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Double-balloon Enteroscopy: The results of a new experience in Iran

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Abstract

Background: Approach to the small intestine has been difficult even with newer methods. Double-balloon enteroscopy (DBE) has been created for diagnostic and therapeutic interventions in diseases of the small intestine. Small intestinal diseases have different etiologies in each country. The DBE has been introduced in recent years in Iran. Our aim was to study the indications and results of DBE in some academic centers in Iran.

Methods: Fifty-five patients with symptoms and signs related to small intestine without definitive diagnosis but with previous workup were enrolled in the study. The DBE was performed in three different medical universities in Iran.

Results: The mean age of the patients that underwent the DBE was 47.2 ± 17.3 years. Abdominal pain (54.5%) and occult gastrointestinal bleeding (23.6%) were the most common presentations. Small bowel lesions were detected in 26 patients (47.3%); the most common lesions were ulcer (46.2%) and polyps (19.2%). Crohn's disease (12.7%) was the commonest diagnosis found in DBE procedure. Patients presenting with abdominal pain or lower hemoglobin level were more likely to be diagnosed (both $p \leq 0.05$). Small intestinal diseases were ultimately diagnosed in 47.3% of the patients. Twenty percent of the patients had another disease outside the small bowel.

Conclusions: DBE is an effective and relatively safe diagnostic and therapeutic option for small bowel evaluations. Accurate selection of patients and more experience technicians and physicians will improve the efficacy of this procedure in Iran.

Keywords: Double-balloon enteroscopy, Small intestinal disease, Crohn's disease.

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Introduction

Evaluation of the small intestine is difficult for gastroenterologists because of its long length, distance from the gut orifices, and redundancy, among others.

Conventional methods used for diagnostic purposes of small intestine have many limitations. Barium follow-through has only 0–20% diagnostic yield (1). Push enteroscopy visualizes the first 50- to 100-cm initial part of the jejunum, and intraoperative endoscopy has risks of a surgery. Using capsule endoscopy, most of the small bowel could

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be visualized but without capability of any diagnostic or therapeutic interventions (2, 3); also, there are several studies suggesting the low sensitivity of capsule endoscopy in finding solitary and/or mass lesions (4, 5).

Double-balloon enteroscopy (DBE) was developed by Yamamoto et al in 2001, and its first workshop was held in 2006 (3, 6).

The DBE, a panendoscopy procedure, was developed for visualization of entire small bowel with the aim of diagnostic and therapeutic interventions. The most common indication used in DBE was obscure gastrointestinal bleeding (OGIB); the cause of gastrointestinal bleeding (GIB) after upper endoscopy and colonoscopy in 5% of cases; is not known, but, the most common cause is small intestinal lesions. Nowadays, with utilization of double and triple anticoagulations for vascular disorders, the rate of GIB and its obscure ones are on a rise. Other applications of DBE include diagnostic evaluation for Crohn's disease, polyposis syndromes, chronic diarrhea, malabsorption, refractory celiac and therapeutic interventions such as polypectomy, dilatation, control of bleeding, and jejunostomy tube placement (2, 6).

There are many studies with different results about DBE in recent years. The etiologies of small intestinal diseases vary in different countries (6). The aim of this study was to evaluate the results of recently provided DBE in 3 academic centers in Iran regarding the indications, diagnostic yields, and clinical outcomes, for this procedure.

Methods

This prospective study was conducted in 3 academic hospitals of medical universities: Tehran, the metropolitan city; Mashhad, the center of Khorasan Razavi province in the north east, and Kerman, the center of Kerman province in the south of Iran. In all these centers, performing DBE procedure (Fujinon Co., Saitama, Japan) was started in recent years; between December 2009 and November 2010, 55 consecutive patients with suspected small intestinal diseases underwent DBE.

Inclusion criteria were suspected small intestinal diseases after negative previous workup or suggestive of small intestinal diseases. All patients had at least one normal upper endoscopy and colonoscopy. Several other diagnostic procedures had been performed regarding small bowel including small bowel follow-through and/or abdominal computed tomographic (CT) scan. None of the patients had a definitive diagnosis before performing the DBE.

Data collection was based on demographic characteristics of the patients, indications for DBE, hemoglobin levels, patient's history of transfusion before DBE, use of nonsteroidal anti-inflammatory drugs (NSAIDs), complications, and follow-up after 3 months.

Informed consent was taken from all patients before the procedure. The DBE performed after bowel preparation with polyethylene glycol solution and dimethicone for clearing the small intestinal bubbles. In all patients, oral route was preferred as the initial procedure. Conscious sedation was achieved by intravenous propofol, with monitoring of pulse oximetry, heart rate, and blood pressure during the procedure. DBE was stopped if the lesion was found or the endoscopist visualized the cecum. The procedure also terminated if these goals were not achieve after 2 hours. For all lesions detected during the procedure, biopsy was obtained and, if possible, treated appropriately.

