The Safety and Feasibility of a New Through-the-scope Balloon-assisted Enteroscopy in Children

*†Efrat Broide, *Tzippora Shalem, †Vered Richter, †Shay Matalon, and †Haim Shirin

ABSTRACT

Objectives: Small bowel involvement in Crohn disease (CD) is clinically important for diagnosis and treatment. Single and double-balloon enteroscopy have already become important diagnostic tools in such cases. The on-demand NaviAid AB device enables deep advancement into the small bowel, using an anterograde or retrograde approach. In adults, this procedure is feasible, safe, and rapid. This work aimed to assess the safety and feasibility of NaviAid AB enteroscopy in pediatric patients.

Methods: Single-center, prospective study using the through-the-scope balloon-assisted-enteroscopy (TTS-BAE) NaviAid AB device for the evaluation of the small bowel in children with suspected or known inflammatory bowel disease (IBD). The system consists of a single-use balloon catheter inserted through the instrument channel of a standard colonoscope. It consists of an inflation/deflation system (NaviAid SPARK), which is inflated to anchoring pressure. The repetitive push-pull technique enables the advancement of the colonoscope along the small intestine.

Results: Fifty analyzed endoscopic procedures (30 retrograde, 20 anterograde) were performed in 34 children (52.9% boys, mean age 13.7 years). Average maximal depth of insertion (MDI), advancement depth using the NaviAid AB and average total procedure time were 138 cm (range 100–190 cm), 81 cm (range 40–120 cm), and 12.8 minutes (range 7.3–19.0 minutes), respectively, for the anterograde approach and 143 cm (range 100–170 cm), 64 cm (range 20–95 cm), and 21.9 minutes (range 13.9–32.0 minutes), respectively, for the retrograde approach. No serious or device-related adverse events were reported.

Conclusions: NaviAid AB enteroscopy in children is safe, feasible, and enables assessment of the small intestine in a short period of time.

Key Words: children, deep enteroscopy, NaviAid AB, small intestine

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What Is Known

- The small bowel is difficult to assess because of tortuous anatomy, incredible length, and significant looping.
- In adults, the NaviAid AB through-the-scope balloon-assisted enteroscopy is a safe and an effective alternative for deep enteroscopy using a conventional colonoscope.

What Is New

- This is the first prospective study exploring the safety and feasibility of NaviAid AB system through conventional colonoscope in pediatric patients.
- Unlike single and double balloon enteroscopies, the NaviAid AB learning curve is swift, intuitive, and simple to use, thus may help to assess disease extension of the small bowel and to obviate the need for imaging investigations.

Classification and extension of inflammatory bowel disease (IBD) affect medical management and prognosis (1,2). In two-thirds of pediatric Crohn disease (CD) patients, upper gastrointestinal tract and distal ileum are involved (3). Single balloon enteroscopy (SBE) and double balloon enteroscopy (DBE) are available (4–7). Several factors, however, limit their use in children including, cost of purchasing a new enteroscope, the need to set-up the overtube balloons, and procedure time with a long learning curve (8). Looping in the small intestine often prevents advancement (9–12).

Through-the-scope balloon-assisted-enteroscopy (TTS-BAE), NaviAid AB (Smart Medical Systems Ltd, Ra'anana, Israel), is a novel on-demand enteroscopy system (ODE) cleared by FDA, CE marking (indication of conformity to the regulation of the European Union) and AMAR (Israeli Health Department approval for the use of medical device). By using a standard endoscope with a working channel of at least 3.7 mm by a push-pull technique, deep advancement into the small bowel is possible (Fig. 1). It should be mentioned that not all pediatric colonoscopes across all vendors are compatible. In such cases, an adult colonoscope may be required.

In a multicenter study in adults, the average maximal depth of insertion (MDI) was 158 cm (50–350 cm) from the pylorus and 89 cm (20–150 cm) beyond the ileocecal valve (ICV), with average advancement time of 15.5 minutes, without adverse outcomes (8). In a single-center study (28 consecutive deep ODE procedures) in adults, for anterograde enteroscopy, the mean MDI was 120 ± 30 cm with a mean procedure time of 24.1 ± 6.4 minutes. For retrograde enteroscopy, the mean MDI was 110 ± 30 cm with a mean time of 19.7 ± 4.0 minutes. The procedures were feasible, safe, and rapid without adverse events (13).

