

Outcomes of Double Balloon Enteroscopy for Managing Overt Small Bowel Bleeding

Ankit Dalal¹ Gaurav Patil¹ Amit Maydeo¹

¹Baldota Institute of Digestive Sciences, Gleneagles Global Hospital, Mumbai, Maharashtra, India

Address for correspondence Ankit Dalal, MBBS, MD, DNB, Baldota Institute of Digestive Sciences, Gleneagles Global Hospital, Mumbai 400012, Maharashtra, India (e-mail: ankit.dalal@gmail.com).

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Abstract

Background The commonest therapeutic indications for double balloon enteroscopy (DBE) includes removal of retained video capsules, dilatation of strictures, polypectomy, and managing obscure small bowel bleeding. We review our experience in managing active small bowel bleeding with DBE.

Methods A retrospective review was done for all the cases undergoing DBE from August 2017 to July 2019. Patient follow-up data was collected.

Results Among 25 cases with a median age of 46.8 (range 25–65 years), 17 males (68%) underwent DBE for suspected small bowel bleeding. The commonest presenting complaint was melena 19 (76%). The findings were positive (diagnostic yield) in 18 (72%) patients with an antegrade approach. Active bleeding was associated with Dieulafoy's lesion ($n = 6$), gastrointestinal stromal tumors (GIST) ($n = 4$), jejunal varices ($n = 3$), angioectasia ($n = 3$), and ulcer ($n = 2$), who then underwent successful intervention. The rest of the patients underwent both antegrade and retrograde approach but failed to immediately identify an alternative diagnosis. Mean (standard deviation [SD]) time taken for antegrade enteroscopy was 96.7 (15.3) mins and 67.8 (13.6) mins for retrograde enteroscopy. The median duration between the last bleeding episode and timing of DBE was 9 (range 6–15 hours). No major complications were seen during or immediately postprocedure.

Conclusion DBE is useful in identifying and treating active small bowel bleeding. Being invasive and time-intensive, it is easy to miss lesions and, therefore, needs appropriate expertise. DBE does appear to be relatively cheaper, with better patient acceptance and time saving.

Keywords

- ▶ double balloon enteroscopy
- ▶ small bowel
- ▶ anemia
- ▶ gastrointestinal bleeding
- ▶ outcomes

Introduction

With advances in endoscopic techniques and availability of double balloon enteroscopy (DBE), the mucosa in small bowel can be visualized in a more efficient manner.¹ Prior to the advent of enteroscopy, there was a delay in diagnosis and therapy of pathological conditions involving the small bowel, thereby withholding appropriate management. Conditions involving the small bowel need adequate expertise as the signs and symptoms are minimal. Since early 2002, with more than a decade of experience, DBE has been widely used for small bowel evaluation using the antegrade

and/or retrograde approach.^{2–4} Indications for DBE includes taking targeted biopsies, therapy for bleeding lesions, foreign body removal, dilatation of strictures, polypectomy, or when capsule endoscopy (CE) is contraindicated.⁵ Presently, CE has only diagnostic role. On the other hand, DBE has diagnostic and therapeutic ability, but it is invasive and requires appropriate sedation. CE is time consuming and patients need to subsequently undergo an enteroscopy for any lesion found.⁶ This may lead to loss of precious time in patients with active small bowel bleeding and increase in overall cost. Managing small bowel bleeding requires a multidisciplinary approach and enteroscopy plays an important role. We present this

2-year case series with technical tips of managing an active small bowel bleeding with DBE without CE.

Methods

A retrospective review of a prospectively maintained database was performed for all the cases undergoing DBE at a tertiary care referral center between August 2017 to July 2019. The study conforms to the ethical guidelines of the 1975 Declaration of Helsinki (7th revision, 2013). The conduct of this study was approved by the Institutional Ethics Committee. Waiver of informed consent was obtained for the study. All patients were adults and had previously given their written informed consent for the procedure.

Patients Selection

Records of all patients undergoing DBE were evaluated. Out of these, patients with active gastrointestinal (GI) bleeding in the form of melena or fresh bleeding per rectum with a normal esophagogastroduodenoscopy (EGD) and colonoscopy were included in this study for analysis. These patients with suspected active small bowel bleeding had undergone DBE without prior CE. Patients who underwent DBE for other indications were excluded from the final analysis. The demographic details, procedural indications, and clinical and physical findings of all the patients were extracted from their case record files. All patients were hospitalized and underwent routine laboratory investigations. Hemodynamic stability was ensured prior to DBE. Packed cell transfusions had been given to those with a low-hemoglobin (Hb) count to maintain Hb more than 8.0 g/dL. Contrast-enhanced CT of the abdomen with angiography was done in all patients prior to a DBE.