This project was approved by Ethical Committee at Tehran University of Medical Sciences.

Statistical analysis

All data were collected and analyzed using SPSS software (SPSS 11.5 Inc., Chicago, IL, USA). Distributions of quantitative variables were analyzed using one-sample Kolmogorov-Smirnov test. Quantitative variables in the two groups were compared using the t-test. Chi-square or Fisher exact tests were also used to evaluate the relation of two qualitative variables as appropriate.

Finally one stepwise multiple logistic re-

gression analysis was used to identify predictors of final diagnosis. In this model, independent variables were level of blood hemoglobin (g/dl), symptoms at presentation, and number of packed red cells transfused. Symptoms at presentation were divided into two groups; patients presenting with abdominal pain or both abdominal pain and diarrhea together constitute pain group and those with occult or frank GIB were collectively considered as GIB group.

Quantitative variables are presented as mean ± SD (standard deviation) and range, and value at $p \leq 0.05$, considered significant.

Results

General points

Thirty-three (60%) DBE procedures were performed at Mashhad, 17 (30.9%) at Tehran, and 5 (9.1%) at Kerman. Table 1 shows the demographic features of patients and clinical indications for this procedure. Obscure-occult GIB characterized by iron-deficiency anemia without known cause was the only presentation in 13 patients (23.6%). Of 41 patients who performed small bowel follow-through, 29 (70.7%) had abnormal findings. The results of 9 (56.3%) out of 16 abdominal CT scan also were abnormal; mucosal thickening as the most common finding in both imaging procedures. Upper endoscopy and colonoscopy were normal in 47 patients (85.5%). Two cases with Peutz-Jeghers syndrome had polyps in the colon and the stomach in addition to small bowel. In the remaining patients, the trivial lesions like hemorrhoids or diminutive polyps could not explain the patient's problems.

Five patients (9.1%) were NSAIDs users. We found no significant difference among patients' characteristics in these 3 centers.

Technical points

Most (69.1%) DBE procedures were performed in an outpatient setting, and mainly by oral route (98.2%), and it was performed via both oral and anal route in only one patient.

In 4 cases (7.3%), the cecum was seen at the end of the oral DBE; other reasons for DBE termination were as follows: finding of lesion in 23 cases (41.8%), duration of more than 2 hours in 17 cases (30.9%), failure of propagation in 10 cases (18.2%), and cardiopulmonary instability in 1 case (1.8%).

Endoscopic findings

Overall DBE disclosed pathologic lesions in 26 cases (47.3%). The lesions were present equally in the jejunum and the ileum (n= 12, 46.2% each). In 2 cases of Peutz-Jeghers syndrome, both jejunum and ileum were involved by polyps (Table 2).

Regarding the type of small bowel lesions, the most common finding was ulcer

Table 1. Demographic features of patients and clinical indications for DBE (N= 55)

	mean ± SD (range)
Age	47.2 ± 17.3 (13-82)
Hemoglobin (g/dl)	10.3 ± 2.6 (5-16.3)
Blood transfusion (unit)	O.65 ± 1.6 (0-8)
Sex	Percentage (number)
Male	63.6 (35)
Female	36.4 (20)
Indications for DBE	
Chronic abdominal pain	54.5 (30)
Occult obscure GI bleeding	23.6 (13)
Overt GI bleeding	9.1 (5)
Chronic pain and diarrhea	7.3 (4)
Diarrhea	1.8 (1)
Refractory celiac	1.8 (1)
Vomiting	1.8 (1)

Table 2. The DBE findings, final diagnoses, and managements in 55 patients

Lesion/diagnosis	Patient No.	Location	Treatment
Ulcer	12		
Crohn's disease	7	6 Ileum, 1 jejunum,	5 Medical (2 surgery)
Lymphoma	2	Jejunum	Chemotherapy
Nonspecific	3	2 Jejunum, 1 ileum	Conservative
Polyp	5		
Peutz-Jeghers syndrome	3	2 Throughout GI, 1 only jejunum and stomach	Polypectomy
Other polyps	2	1 Ileum, 1 colon	Polypectomy
Stenosis	4		
Diaphragm-like	3	Ileum	Dilation (1 case)
Lymphoma	1	Jejunum	Chemotherapy
Mass	3		
Adenocarcinoma	1	Jejunum	Surgery
GIST	1	Jejunum	Surgery
Leiomyoma	1	Jejunum	Surgery
Telangiectasia	1	Jejunum	APC*
Diverticulum	1	Jejunum	-

*APC, argon plasma coagulation

in 12 cases (46.2%), followed by polyps in 5 (19.2%), stenosis in 4 (15.4%), mass in 3 (11.5%), and telangiectasia and diverticulum in 1 case (3.8%) each.