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From the *The Jecheskiel Sigi Gonczarowski Pediatric Gastroenterology Unit, and the †The Gonczarowski Family Institute of Gastroenterology, Shamir (Assaf Harofeh) Medical Center and the Sackler School of Medicine, Tel Aviv University, Israel.

Address correspondence and reprint requests to Efrat Broide, Shamir (Assaf Harofeh) Medical Center, Zerrifin, 70300, Israel (e-mail: efibroide@yahoo.com).

Drs Efrat Broide and Tzippora Shalem contributed equally to this work.

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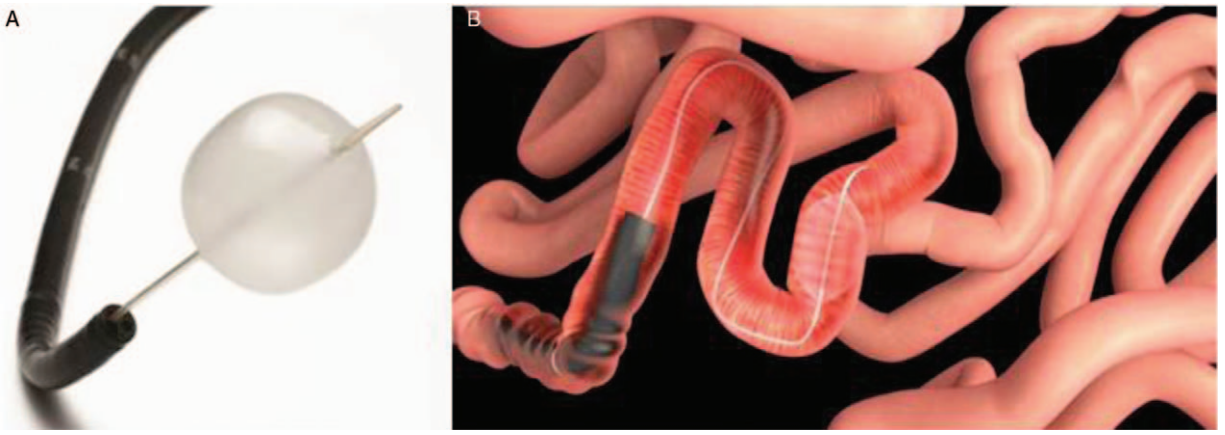

FIGURE 1. (A) NaviAid AB. (B) Advancement of the inflated NaviAid AB balloon.

As there are no published data on TTS-BAE in children, we aimed to assess the feasibility and safety of this new technique.

MATERIALS AND METHODS

Study Population

This prospective, single-center study was conducted at Shamir (Assaf Harofeh) Medical Center, Israel, between June 2016 and January 2018. Written informed consent was obtained from the participants' parents. The protocol was approved by the local institutional review board of Shamir (Assaf Harofeh) Medical Center (0264), and the study was registered at clinicaltrials.gov (NCT02629211).

Eligible patients were defined as those ages 8 to 18 years, fulfilling one of the following criteria: suspected IBD defined according to the Porto criteria (14,15), known CD, with suspected small bowel disease activity or known IBD for children with undetermined colitis, in need of investigation of the small intestine to exclude CD. Suspicion of small bowel disease activity in children with a known diagnosis of CD was defined as persistent abdominal pain or diarrhea despite medical treatment, or elevated inflammatory markers, such as C-reactive protein (CRP) or fecal calprotectin. The following laboratory data were obtained from patient electronic records: complete blood count; hemoglobin, white blood, absolute neutrophil and platelet count, as well as serum CRP, iron, and ferritin levels. Demographic, clinical, and medical data were also obtained from the patient's electronic data.

