Double-balloon enteroscopy for obscure gastrointestinal bleeding: A single center experience in China

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AIM: To evaluate the diagnostic value of double-balloon enteroscopy (DBE) for obscure gastrointestinal bleeding (OGIB).

METHODS: The data about 75 OGIB patients who underwent DBE in January 2007-June 2009 in our hospital were retrospectively analyzed.

RESULTS: DBE was successfully performed in all 75 patients without complication. Of the 75 patients, 44 (58.7%) had positive DBE findings, 22 had negative DBE findings but had potential bleeding at surgery and capsule endoscopy, etc. These 66 patients were finally diagnosed as OGIB which was most commonly caused by small bowel tumor (28.0%), angiodysplasia (18.7%) and Crohn's disease (10.7%). Lesions occurred more frequently in proximal small bowel than in distal small bowel (49.3% vs 33.3%, P = 0.047).

CONCLUSION: DBE is a safe, effective and accurate procedure for the diagnosis of OGIB.

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Key words: Double-balloon enteroscopy; Capsule endoscopy; Obscure gastrointestinal bleeding; Diagnosis

INTRODUCTION
Obscure gastrointestinal bleeding (OGIB) is defined as recurrent or persistent gastrointestinal bleeding when gastric and colonic endoscopy is negative[1]. OGIB accounts for approximately 5% of all gastrointestinal bleeding events[2]. Most OGIB events are attributable to small bowel diseases.

The detection and management of small bowel bleeding are a challenge in the past due to the length and ana-
tomical position of small bowel. The diagnostic rate of conventional diagnostic strategies including small intestine radiography, abdominal computed tomography (CT), angiography, and red blood cell scan for small intestine disease is low[8]. Introduction of capsule endoscopy (CE) has significantly revolutionized the study of small bowel as it is a reliable method to evaluate the entire small bowel[9]. However, application of CE in diagnosis of OGIB is limited by the handing controllability, biopsy, endoscopic treatment, retention of capsule in stenosis intestine[10].

Etiological diagnosis of OGIB has been markedly improved with the development of double-balloon enteroscopy (DBE) since 2001[6]. DBE can be performed either through the mouth or through anus, and is thus able to explore a large part of the small bowel. DBE has the advantages including image clarity, handing controllability, biopsy, and endoscopic treatment over CE[7]. It has been demonstrated that DBE is a safe and useful procedure for the diagnosis of small intestinal disease, especially for OGIB[9]. In China, very few data are available on the diagnostic value of DBE for OGIB.

In this study, the data about 75 OGIB patients admitted to our hospital from January 2007 to June 2009 were retrospectively analyzed and the diagnostic value of DBE for OGIB was evaluated.

MATERIALS AND METHODS

Patients
DBE was performed in 75 OGIB patients (37 males, 38 females, at a mean age 51.5 ± 16.6 years, range 16-86 years) admitted to our hospital in January 2007-June 2009. Melena, hematemesis, hemafecia, and fecal occult bleeding were detected in the patients enrolled in this study. The duration of symptoms ranged 1 d-over 10 years. The causes of OGIB were expressed as mean ± SD. Difference was detected by χ² test. P < 0.05 was considered statistically significant.

DBE system
OGIB was detected in patients using a Fujinon enteroscope (EN450-P5/20, Fujinon Inc, Saitama, Japan) consisting of a mainframe, an enteroscope, an overtube, and an air pump. Two soft latex balloons that can be inflated and deflated are attached to the tip of enteroscope and overtube. The balloons are connected to a pump through an air channel in the endoscope that can automatically modulate the air according to the different balloon pressures. By utilizing the overtube in combination with serial inflation and deflation of the balloons, endoscope can be inserted into the small bowel.

Preoperative preparation
The patients were fasted overnight and 2 boxes of polyethylene glycol electrolyte mixed with 3000 mL water were taken 4-5 h prior to DBE through anus or mouth. At the same time, 5-10 mg of midazolam and 10 mg of scopolamine butylbromide were also injected intramuscularly 10 min before DBE. The patients were anesthetized with 10 mL of oral 2% lidocaine hydrochloride before DBE through mouth. Oxygen was inhaled with electrocardiography monitored when necessary.

Procedure
DBE through mouth or anus was performed according to the suspected site of lesions. When the site was uncertain, DBE was performed through mouth.

DBE was not performed when the cause of bleeding could be explained, the operation time was too long to be tolerated, and more than half of the small intestine examined was negative.

Statistical analysis
Statistical analysis was performed using SPSS 11.5. Data were expressed as mean ± SD. Difference was detected by χ² test. P < 0.05 was considered statistically significant.

RESULTS

General information
DBE was performed 84 times in 75 patients, including 57 times through mouth and 27 through anus. Two patients completed DBE of the entire small bowel through mouth at one time.

