Acute Effects of a Glucagon-Like Peptide 2 Analogue, Teduglutide, on Gastrointestinal Motor Function and Permeability in Adult Patients With Short Bowel Syndrome on Home Parenteral Nutrition

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Abstract

Background: Glucagon-like peptide 2 (GLP-2) agonists decrease the need for parenteral nutrition (PN) in short bowel syndrome (SBS); mechanisms evaluated to date have focused on the intestinotrophic effect of GLP-2 agonists such as increased absorptive capacity of the remnant intestine and increased citrulline levels. Other mechanisms may also play a role in effects of GLP-2 agonists. Aim: To measure effects of a GLP-2 agonist, teduglutide (TED), compared with placebo (PLA) on gastric emptying (GE), overall gut transit, fluid balance, intestinal monosaccharide absorption, and permeability in patients with SBS on home PN (HPN). Materials and Methods: In 8 adults with SBS on HPN, we compared daily subcutaneous TED (0.05 mg/kg) and PLA (crossover design, each treatment 7 days with a 14-day washout) on gut transit, intestinal absorption, and permeability after oral mannitol (200 mg) and lactulose (1 g), as well as stool weight and urine volume over 8 hours. Analysis used the paired t test. Results: Of 8 patients, 4 were men, with a mean ± SD age of 54 ± 1 years, body mass index of 25 ± 4 kg/m², residual small intestine of 63 ± 12 cm, and 25% ± 15% of residual colon. The overall gut transit (% emptied at 6 hours) was 53.4% ± 15% for TED vs 62.4% ± 15.2% for PLA (P = .075), with no effect on GE (P = .74). TED increased urine mannitol excretion at 0–2 hours (16.2 ± 3.6 mg TED vs 11.3 ± 2.2 mg PLA, P = .20) and 0–8 hours (32.7 ± 5.9 mg PLA vs 48.8 ± 8.9 mg TED, P = .17). There were no differences in urine lactulose excretion or lactulose/mannitol ratio (0.024 ± 0.005 TED vs 0.021 ± 0.005 PLA). Over 8 hours, TED (vs PLA) numerically reduced stool weight (mean ± SEM, 77 ± 18 g TED vs 106 ± 43 g PLA, P = .42) and increased urine volume (408.9 ± 52.2 mL TED vs 365.7 ± 57.3 mL PLA, P = .34). Conclusion: Seven-day TED treatment in 8 participants suggests beneficial effects on fluid balance and monosaccharide absorption, and it retarded overall gut transit with no effects on GE or mucosal permeability. Larger, longer, mechanistic studies of TED in SBS are warranted. This trial was registered at clinicaltrials.gov as NCT02099084. (JPN J Parenter Enteral Nutr. XXXX;xx:xx-xx)

Keywords
short bowel syndrome; teduglutide; GLP2; gastrointestinal transit; permeability

Clinical Relevancy Statement

In a pilot crossover trial, the recombinant glucagon-like peptide 2 agonist, teduglutide, compared with placebo, retarded overall gut transit without affecting gastric emptying and enhanced fluid balance and intestinal monosaccharide absorption. These data provide further insights on the mechanism of action of teduglutide and appraise the magnitude of the variation in responses for planning definitive studies to understand mechanism and provide evidence of pharmacodynamic efficacy.

Introduction

Intestinal failure (IF) is defined as the reduction of gut function below the minimum necessary for absorption of macronutrients and/or water and electrolytes, such that intravenous (IV) supplementation is required to maintain health and/or growth.1

Short bowel syndrome (SBS) is the main cause of IF and is mostly attributed to extensive intestinal resection, resulting in
malabsorption, malnutrition, dehydration, and weight loss. Treatment for SBS includes lifestyle modification such as hyperphagia, oral rehydration solutions, antimotility or antisecretery drugs, and avoidance of hyperosmotic food. Depending on the extent and sites of resection, these approaches may not achieve complete success, leaving patients dependent on long-term or lifelong home parenteral nutrition (HPN) support with its associated morbidity and impact on quality of life.

Strategies improving intestinal adaptation may allow patients with IF to discontinue HPN; these strategies include growth factors (growth hormone, epidermal growth factor, insulin-like growth factor 1, and glucagon-like peptide 2 [GLP-2]), somatostatin analogues (octreotide), and luminal nutrients (glutamine, soluble fibers, short-chain fatty acids, and pancreaticobiliary secretions). At present, the most promising growth factor for treatment of SBS appears to be GLP-2.

GLP-2 is a product of the preproglucagon gene and is secreted by the L cells in the distal intestine after food ingestion. In animal models, GLP-2 has been shown to stimulate growth of the small and large intestine by inducing crypt cell proliferation and by inhibiting enterocyte apoptosis. GLP-2 has also been shown to be involved in a variety of physiologic effects such as inhibiting vagally induced gastric secretion (potentially inhibiting antral motility and delaying gastric emptying), increasing intestinal nutrient absorption, increasing intestinal barrier function in mouse small intestine studied in vitro, stimulating intestinal blood flow, and acting as an anti-inflammatory agent. In humans, GLP-2 has been shown to reduce gastric acid secretion and to increase superior mesenteric artery flow.