The usual plan for upper GI bleed at our center is EGD, followed by colonoscopy. If negative, we do CT scan of abdomen followed by DBE or CE. We preferred to initiate with an antegrade approach at our center. Melena is the indication for antegrade DBE. At our center, we do retrograde only when antegrade approach has failed to identify any pathology. Eight hours of fasting for antegrade was considered necessary. Colonoscopy preparation was given to all patients, keeping in mind the possibility of requiring the retrograde approach as well. Patients were advised not to eat any colored foods a day prior to DBE. Management of patients was done as described under the guideline for enteroscopy.⁷ Actively bleeding lesions found at DBE were managed with interventions such as argon plasma coagulation (APC), hemoclips, *n*-butyl cyanoacrylate glue injection, or dilute epinephrine injection. Procedures were done by a single endoscopist with an experience of >300 enteroscopy procedures. Statistical analysis was done with SPSS (v.23.0, Chicago, USA). Descriptive statistics was used as appropriate.

Anesthesia Care

Vascular access was secured in all patients via peripheral vein. Total intravenous anesthesia was used in the form of opiates (nalbuphine, butorphanol), anticholinergics (glycopyrrolate).

Sedation was maintained with continuous/intermittent injection of propofol.

Procedure–Technical Tips

A DBE (EN-580T, Fujifilm, Japan)⁸ attached to high-definition digital video processor (VP-4440HD) with flexible spectral imaging color enhancement and 300-W xenon light source (XL-4450) was used. This has a 200 cm long insertion tube and a 3.2 mm working channel along with an overtube (TS13140), which helps in positioning of the endoscope in the small bowel. The overtube is inserted, while the endoscope balloon is inflated. The ST-10 setting tool enables smooth attachment of rubber bands when setting the balloon onto the DBE. The two latex balloons (one at the end of the endoscope and the other at the end of the tube) were controlled with an electronic balloon pump controller (PB-30, Fujinon, Japan) and peripheral remote control switch. Controlling the amount of balloon dilation and contraction helps to perform test smoothly. The enteroscope could be moved back and forth in a controlled manner by the endoscopist with an assistant to visualize the small bowel. Air insufflation was used during examination. Use of air during enteroscopy can lead to distension and difficulty in continuing the procedure. In cases with prolonged procedure time, or when the need of retrograde endoscopy was anticipated, we overcame it by reducing the air flow and using water irrigation with a syringe. Fluoroscopic guidance was used to verify direction of the rotation of the scope in rare cases. We marked the small bowel with injection of methylene blue during the antegrade approach, when the scope could not be advanced any further. Pan enteroscopy was successful when this point was visualized during the retrograde approach. The retrograde endoscopy was undertaken immediately in the same sitting. The Yano–Yamamoto classification was used to identify vascular lesions of small bowel.⁹

Results

One hundred and twelve DBEs had been performed over the past 2 years. A total of 25 (22.3%) patients had undergone DBE for suspected active small bowel bleeding without a prior CE. There were 17(68%) male patients with a median age of 46.8 (range 25–65) years. All patients had a normal gastroscopy. Presence of altered blood was noted during colonoscopy, but no pathology was found. Contrast-enhanced CT of the abdomen showed presence of jejunal varices in three patients, jejunal polypoid lesion in two, and wall thickening in five patients. No contrast extravasation was seen in any patients. In view of the ongoing blood loss, a prior CE was not performed in these cases and patients underwent an enteroscopy directly. The findings were positive in 18 (72%) of the patients. These findings were noted during the antegrade approach. One patient had undergone a previous hepaticojejunostomy. Others had not undergone any previous surgery. During enteroscopy, active bleeding was associated with small bowel Dieulafoy's lesion (DL) ($n = 6$), gastrointestinal stromal tumor (GIST) ($n = 4$), jejunal