Patients who underwent a retrograde enteroscopy were prepared by a standardized full bowel cleansing according to age and body weight, and bowel preparation was graded according to the Boston Bowel Preparation Quality Scale Score (16). Patients who were referred to an anterograde procedure alone, just fasted for 8 hours. Patients were assigned to anterograde approach, retrograde approach, or both based on the physician's decision. Colonoscopies and gastroscopies were performed using a pediatric video-colonoscope (Pentax, Tokyo, Japan). For optimal conditions during the examination, endoscopies were performed when patients were in a deeply sedated state and monitored by an anesthesiologist.

Endoscopic Procedure

NaviAid AB is an on-demand, single-use balloon catheter, supported by an inflation-deflation apparatus (NaviAid SPARK), which is a software-based inflation system. The balloon is inflated to a set pressure level that allows anchoring of the balloon in the small intestine. The pressure level is fixed and cannot be modified by the physician, thus eliminating the option of over-inflation. The latex-free balloon requires a working channel of at least 3.7 mm. The catheter has a soft flexible tip that enables the safe advancement of the catheter. All procedures were performed by the same endoscopist (E.B.) to avoid procedure information bias. This endoscopist previously performed push enteroscopy in adults but not ODE procedures. The balloon catheter was deployed when the colonoscope reached the papilla of Vater for anterograde enteroscopy and immediately after intubation of the ICV for retrograde enteroscopy. The balloon catheter was advanced ahead of the colonoscope (Fig. 2A) and the balloon was inflated at the point where resistance was encountered (Fig. 2B).

After the inflation of the balloon, the colonoscope was pushed forward with simultaneous counter traction (push-pull technique), provided on the balloon catheter. Once the colonoscope met the balloon, the balloon was deflated and the cycle was repeated until the point of possible maximal insertion was reached or upon the physician's decision that no additional evaluation of the intestine was necessary. The controlled withdrawal was performed while measuring the length of insertion. Whenever necessary, the balloon catheter was removed and biopsies were taken, after which, the balloon catheter was re-introduced and the controlled withdrawal continued.

Safety of the NaviAid AB was assessed by examining the patient immediately following the endoscopic procedure. In addition, follow-up telephone calls to the parent were made 24 and 48 hours after the procedure. Reported adverse events were graded as mild, moderate, or severe. The estimation of the advancement length and MDI is difficult as the bowel is pleated and reduced, making this issue very difficult and using the endoscope measurements on the shaft unreliable. We adopted the ESGE recommendations, which states that small-bowel insertion depth should be estimated by counting net advancement of the enteroscope during the insertion phase, with confirmation of this estimate during withdrawal (17). The MDI and advancement length from the ICV or the papilla were measured during withdrawal from the point of maximal insertion and are expressed in centimeters. Fluoroscopy, which may improve the estimation of the MDI was not utilized in order to prevent the exposure of the children to radiation. Total procedure time was defined as the time needed to reach the MDI, while advancement time was measured as the time required to reach from the ICV or the papilla of Vater to MDI. Technical success was defined for the anterograde approach as an advancement depth of at least 40 cm beyond the papilla of Vater and for the retrograde approaches as an advancement depth of at least 20 cm beyond the ICV. As this was a preliminary safety and feasibility study, these

