65±90.3
Anal	166.8±80.2

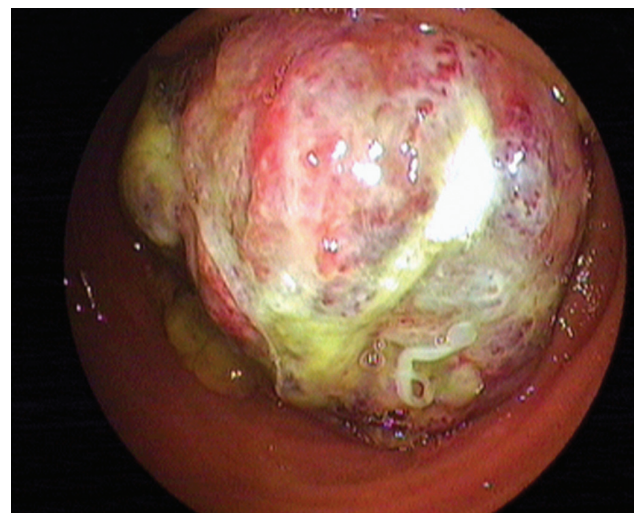DBE: Double balloon enteroscopy. SD: Standard deviation.

Figure 1. Polypoid ulcerated lesion in the distal ileum (histopathologic examination revealed leiomyosarcoma).
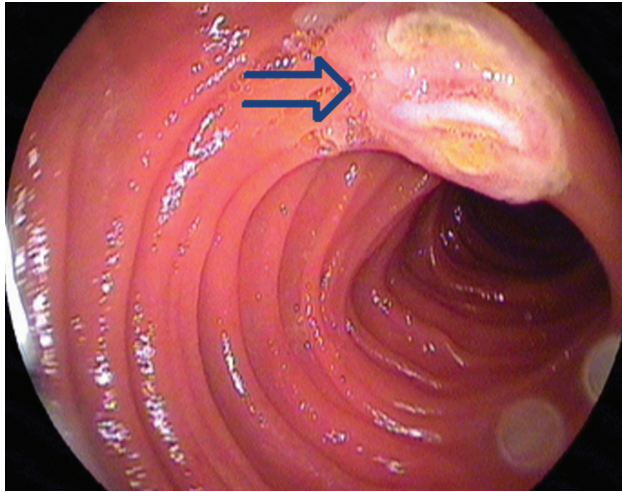
Figure 2. Ulcerated lipoma (confirmed by histology) in the proximal jejunum.

The anatomic locations of most detected lesions are presented in Table 2. Patients diagnosed with adenocarcinoma were older when they were compared to patients who had gastrointestinal stromal tumor (GIST), but there was no statistically significant difference. All malignant lesions were localized in the proximal jejunum. Vascular malformations were seen at similar ratios through all parts of the small intestine.

Twenty-three percent of patients (n=17) were using acetylsalicylic acid and/or clopidogrel because of comorbidities (ischemic or valvular heart disease). There was no correlation between vascular lesions and comorbidities (r=0.106, p=0.367). All patients with a diagnosis of non-specific ulcer, except one, were using non-steroid anti-inflammatory drugs.

Therapy

Endoscopic therapeutic procedures were performed in 30.7% of patients (APC in 20 patients, polypectomy in 2 patients, bipolar electrocautery in 1 patient). Surgical excision was performed in 29.3% of patients (n=22), and 40% of patients (n=30) had medical observation. Capsule endoscopy (CE) was performed in 4 patients before DBE, and vascular malformation was detected in 1 of them. In the other 3 patients, CEs were reported as normal, and GIST was detected by DBE in these patients.

Final diagnoses of patients are presented in Table 3. Six patients diagnosed with Crohn's disease were referred because of occult obscure bleeding. The mean age of the patients was 35±12 years (range: 16-50 years), and 66% of them were male. In these patients, ulcers were multiple and localized in the distal jejunum and ileum. Biochemical inflammatory markers were negative in these patients. Diagnosis was made by pathologic examinations. Three patients diagnosed with ulcerative jejunoileitis were also referred because of occult obscure bleeding. The mean age of these patients was 48.6±17.9 years (range: 28-60 years) and 2 of them were male. All lesions were in the jejunum. Diagnosis was made by histopathologic examinations and serological tests.

Radiologic imaging (CT and/or small bowel imaging) was helpful in 12% of patients.