varices ($n=3$), angioectasia ($n=3$) and ulcer ($n=2$), which then underwent successful interventions. Retrograde enteroscopy was performed subsequently in those seven patients with a negative antegrade DBE. Pan enteroscopy was achieved in 4/7 (57.1%) patients. No lesion was identified in these patients. One of these seven patients had history of using nonsteroidal anti-inflammatory drugs (NSAIDs) which could have led to drug-induced enteropathy and possible GI bleeding. For the other six patients, no cause was identified (►Fig. 1). All patients were stable at follow-up without any further episodes of GI bleeding. Mean (SD) time taken for antegrade enteroscopy was 96.7 (15.3) mins and 67.8 (13.6) mins for retrograde enteroscopy (►Table 1). The median duration between the last bleeding episode and timing of DBE was 9 (range 6–15 hours). No major complications like bleeding, perforation or pancreatitis were seen immediately after the procedure. Six (24%) patients had postprocedural abdominal distension and pain which was managed conservatively.

Scenario 1—Managing Dieulafoy's Lesion (DL)

Six patients at DBE had DL. There were five (83.3%) male patients and the median age was 50 years. The presenting complaint was melena in all patients, with four (66.7%) patients requiring blood transfusion. None had prior history of NSAIDs or antiplatelet use. Altered blood was seen in all patients when enteroscope was in proximal-to-mid jejunum.

DL was seen in proximal jejunum ($n=2$) and mid jejunum ($n=4$). These lesions appeared as punctuate lesions measuring <1 mm with active pulsatile bleeding (Type 2a). Water irrigation by an accessory was used to visualize the bleeding lesion with accuracy. Diluted epinephrine (1:20000) was injected at the surface of these lesions. Hemostasis was achieved with APC, followed by application of hemoclips. Olympus rotary reusable delivery system, HX-110UR (2300 mm in length) with an EZ clip was used. Medorah clips were also used in some patients. Hemostasis was achieved in all patients, and they had a quick recovery with no further episodes of bleeding (►Fig. 2 a, b, c).

Scenario 2—Managing Gastrointestinal Stromal Tumor (GIST)

Three patients, two males (66.7%), who underwent DBE had a submucosal lesion with surface ulceration and stigmata of a recent bleed. The appearance was suggestive of a small bowel GIST (►Fig. 3 a, b). Their median age was 58 years. Majority of them presented with melena and one patient with hematochezia. One patient required blood transfusion prior to the procedure. These lesions were seen in proximal jejunum in two patients and in midjejunum in the third patient. The largest lesion measured 3 cm. An endoloop was placed at the base of the lesion and tightened until signs of tissue congestion were noticed. Multiple biopsies were taken from this