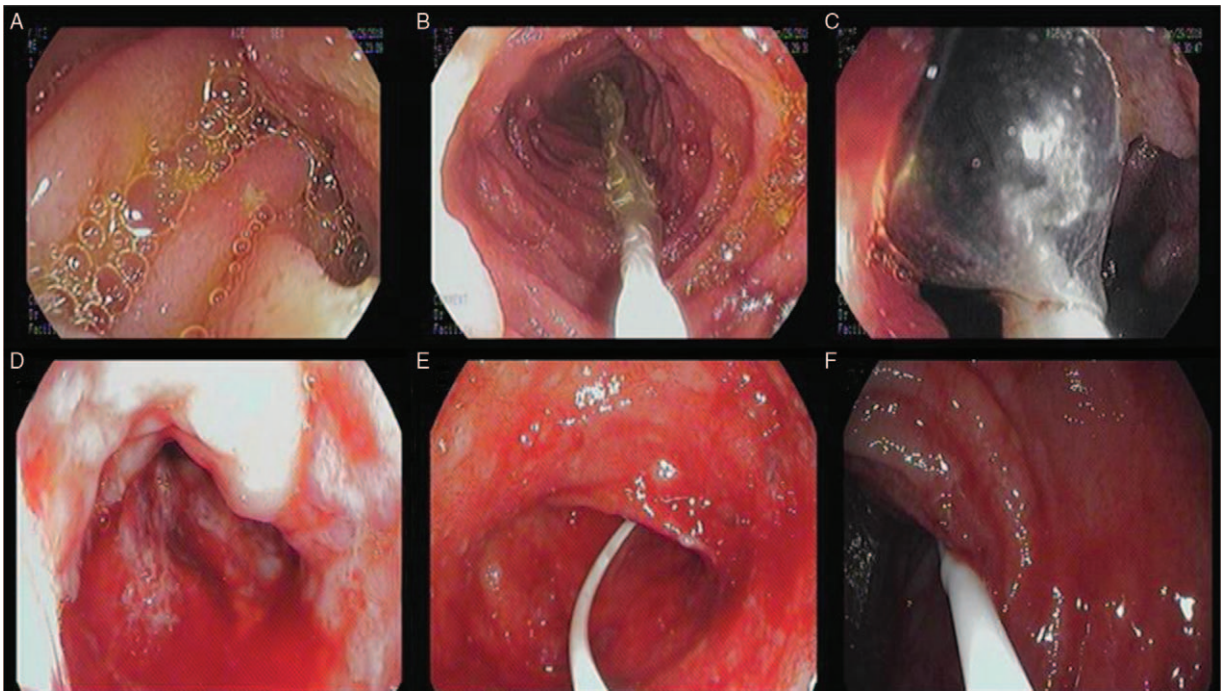

FIGURE 2. Endoscopic findings and NaviAid AB, as captured during anterograde (A–C) and retrograde (D–F) enteroscopy procedures. (A) Small erosion in duodenal bulb. (B) Normal proximal jejunum. (C) Advancement of the balloon catheter in the jejunum. (D and E) Crohn disease in the distal ileum. (F) Normal proximal ileum of the same patient.

were based on the mean depth of insertion from the standard esophagogastroduodenoscopy or the colonoscopy, 50 to 80 cm to the jejunum and 15 to 25 cm into the ileum, respectively (18–23). The ease of the procedure was graded and reported by the endoscopist as very easy, easy, moderate, difficult, or very difficult.

Patients were excluded from the statistical analysis when protocol deviation that could have influenced study outcomes occurred. This included administrative error/missing data and cases of insufficient bowel preparation.

Statistical Analysis

Descriptive statistics were calculated for all measured variables and delivered parameters (eg, demographics). The results are tabulated as mean, median, standard deviation (SD), and range. Categorical data are expressed as absolute and relative frequencies. All statistical analyses were performed using SPSS version 23 (IBM SPSS, statistics, Armonk, NY).

RESULTS

A total of 39 patients (56.4% boys), with a mean age of 14.68 ± 2.76 years (range 8–18 years) were recruited to the study. Overall, 60 endoscopic procedures were performed. One patient was assigned to anterograde procedure alone, 17 patients were assigned to retrograde procedure alone and 21 patients to both. Out of the 60 procedures, 22 were anterograde and 38 were retrograde. Figure 3 summarized the flow chart of the study.

Anterograde Outcome

Twenty-two anterograde procedures were performed (50% boys, with a mean age of 14.34 ± 2.77, range 9–18 years). One out of the 22 procedures was excluded because of missing data/protocol deviation. One out of the 21 performed procedures failed because of technical difficulty with the endoscope camera. AB was connected, but not inflated, leading to a success rate of 95.23% (21/22) (Fig. 3). The indications for the anterograde procedure were: suspected IBD (14 patients), known CD (6 patients), and undetermined colitis (2 patients). The average MDI was 138 cm (range 100–190 cm), with an average MDI beyond the papilla of Vater of 81 cm (range 40–120 cm) (Table 1). The average advancement time beyond the papilla of Vater was 8.0 minutes (range 3.3–10.6 minutes) and the average total procedure time was 12.8 minutes (range 7.3–19.0 minutes). NaviAid AB ease of use was graded as very easy in 20%, easy in 55%, and moderate in 25% of the procedures. No significant technical and learning difficulties were reported.