According to endoscopist assessment and result of pathologic examination, the frequency of final diagnoses was as follows: Crohn's disease in 7 cases (12.7%); nonspecific ulceration, lymphoma, Peutz-Jeghers syndrome, and diaphragm-like lesions each in 3 cases (5.5%); and gastrointestinal stromal tumor, leiomyoma, and adenocarcinoma each in one case.

Logistic regression analyses have shown that each one g/dl increase in the serum hemoglobin level could decrease the chance of diagnosis (OR= 0.7 (95% CI: 0.5-1)). Pain was more predictive than GIB in diagnosis (OR= 5.6 (95% CI: 1-29)), and the number of packed red cells received by patients was not predictive of diagnosis (Table 3).

In 18 cases (32.7%) showed no final diagnosis, In 11 (20%) without significant finding on DBE, the additional workup disclosed other diagnoses such as irritable bowel syndrome (2 cases), biliary stone (2), fasciolosis (1), aplastic anemia (1), leukemia (1), marginal ulcer in a case of previous gasterectomy (1), pain due to diabetic neuropathy (1), partial bowel obstruction by adhesion bands from previous laparotomies (1), and visceral involvement of rheumatoid arthritis (1).

Patient outcomes and complications

Of 26 patients 19 had follow up with small intestinal diseases 3 months after the DBE procedure: in which16 (61.5%) were improved or cured by medical treatments, two cured by surgery (7.4%), and one case with polyps was still symptomatic.

In 14 of 18 cases without definitive diagnosis, 10 were improved, and 3 had symptom; one with abdominal pain and ileal ulcers died two months later.

Bowel perforation occurred after polypectomy in a patient with Peutz-Jeghers syndrome that improved after laparotomy.

Discussion

Overall, the indications for DBE among the three different centers were comparable, especially when we considered both obscure-occult and frank GIB as a possible source of OGIB (p= 0.10). Also, there was

Table 3. Logistic regression analyses to identify predictors for final diagnosis.

	p value	Odds ratio	95% Confidence interval
Hemoglobin level (g/dl)	0.05	0.7	0.5-1
Symptom at presentation♠	0.04	5.6	1-29
Number of transfused packed cell	0.3	0.8	0.5-1.2

♠ Pain and GIB; GIB is reference group

no significant difference regarding the laboratory and imaging results between these centers before DBE procedure.

In other studies, the most common indication to perform DBE was OGIB (3, 7-12); whereas chronic abdominal pain was more common in our patients (54.5%).

We found small bowel lesions in 47.3% of cases with unclear as the most common lesion was ulcer (46.2%). Vascular lesions were the most common lesions in American and European studies, but ulcer was more common in studies from both China and Japan (3, 8-15).

In our series of 55 cases, DBE demonstrated a small intestinal diagnostic rate of 47.3% in this study; which is varied from other studies as 43 to 79% (3, 7, 16). The high diagnostic and especially therapeutic yield (in comparison with other modalities) makes DBE the most efficient endoscopic procedure for the direct inspection of the small intestine.

The most common diagnosis found with this technique was Crohn's disease (12.7%), and the most common neoplasm as lymphoma (5.5%). Prevalence of different diseases varies in different countries, but it seems that lymphoma is more common in Asian and North European than American population (3, 9, 11-13).

Final diagnosis established more commonly in those with abdominal pain than GIB (P=0.04); also, lower hemoglobin level was predictive of the disease (P = 0.05). Other studies have suggested that patients with OGIB is more likely to reach diagnosis (almost 81% for OGIB versus 37% for diarrhea and 38% for abdominal pain) (7, 13).

The incidence of major complications associated with DBE has been reported as nearly 1% including acute pancreatitis (11, 17); we had one perforation after therapeutic polypectomy and no complication after diagnostic procedure with the DBE.

There were several limitations in our study; we only performed oral DBE in most cases because the thin and extremely flexible nature of enteroscope which could only loop into the colon, along with prolonged procedures. Thus we preferred oral approach with deeper insertion into the small intestine, even though this route was occasionally less comfortable to patient compared to the rectal one.

We usually terminated the DBE after finding the first lesion; since it could be found in multiple fashions, it is better that endoscopist inspect the entire small bowel and not be satisfied with finding the first lesion (13). Ulcers in small bowel may be due to lymphoma, tuberculosis, Crohn's disease, and other disease as well. The concordance rate between endoscopic biopsy and postoperative samples in small bowel ulcers was only 57% in one study (13); therefore, care should be undertaken to assign any ulcer in the small bowel to a nonspecific lesion especially in the lack of history of the offending drugs like NSAIDs (1).

Conclusion

The DBE really has been a great success in the management of small bowel disorders. It is time for the development of an algorithm for diagnostic and therapeutic workup of small bowel disorders on the basis of DBE procedure.

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