DISCUSSION

The advent of DBE has enabled the observation of small intestinal lesions that cause OGIB. Particularly, the diagnostic ratio of DBE is higher for bleeding when compared with other indications of DBE (11). The diagnostic ratio of DBE was 75% for OGIB in our study. This ratio was statistically higher in patients with overt OGIB compared to those with occult OGIB. Byeon et al. (12) reported that the diagnostic ratio of DBE was 69.8% in 43 patients with OGIB. Arakawa et al. (13) evaluated

Table 2. Anatomic locations of the most commonly detected lesions by double balloon enteroscopy

	Jejunum		Ileum		Mean age±SD (years)	M/F
	Proximal (%)	**Distal (%)**	**Proximal (%)**	**Distal (%)**		
Malignant lesions						
Adenocarcinoma	4 (57.1%)	3 (42.9%)	-	-	58.8±7.3	3/4
GIST	3 (50%)	3 (50%)	-	-	46.3±22.9	4/6
Benign lesions						
Vascular malformation	6 (30%)	5 (25%)	5 (25%)	4 (20%)	54.8±16.2	10/10
Nonspecific ulcers	-	3 (50%)	1 (16.7%)	2 (33.3%)		
All lesions	**17 (30.4%)**	**21 (37.5%)**	**7 (12.5%)**	**11 (19.6%)**	**50.8±16.2**	**43/32**

GIST: Gastrointestinal stromal tumor. M/F: Male/female. SD: Standard deviation.

Table 3. Final diagnosis of patients with obscure gastrointestinal bleeding

Final diagnosis	*n* (%)
Vascular malformations	**20 (26.7)**
Angiodysplasia	18 (24.0)
Dieulafoy's lesion	1 (1.3)
Hemangioma	1 (1.3)
Ulcerations	**15 (20.0)**
Crohn's disease	6 (8.0)
Nonspecific ulcer	6 (8.0)
Ulcerative jejunoileitis	3 (4.0)
Tumors and polyps	**19 (25.3)**
Adenocarcinoma	7 (9.3)
GIST	6 (8.0)
Lipoma	3 (4.0)
Lymphangioma	1 (1.3)
Leiomyosarcoma	1 (1.3)
Adenomatous polyp	1 (1.3)
Meckel's diverticulum	**1 (1.3)**
None	**19 (25.3)**
Total	**75 (100)**

GIST: Gastrointestinal stromal tumor.

162 cases with OGIB, and reported the diagnostic ratio of DBE as 64%. In that study, the detected lesions were mostly vascular malformations. In our study, the most frequent lesions were vascular malformations and tumoral lesions. Adenocarcinoma and GIST were the most commonly detected small bowel tumors. In a multi-center study from Japan, 1035 patients were evaluated with DBE and small bowel tumor ratio was found as 13.9%. Malignant lymphoma and GIST were detected as the most frequent small bowel tumors (14).

There are studies that have compared the diagnostic yield of CE and DBE in small intestinal pathologies (5,13,15). The diagnostic ratio of CE was comparable to DBE in those studies. DBE has the advantages like giving air and cleaning secretions, but CE is well tolerated and is an outpatient procedure. CE can guide the insertion route of DBE and can be used as a complementary procedure. Using CE before DBE increases the costs of diagnostic procedures and may not be cost-effective.

Gerson et al. (16) reported that an initial DBE is a cost-effective approach for patients with obscure bleeding. In our study, only four patients underwent investigation with CE before DBE, and GISTs were detected in three of the patients, although CE was reported as normal. Because of false-positivity (submucosal prolapsus and small intestinal intussusception that mimic submucosal tumors) and false-negativity (angiectasis, tumor) of CE, it can misdiagnose very large polypoid lesions (17-19). Some algorithms advise the first choice of DBE from a cost minimization perspective.

The anatomic location of small intestinal lesions can guide the insertion route of DBE. Schwartz et al. (20) reported that benign and malignant lesions are generally detected in the jejunum. In a study that evaluated OGIB with CE, Hindryckx et al. (21) showed that 60% of lesions that lead to bleeding were localized in the proximal part of the intestine. In our study, 70% of lesions leading to OGIB were detected in the jejunum. All GISTs and adenocarcinomas were localized in the jejunum. Malignant lesions are mostly in the proximal part of the jejunum. Although vascular malformations were distributed through the small bowel equally, approximately half of them were localized in the jejunum. These findings proved that the oral route may be preferred as a first choice in most patients.

We did not record any serious complications during the study. However, the ratio of pancreatitis was higher than in the literature (13% vs. 0.3%) in our study (22). In our previous study, we reported that the duration between first inflation and second inflation of balloons of the flexible tube was a risk factor for pancreatitis (23). The procedure technique and total time of DBE may be associated with a high ratio of pancreatitis. None of the patients had severe pancreatitis.

In conclusion, the detected intestinal lesions causing OGIB were localized most commonly in the proximal part of the small bowel, at least in our limited cases. The oral route may be preferred as a first choice.

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