Retrograde Outcome

Thirty-eight retrograde procedures were performed (55.23% boys, with a mean age of 14.7 ± 2.79, range 9–18 years). Three patients were excluded, 1 because of missing data/protocol deviation and 2 because of insufficient bowel preparation. One procedure failed because of system failure, 3 because of technical difficulties, and 1 because of nontransferable ileocecal stricture-yield a success rate of 85.71% (30/35) (Fig. 3). In order to avoid biasing the success rate, we considered the 4 patients with difficult anatomy and nontransferable stricture as a failure, although we believe that the procedures would probably not have been successful with other devices.

The indications for the retrograde procedures were suspected IBD (23 patients), known CD (9 patients), and undetermined colitis (6 patients). The average MDI using the NaviAid AB was 143 cm (range 100–170 cm) with an average MDI beyond the ICV of 64 cm (range 20–95). The average advancement time beyond the ICV was 7.2 minutes (range 3.6–14.6 minutes). The average total procedure time was 21.9 minutes (range 13.9–32.0 minutes) (Table 1).

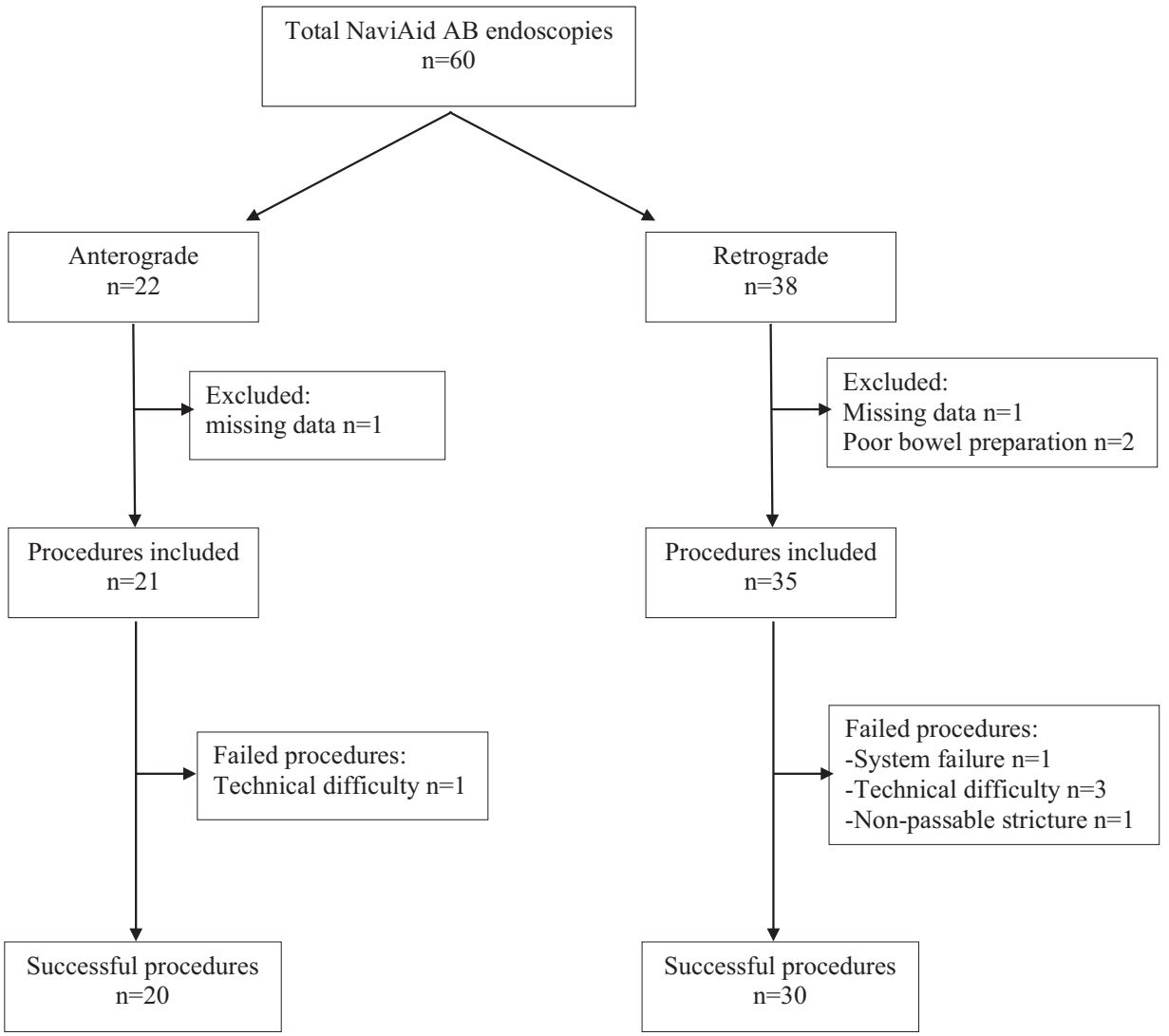

FIGURE 3. Procedures flow chart.

Endoscopic Findings

The endoscopic findings of the 31 patients who completed the scheduled procedures were evaluated; 15 of these patients had suspected IBD and 16 had known IBD (undetermined colitis n = 7; known CD n = 9) at enrollment. In the suspected IBD group, 3 patients were diagnosed with UC and 3 patients with CD; the remaining 9 patients showed no intestinal abnormalities. In the known IBD group, 6 patients with undetermined colitis at baseline were confirmed to have an active UC and 1 patient exhibited mucosal healing. Out of the 9 patients with known CD, 8 were confirmed to have active CD and 1 patient exhibited mucosal healing. Figure 2 presents some endoscopic findings and procedure images obtained during anterograde enteroscopy (A, B, C) and by the retrograde enteroscopy procedures performed in CD patients (D, E, F). NaviAid AB device ease of use was reported as very easy (13%), easy (57%), or moderate (27%), and in 1 procedure, it was reported as difficult (3%) because of difficult patient anatomy. No significant learning difficulties were reported.