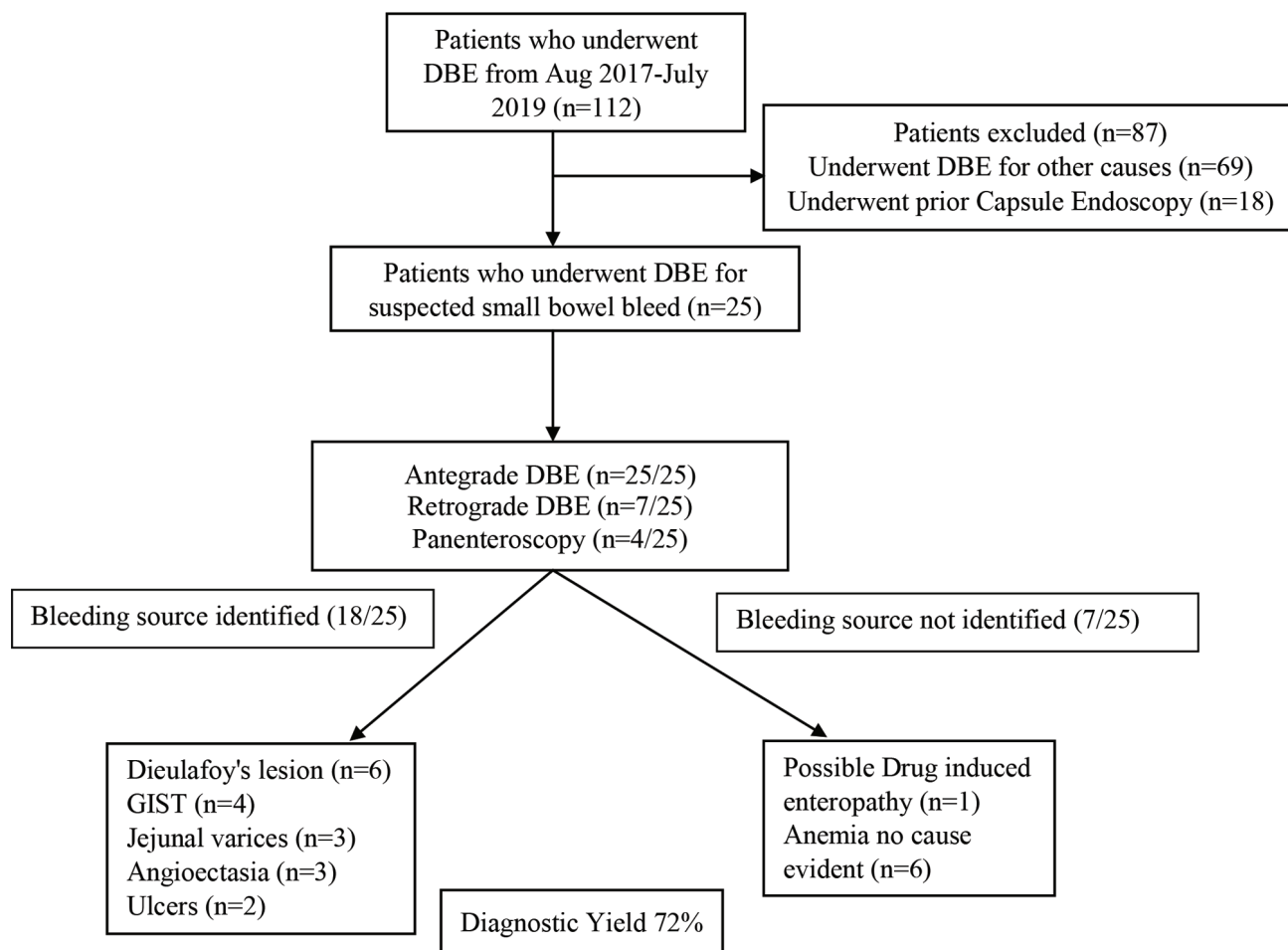


Fig. 1 Shows study flowchart.

site. These patients were subsequently referred for surgical excision. DBE diagnosis of GIST obtained using biopsies was reconfirmed by histopathology examination.

Table 1 Shows patient characteristics

Parameters	N (%)
Total DBE	112
DBE without prior capsule	25 (22.3)
Median age (years)	46.8 (range 25–65)
Male	17 (68)
M:F	2.1:1
Presenting Complaint#	
Pain abdomen	7 (28)
Melena	19 (76)
Hematochezia	6 (24)
Weight Loss	3 (12)
Approach	
Antegrade	18 (72)
Antegrade + retrograde	7 (28)
Pan enteroscopy completed	4 (57.1)
Diagnosis	
Dieulafoy's lesion	6 (24)
GIST	4 (16)
Jejunal varices	3 (12)
Angioectasias	4 (16)
Small bowel ulcer bleed	2 (8)
Mean (SD) procedure duration (mins)	
Antegrade	96.7 (15.3)
Retrograde	67.8 (13.6)
Mean procedure extent (cm)	
Antegrade	156.5 (22.7)
Retrograde	85.1 (12.3)
Interval (median in hrs) between the last bleeding episode and timing of DBE.	9 (range 6–15)

Some patients may have multiple presenting complaints and indications
Abbreviations: DBE, double balloon enteroscopy; GIST, gastrointestinal stromal tumor; SD, standard deviation.

Scenario 3–Managing Jejunal Varices

Three patients, two females (66.7%), who underwent DBE had jejunal varices. Patients had underlying extrahepatic portal vein obstruction. One patient had undergone a hepaticojejunostomy previously for bile duct stricture. Hematochezia was the presenting complaint in all patients, and they required multiple blood transfusions. Gastroscopy showed small esophageal varices and no gastric varices. Their median age was 37 years. A contrast CT of the abdomen showed presence of jejunal varices in all three but did not reveal any active bleeding. Jejunal varices were seen in proximal jejunum ($n = 2$), and at the anastomotic site of hepaticojejunostomy in one patient. One patient developed active spurting at the time of DBE. All patients were injected with *n*-butyl cyanoacrylate glue without any adverse events (►Fig. 4 a, b). Their follow-up was uneventful.