All the procedures were successful without anesthesia. No hemorrhage, perforation, acute pancreatitis or other serious complications occurred. Nausea, vomiting, abdominal distension, and abdominal pain occurred in some patients during the procedure. However, these symptoms were transient and tolerable. In general, DBE through anus was more tolerable than through mouth.

DBE findings
Of the 75 patients, 44 (58.7%) had positive DBE and 22 had negative DBE with potential bleeding sites observed at surgery and CE, etc. The distribution of OGIB patients

| Characteristics | n = 75 |
|-----------------|-------|
| Age (yr)        | 51.5 ± 16.6 (16-86) |
| Sex (male/female)| 37/38 |
| Causes of OGIB  |       |
| Melena          | 45 (60.0) |
| Hematemesis and melena | 7 (15.6) |
| Hemafecia       | 17 (22.7) |
| Occult bleeding | 6 (8.0) |
| Duration of symptoms (mo) | |
| < 1             | 29 (38.7) |
| 1-12            | 24 (32.0) |
| > 12            | 22 (29.3) |

OGIB: Obscure gastrointestinal bleeding.
Table 2  DBE findings in OGIB patients

| Lesion                  | Diagnosed by DBE | Diagnosed by other methods | Location                     | Difference in proximal and distal small bowel |
|-------------------------|-------------------|----------------------------|------------------------------|-----------------------------------------------|
|                         | (n = 75)          | (n = 44)                   | Stomach and duodenum         |                                               |
|                         |                   |                            | Jejunum                      |                                               |
|                         |                   |                            | Ileum                        |                                               |
| Tumor                   | 17                | 4                          | 3                            | 14                                            | 4       |
| Gastrointestinal stromal tumor | 7       | 1                          | 1                            | 6                                             | 1       |
| Non-hodgkin lymphoma    | 2                 | 3                          | 0                            | 3                                            | 2       |
| Adenocarcinoma          | 3                 | 0                          | 1                            | 1                                            | 1       |
| Lipoma                  | 3                 | 0                          | 0                            | 3                                            | 0       |
| Brunner adenoma         | 1                 | 0                          | 1                            | -                                            | -       |
| Angioma                 | 1                 | 0                          | 0                            | 1                                            | 0       |
| Angiodysplasia          | 7                 | 7                          | 1                            | 9                                            | 4       |
| Crohn's disease         | 7                 | 1                          | 0                            | 2                                            | 6       |
| Diverticulum            | 3                 | 2                          | 0                            | 4                                            | 1       |
| Henoch-Schönlein purpura| 4                 | 0                          | 0                            | 2                                            | 2       |
| Single ulcer            | 0                 | 4                          | 0                            | 1                                            | 3       |
| Others                  | 7                 | 5                          | 3                            | 3                                            | 4       |
| Un-diagnosed            | 0                 | 9                          | -                            | -                                            | -       |
| Total                   | 45                | 32                         | 7                            | 36                                           | 24      |

66.7% vs 19.0% (P = 0.002)

64.3% vs 28.6% (P = 0.128)

33.3% vs 66.7% (P = 0.132)

49.3% vs 33.3% (P = 0.047)

One case was accompanied with ancylostomiasis; One case was accompanied with heterotopic pancreas. DBE: Double-balloon enteroscopy.

Figure 1  Distribution of obscure gastrointestinal bleeding (OGIB) patients enrolled in this study. DBE: Double-balloon enteroscopy.

75 OGIB patients (nondiagnostic gastroscopy and colonoscopy)

DBE was performed (n = 75)

Not diagnosed with DBE (n = 31)

Further examinations (surgery, capsule endoscopy, etc.)

Diagnosed with DBE (n = 44)

Surgery (n = 18)

Positive diagnosis (n = 22)

Negative diagnosis (n = 9)

Follow-up

OGIB was most commonly caused by small bowel tumor (28.0%, 21/75), angiodysplasia (18.7%, 14/75) and Crohn's disease (10.7%, 8/75). Small bowel tumor was detected in duodenum of 3 cases, in jejunum of 14 cases, and in ileum of 4 cases, respectively. The incidence of small bowel tumor was higher in jejunum than in ileum (66.7% vs 19.0%, P = 0.002). Histological analysis showed that the tumor was benign in 7 cases (gastrointestinal stromal tumor in 2, lipoma in 3, duodenum adenoma in 1 and angiomma in 1) and malignant in 14 cases (gastrointestinal stromal tumor in 6, non-hodgkin lymphoma in 5 and adenocarcinoma in 3) (Figure 1). The detection rate of benign tumor was lower than that of malignant tumor (33.3% vs 66.7%, P = 0.031).

Angiodysplasia was detected in jejunum of 9 cases, in ileum of 4 cases, and in duelafy of gastric fundus of 1 case, respectively, accounting for 18.7% of all the cases with no significant difference between them (P = 0.128).