Safety

No device-related serious adverse events were reported throughout the study. One patient reported moderate abdominal discomfort immediately after the retrograde procedure, which was resolved within 1 hour (Table 1).

DISCUSSION

The TTS-BAE using a NaviAid AB overcomes many of the limitations presented by using SBE and DBE and is designed to be as benefit as small bowel evaluation with deep enteroscopy. The device allows advancement and visualization of the small bowel, with the push-pull technique that helps in overcoming looping of the device during intubation. Previous studies in adults that compared the various enteroscopy techniques suggested that DBE was superior to SBE for visualization of the entire small bowel. In addition, DBE and SBE were similar with regards to diagnostic and therapeutic yield as well as procedure time (24–27). The limited published literature on DBE and SBE usage in the pediatric population has not demonstrated significant differences in

TABLE 1. Patient and procedure data

	Anterograde approach	Retrograde approach
Demographics	n = 22	n = 38
Gender: male, %	11 (50)	21 (55.23)
Age (years), mean (range) ±SD	14.34 (9-18) ± 2.77	14.7 (9–18) ± 2.79
Indication for endoscopy, n	n = 22	n = 38
Suspected IBD, %	14 (63.63)	23 (60.52)
Known IBD: CD, %	6 (27.27)	9 (23.68)
Undetermined colitis, %	2 (9.09)	6 (15.79)
procedure data, mean (range) ±SD	n = 20*	n = 30**
Depth of insertion, cm	138 (100–190) ± 22	143 (100–170) ± 20
Depth of insertion beyond the papilla/ICV, cm	81 (40–120) ± 22	64 (20–95) ± 19
Total procedure time, minutes	12.8 (7.3–19.0) ± 3.5	21.9 (13.9–32.0) ± 5.7
Total advancement time beyond the papilla, minutes	8.0 (3.3–10.6) ± 2.0	7.2 (3.6–14.6) ± 2.6
Reported adverse event	n = 20*	n = 30**
Immediately after procedure		
Moderate abdominal pain	0	1
24-h follow-up	0	0
48-h follow-up	0	0

CD = Crohn disease; IBD = inflammatory bowel disease; ICV = ileocecal valve; SD = standard deviation.
*Excluded, n = 1; failed procedure, n = 1.
**Excluded, n = 3; failed procedure, n = 5.

visualization. Moreover, it has reported comparable diagnostic yield (5–7,9).