Scenario 4–Managing Angioectasia

Four patients, males ($n = 4$), who underwent DBE had angioectasia. Their median age was 41.5 years. Melena was the presenting complaint in all patients. Angioectasias were seen in proximal and midjejunum (►Fig. 5 a, b). They appeared as punctuate erythematous lesions measuring <1 mm (Type 1a). One patient had active ooze while the others did not have any active bleeding. APC was done in all patients to eradicate angioectasia, and hemostasis was achieved. No major complication was encountered during the procedure.

Scenario 5–Ulcer-related Bleeding

Two patients, males ($n = 2$), had an ulcer-related bleed. DBE showed multiple discontinuous linear ulcers throughout the distal jejunum in one patient (45 years), and discrete ulceration in the terminal ileum in the other patient (53 years) (►Fig. 6). The ulcers showed stigmata of a recent bleed. Hemostasis was achieved using coagulation grasper forceps and hemoclip application. Histopathology confirmed the presence of Crohn's disease (CD) in the former. The patient received treatment with controlled-release mesalamine and azathioprine.

Follow-up–Patients with GIST, who had endoloop placement, underwent resection for the GIST. In patients with angioectasia, two developed repeat bleeding after few weeks,

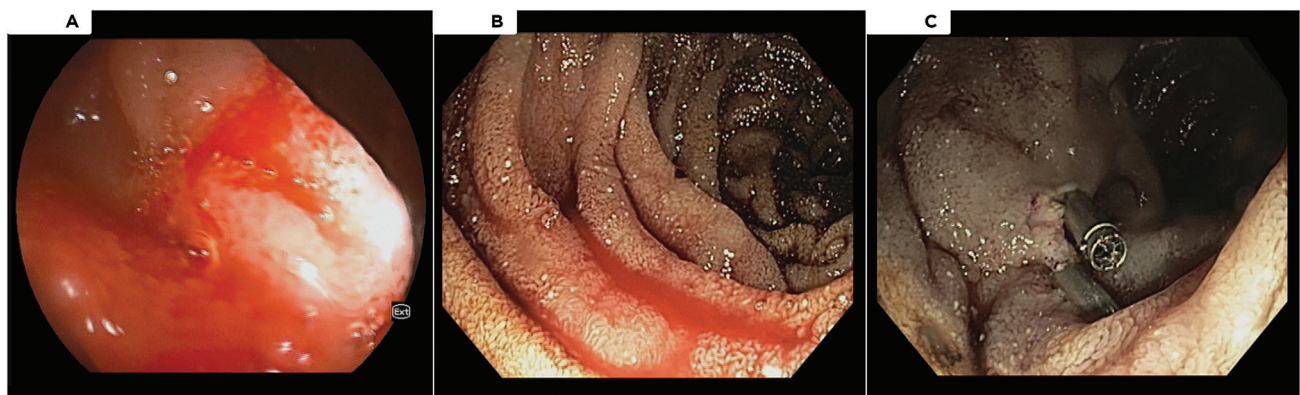


Fig. 2 (A, B, C) shows bleeding from Dieulafoy's lesion and hemoclip applied to it.

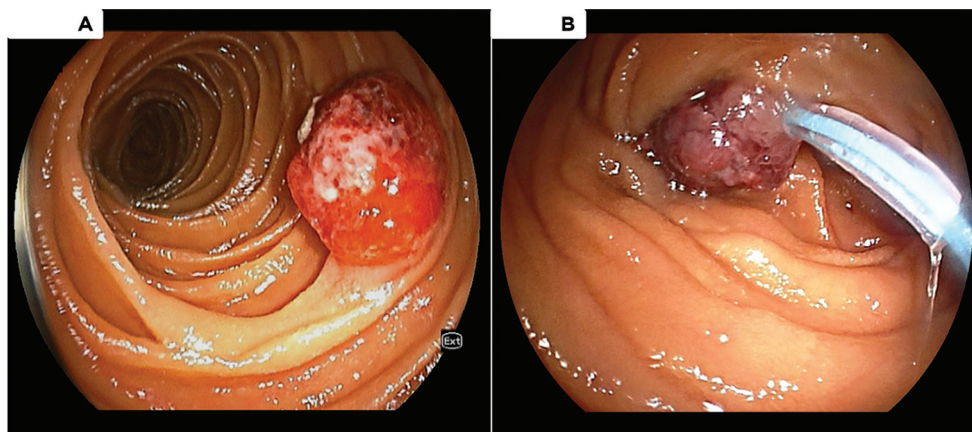


Fig. 3 (A, B) shows gastrointestinal stromal tumor in the small bowel and endoloop applied to it.