Crohn's disease was detected in jejunum and ileum of 2 and 6 cases, respectively, accounting for 10.7% of all the cases with no significant difference (P = 0.132). In addition, diverticulum, Henoch-Schönlein purpura, single ulcer, polyp, ancylostomiasis, tuberculosis, and non-specific inflammation were also detected (Figure 2).

DBE detection rate of bleeding and duration of symptoms

Of the 75 cases, 45 presented with melena and 25 (55.6%) with positive DBE. Symptoms of hemafecia were detected in 17 cases with a DBE detection rate of 47.1% (8/17). There was no significant difference between the DBE detection rates of melena and hemafecia (55.6% vs 47.1%, P = 0.55). The DBE detection rates of occult bleeding, hematemesis and melena were not compared because of the limited number of cases.

The 75 patients were divided into 3 groups according to their bleeding time. There was no significance between the duration of OGIB symptoms and the DBE detection rates (Table 3).

Operation results

Of the 75 patients, 18 (24.0%) underwent operation. Gastrointestinal stromal tumor, non-hodgkin lymphoma, adenocarcinoma, lipoma and angionioma were the most commonly detected tumors. Both gastrointestinal stromal tumor and bleeding from heterotopic pancreas were detected in 1 patient.
OGIB is a common problem encountered by gastroenterologists. Its diagnostic rate has been greatly improved due to CE since 2000[9]. CE has a higher diagnostic rate of OGIB than conventional methods including small bowel barium radiography, push enteroscopy, and cross-sectional imaging[10]. However, CE may fail to identify lesions such as Meckel’s diverticulum, angiodysplasia, and malignancies[11]. DBE can explore a large part of the small bowel, during which targeted tissue for biopsy can be taken. Moreover, endoscopic treatment procedures, including hemostasis, polypectomy, endoscopic mucosal resection, balloon dilation, and stent placement, can be performed at DBE[12].

In this study, the diagnostic value of DBE for OGIB was evaluated. The DBE detection rate of OGIB is consistent with the reported data[13,14]. No complication occurred in the 75 patients who underwent DBE without anesthesia, suggesting that DBE is a safe, tolerable, and effective procedure for the diagnosis of OGIB.

It was reported that 3%-6% of OGIB events are caused by small bowel tumor[15,16]. Sun et al[17] showed that the prevalence of gastrointestinal stromal tumor is the highest among different small bowel tumors. DBE can show lesions in about 50%-66% of the small intestine and even in the entire small intestine, thus providing a high diagnostic rate of small bowel tumor[18].

In this study, angiodysplasia was found to be another common etiology of OGIB, which is also in agreement with the reported data[19]. The detection rate of lesions was higher in jejunum than in ileum. Since Crohn’s disease has been found to be the third commonest etiology of OGIB, and shows a higher incidence in distal intestine, DBE via anus is usually recommended[20].

The selection of DBE is still controversial. For those with no site of lesion indicated, DBE through mouth is preferred because our study and other studies showed that it has a higher diagnostic rate of lesions in proximal small bowel[21,22] and is relatively easier to perform without twisting the colon, which is also supported by Safatle-Ribeiro et al[23]. However, DBE through anus is also preferred by some endoscopists, since it has a better tolerance[18].

In summary, DBE is a safe, tolerable, accurate and effective procedure for the diagnosis of OGIB. OGIB is most commonly caused by small bowel tumor and angiodysplasia. Lesions occur more frequently in proximal small bowel and DBE through mouth is recommended as a prior consideration if no evidence indicates the location.
COMMENTS

Background
The diagnosis of obscure gastrointestinal bleeding (OGIB) was rather difficult in the past. Double-balloon enteroscopy (DBE) and capsule endoscopy (CE) have significantly revolutionized the diagnosis of small bowel lesions. Compared with CE, DBE has unique advantages such as handling controllability, biopsy, diagnosis and treatment, etc. Few data are available on the diagnostic value of DBE for OGIB.

Research frontiers
The data about 75 OGIB patients were retrospectively analyzed in this article. The DBE detection rate of OGIB and the feasibility of operation were evaluated. The incidence of common diseases in small bowel was compared. The DBE detection rate of lesions in proximal or distal small bowel was different.

Innovations and breakthroughs
Patients could tolerate the whole DBE process with no serious complication. The DBE detection rate of different bleeding events and symptoms of OGIB were compared. DBE through mouth was completed at one time.

Applications
In this study, DBE was proven to be a safe, accurate and effective procedure for the diagnosis of OGIB and can thus be performed in hospital for the diagnosis of OGIB.

Terminology
OGIB is defined as recurrent or persistent gastrointestinal bleeding when gastric and colonic endoscopy is negative. DBE and CE are both new methods enabling diagnostic endoscopy of the entire small intestine, which have their own pros and cons in the diagnosis of small bowel diseases.

Peer review
This is an interesting descriptive study concerning a single center experience with DBE for OGIB in China.

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S-Editor Tian L. L-Editor Wang XL. E-Editor Zheng XM