In this first prospective study exploring the safety and feasibility of TTS-BAE using a NaviAid AB system through conventional colonoscope in pediatric patients, technical success was achieved in 95.23% and in 85.7% of the anterograde and retrograde procedures, respectively. This relatively high rates are in line with the results obtained in 28 adult patients in previous research who had undergone endoscopy using the NaviAid AB system and showed 100% technical success (13).

There is great variation in the literature regarding the MDI in children, most probably arising from the starting point of measurement, which varies across studies. In addition, although CO_2 has been proven to extend intubation depth, we used air in this study to inflate the bowel (28). Nevertheless, the physician's target of enteroscopy is the main factor for the differences in MDI. In our study, the target insertion depth was according to the physician discretion. This is in contrary to various SBE and DBE studies, which aimed to examine the entire bowel (4,5,29–33). However, even despite the difference in advancement target, the average advancement depth utilizing the NaviAid AB in the retrograde approach was 64 cm, similar to that reported by Lin and Erdman (34) using DBE (mean 65 cm), less than that reported by Hagiwara et al (35) (mean 75 cm) and superior to the report by de Ridder et al (4) using SBE (mean 25 cm). Studies evaluating MDI by the anterograde approach, have shown deeper small bowel advancement with both SBE and DBE. It has been, however, argued that as the majority of lesions are found in the proximal aspects of the small bowel, deeper intubation is not always an indication for a higher quality examination (8).

One key advantage of this new technique is that TTS-BAE uses a standard colonoscope provided that the working channel is at least 3.7 mm. It is an on-demand, easier, and safe way of intubation of the small intestine for any needed biopsy or therapy through the scope. The balloon in front of the colonoscope enhances deep insertion into the small intestine, and whenever the balloon is withdrawn in order to take a biopsy or to perform a therapeutic intervention, the colonoscope still maintains its position. Moreover, average anterograde total procedure time was 12.8 minutes, with an advancement time of 8.0 minutes, and for the retrograde average total procedure time was 21.9 minutes, with an advancement time of 7.2 minutes. Both are significantly shorter compared with SBE and DBE (78 and 50 minutes, respectively, for SBE and minimum 130 and 92.5 minutes for DBE). It should be, however, remembered that the total procedural time may be longer as deeper insertion is achieved (4,5,31). Additionally, the NaviAid AB procedure time was found to be shorter compared with unassisted push enteroscopy (29.4 ± 12.5 minutes) described by Darbari et al (36), and so enables the performance of the procedure under propofol sedation without the need for an anesthesiologist. Therefore, this device could potentially replace traditional push enteroscopy, which is also limited by its shorter reach.

The on-demand NaviAid AB is a device that introduced through regular endoscope channel and with vastly shorter procedure time is a cost-effective alternative to the SBE and DBE. Moreover, unlike DBE and SBE, the NaviAid AB learning curve was swift, as its operation is intuitive and simple. In children with suspected or diagnosed IBD, TTS-BAE may help to assess the extension of the small bowel disease and to obviate or postpone the need for imaging investigations. Some study limitations should be mentioned, however. First, this was an open, single-center study, with a small number of endoscopy procedures, performed only in children with suspected or known IBD. Second, the main objective of the study was to explore the safety and feasibility of the procedure with NaviAid AB, and not to evaluate the diagnostic yield. Third, no direct comparison to other enteroscopic methods, such as SBE or DBE was done.

CONCLUSIONS

In conclusion, our study demonstrated that utilization of TTS-BAE NaviAid AB in children is safe, feasible and quick. Extended examination of the small bowel is accessible and enables clinical assessment of IBD that could be critical to clinical management. Further prospective studies are needed to assess the MDI and diagnostic yield of the device in small bowel pathologies in children.

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