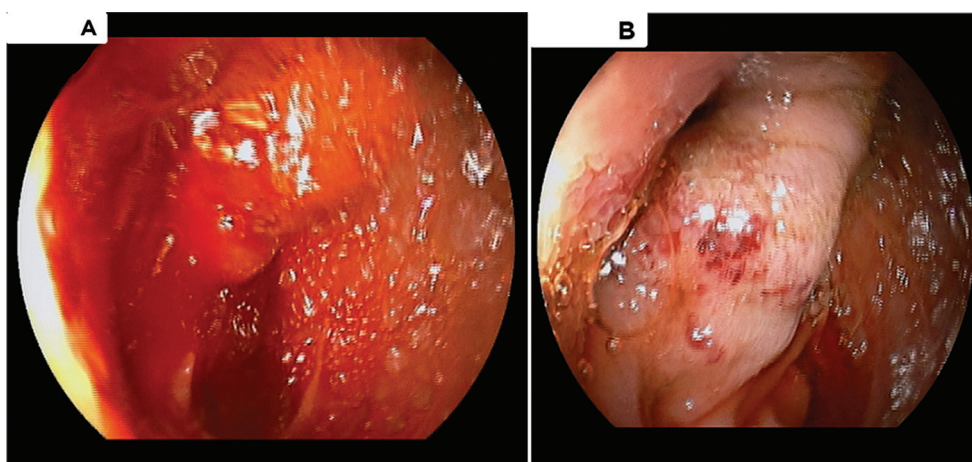


Fig. 4 (A, B) shows bleeding jejunal varices and cyanoacrylate glue injected into the varix.

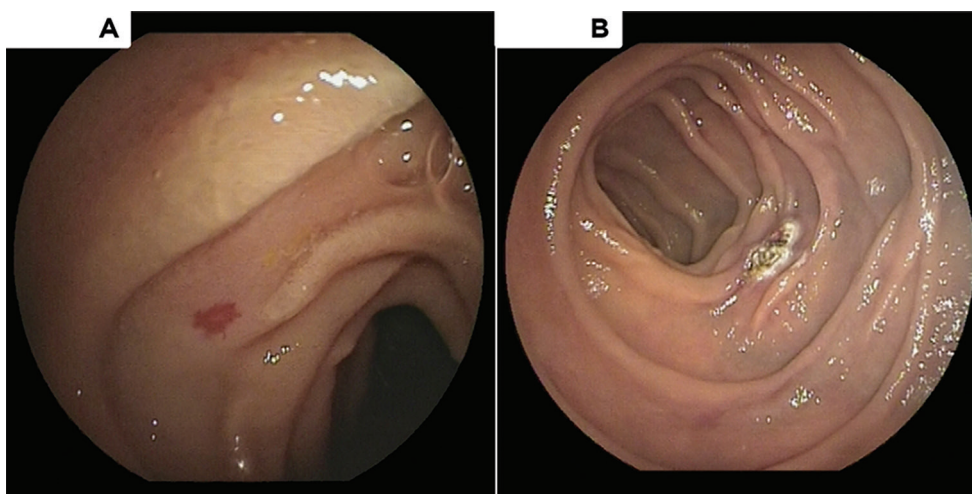


Fig. 5 (A, B) shows angioectasia and subsequent APC. Abbreviation: APC, argon plasma coagulation.

so repeat DBE and APC was done. Patients with varices did not have bleeding. Patient with CD was stable on immunosuppressants. Six (24%) DBE negative patients with unclear etiology of bleeding were followed-up clinically. Of these six patients, three developed repeat small bowel bleeding who underwent evaluation by DBE to reveal angioectasias

in small bowel which were treated successfully with APC. Among those who underwent DBE, angioectasias ($n = 2$) were seen in patients who had undergone antegrade DBE. While bleed was also seen in ($n = 1$) one patient who had undergone panendoscopy. The remaining three did not have any drop in hemoglobin.

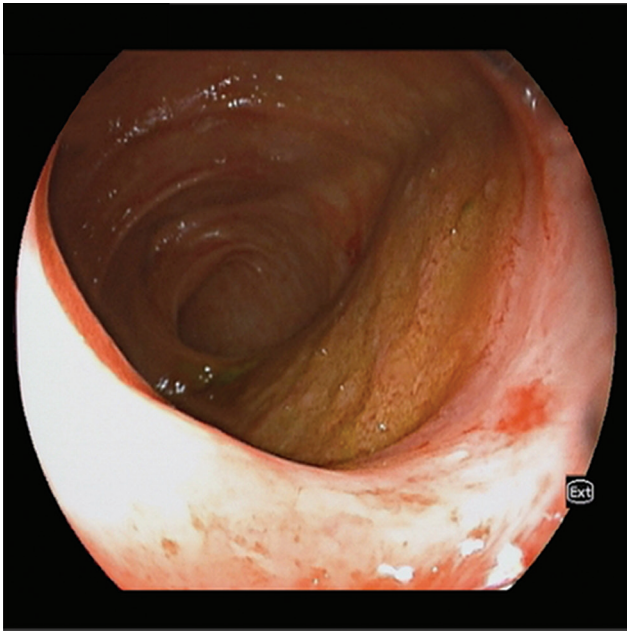


Fig. 6 Shows ileal ulcer.

Discussion

By retrospectively reviewing the endoscopic database, we studied the utility of DBE in managing active small bowel bleeding. DBE helps in the diagnosis and treatment of small bowel pathological conditions, and in majority of the cases, it reduces the need for immediate surgical interventions.¹⁰ A total of 112 DBE were performed over a period of 2 years, out of which 25 patients had undergone DBE without a CE for active small bowel bleeding. Eighteen (72%) of those patients in our study showed positive findings (DL, GIST, jejunal varices, angioectasia, ulcers) at DBE. To the best of our knowledge, this is first of such case series for active small bowel bleed from the Indian subcontinent.

More than 80% of DL have been seen in the stomach. However, they have also been seen in other parts of digestive system.¹¹ It is difficult to visualize them in the small bowel due to its length, contractility, and location. Due to the intermittent bleeding, diagnosis of DL at index endoscopy can be only up to 70%.¹² Mortality rates with DL are as high as 8%.¹³ APC, adrenaline injection, clipping, or banding is useful in 90% of cases.¹⁴ Some need angiography with embolization or resection at surgery. However, our patients recovered with endoscopic therapy and did not need any further interventions.

GIST are mesenchymal neoplasms that accounts for 0.1 to 3% of all GI neoplasms.¹⁵ The commonest site is stomach (60–70%), followed by the small intestine (25–35%). The commonest symptom is GI bleeding, which is seen in half of the patients, followed by pain abdomen in 20 to 50% and GI obstruction in up to 30% patients.¹⁶ Patients can have melena, abdominal fullness, and palpable mass. They can metastasize to the liver but rarely other organs. The detection rates for DBE, CE and CT were 92%, 60% and 67%, respectively.¹⁷ This shows that DBE is more useful than the rest, as seen

with our cases. Endoloop application at the time of endoscopy to strangulate the lesion is effective and can control bleeding.^{18,19} Subsequently surgical resection is the treatment of choice for small bowel GIST.

Angioectasias are seen in the elderly which undergo appropriate management with APC during DBE. They are commonly seen in jejunum (80%).²⁰ Anemia is the commonest indication in them. Vascular lesions are more common in the elderly. These results are concordant with our findings. APC is the most common method to treat these lesions via endoscopic therapy.²¹ DBE is superior to radio diagnosis for aphthous ulcers, erosions, and ileal ulcers.²² Ileal lesions proximal to the terminal ileum were found in 53.3% of patients with CD.²²

A prior CE helps in guiding the approach for enteroscopy. When this information is unavailable, antegrade DBE has been found to be more effective than retrograde for evaluating suspected small bowel disease.² In this study, the diagnostic yield was better with the antegrade approach without the use of CE. Safety and clinical outcomes were comparable as well using this approach. DBE has been found to be therapeutically beneficial, and overall positive yield was 65 to 82% in recent years.^{23–25} We could achieve a positive diagnostic and therapeutic yield of 72%. However, this may be due to the smaller number of patients in the current study as well as the presence of active bleeding. Mean procedural duration (min) with antegrade approach was 97 minutes and 68 minutes via the retrograde. The time utilized in our study for these procedures is way too less as compared with studies across the world.^{26,27} During antegrade enteroscopy, we proceeded till the limit of the scope, and once the bleeding source was identified, appropriate management was done. As a bleeding source was found at the antegrade approach, we decided to clinically follow-up these patients instead of performing a pan enteroscopy at the same time. Patients were better after these procedures, which indirectly suggests that these patients would have had these lesions in the proximal part of small intestine. Only in cases where we did not encounter any pathology, did we go in with a retrograde approach. It is indeed possible, to a very less extent, that there may be some lesions distally. We need to keep in mind that these are very sick patients and doing an additional procedure can sometimes be risky without optimal benefit.

Bleeding from small bowel accounts to approximately 5% of the overall cases with GI bleeding.²⁸ Complications have occurred in DBE, consisting of bleeding, perforation after polypectomy of large polyps, segmental enteritis after APC, and pancreatitis.^{29,30} However, we did not encounter any major complications, and feel this procedure is safe if performed under experienced hands. It is vital to perform this procedure quickly, although with adequate bowel visualization. It seems that increase in the total duration of the procedure time might increase the chances of adverse outcomes, although no substantial evidence is available to the contrary. Six patients (24%) in this study were in the elderly age group. We found that DBE can be done with adequate safety in the elderly population without complications. These results are in line with results across the world.^{31,32}

There is certain degree of diagnostic uncertainty with CE. One cannot steer a capsule, flush or suction, or obtain tissue samples for histopathological examination. Additionally, it is time consuming, video needs to be reviewed, and it is not available at all places. In a recent systematic review, the sensitivity of DBE was 84% and the specificity was 92% in the diagnosis of small bowel bleed, but there was significant heterogeneity among the included studies.³³ It mentioned that by performing DBE after CE, the diagnostic yield of identifying vascular lesion increased to 90%. However, we feel that patients with suspected active small bowel bleeding need immediate intervention; hence, getting a capsule endoscopy would result in wastage of the limited time at hand as well contribute to additional cost of management. Since majority of these studies were conducted retrospectively, it would be inappropriate to comment on its inference. Indeed, we need many more studies wherein radiological findings need to be compared with CE and DBE in a prospective manner to draw definitive conclusion, leading to superiority of one over the other. Also, premedication with mucolytic and defoaming agents³⁴ might add to superior mucosal views but needs additional studies. The polypoidal lesions identified in CT helped in managing GIST. However, CT was not much useful in other cases. DBE, not preceded by CE or angiography, has been proposed as a first-line procedure in occult massive bleeding, while ESGE recommends an emergency CE and DBE to be equally effective.³⁵ Spiral enteroscopy and DBE both have their own advantages and disadvantages. It is vital to choose the right device for the appropriate indication based on individual experience.³⁶ With spiral enteroscopy, there is a shorter procedural time, but it needs two operators. The motorized, spiral enteroscope has a motor attached to the handle of the scope which accelerates the procedure and fastens movement without the need for additional operator.³⁷

The present study does have its limitations. One such shortcoming arises from the chosen study design of retrospective nature. The quality of evidence for such studies is low. Results are from a single center and single observer; hence, generalizing these will not be appropriate. Selection bias could not be eliminated. Seven patients in our study had no pathological finding during DBE. This highlights the limitations clinicians persistently face in managing small bowel diseases. Nevertheless, this case series is unique, since this was targeted to extract data for active bleeding which is currently unexplored.

The current role of DBE looks very promising in identifying and treating lesions of the small bowel. With refinement in technology and the recent introduction of a motorized, spiral enteroscopy, we should be able to finish this procedure quickly. The visualization indeed needs improvement to pick up smaller lesions which can be missed during routine procedures.

Author Contributions

Concept–A.D.; Design–A.D.; Supervision–A.D., G.P.; Data Collection and/or Processing–A.D., G.P., A.M.; Literature Review–A.D.; Writing–A.D.; Critical Reviews–A.M.

Conflict of Interest

AD, GP, and AM declare that they have no conflicts of interest.

Financial Disclosure

Nil.

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