Teduglutide, a recombinant human GLP-2 analogue, has been associated with improved nutrient absorption and nutrition status in patients with SBS and with reduced parenteral nutrition (PN) and IV fluid dependence in patients with SBS, with a small proportion of patients achieving complete independence. In addition, the efficacy of teduglutide has been maintained up to at least 52 weeks, with a safety profile that is considered acceptable for long-term use.

The mechanism(s) by which teduglutide decreases fluid requirements in PN-dependent patients and increases absorption of fluids and nutrients is poorly understood. Previous studies have shown conflicting data regarding the effects of GLP-2 on gastrointestinal (GI) transit, with some studies showing decreased transit in animals and in humans in whom emptying of liquids was measured by antral ultrasonography. In other studies, GLP-2 retarded gastric emptying but not small bowel transit of a solid meal, both measured by radioscintigraphy. Furthermore, other studies reported no difference in the gastric emptying of liquids or solids measured by stable isotope gastric emptying test or by measurement of emptying of a radio-labeled omelet meal using scintigraphy. Such discrepancies in the effects on gut transit may be related to the different methods of measurement of GI transit, GLP-2 analogue doses, and patient heterogeneity between studies.

In addition, a few studies have shown that teduglutide decreases intestinal permeability in mice; this may translate to improved nutrient absorption, decreased risk of infections, and decreased fluid requirements.

To help clarify the mechanisms of action of teduglutide in SBS, we conducted a double-blinded, randomized, crossover pilot study to compare the acute effects of teduglutide vs placebo on GI motor function, intestinal permeability, and monosaccharide absorption in patients with SBS who were dependent on HPN. Our overall hypothesis was that teduglutide retards gastric emptying and overall gut transit of solids, decreases intestinal permeability, and enhances fluid balance by decreasing stool weight and increasing urinary volume compared with placebo.

Materials and Methods

Study Design

In 8 adult patients with SBS who were dependent on HPN, we performed a double-blinded, placebo-controlled, crossover pilot study of once-a-day, subcutaneous (SQ) teduglutide, 0.05 mg/kg, or placebo, administered for 7 days, with a washout period of at least 7 days. The study was approved by the Mayo Clinic Institutional Review Board, and all participants gave written informed consent after the nature of the procedure(s) had been explained. All study participants were closely followed by the Mayo Clinic HPN Program.

The randomization schedule was generated using a computer-generated program by the study statistician and submitted to the Mayo Clinic Research Pharmacy. Allocation was concealed. The study blind (clinical investigators, study personnel, and study participants) was retained until all the data had been recorded and analyzed, and the blinded data were received and locked by the statistician.

Study Medication

The study medication and placebo (saline solution) were provided by NPS Pharmaceuticals (Bedminster, NJ), the manufacturing company, and were dispensed by the Mayo Clinic Research Pharmacy. The study medication and placebo were dispensed in a box (placebo or teduglutide vials and syringes) and were identical.

Participants were excluded from the study if they were pregnant, trying to become pregnant, were lactating, had diabetes, had a history of alcohol or drug abuse within the past year, had active Crohn’s disease, or had a history of pancreatitis, primary renal impairment (estimated glomerular filtration rate [eGFR] <30 mL/min), radiation enteritis, scleroderma, celiac disease, tropical sprue, diabetes, chronic pseudo-obstruction, or a history of or active malignancy. Participants with previous use of teduglutide or potential allergies to teduglutide or its constituents were also excluded from the study. We also excluded...
participants with any hospitalization within 1 month before screening; use of octreotide, IV glutamine, growth hormone, or growth factors such as native GLP-2 within the past 12 weeks; or use of any investigational drug within the past 30 days. We excluded patients who had used tobacco products within 4 weeks before screening and those who had used oral corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), or aspirin within 1 week before screening. Ingestion of artificial sweeteners such as Splenda (sucralose), Nutrasweet (aspartame), lactulose, or mannitol 2 days prior to the study measurement days was discouraged.

Infliximab and other biological agents such as azathioprine, methotrexate, cyclosporine, tacrolimus, and sirolimus were required to be stable for at least 8 weeks prior to baseline and remain stable during the study. Diuretics and oral rehydration solutions were required to be stable for ≥4 weeks prior to baseline evaluations and remain stable during the study. Antimotility or secretory agents were required to be stable from 2 days prior to and throughout the study.

**Experimental Protocol**

The experimental protocol is depicted in Figure 1. Participants presented at the Mayo Clinic Clinical Research Unit and began with a baseline screening visit (visit 1). Informed consent was obtained after determining eligibility by a thorough history and physical examination. Participants were encouraged to maintain a stable oral intake during the entire time of the study, and this was recorded in a daily food diary. Stool quantity, frequency, and consistency were also recorded with a daily stool diary. Participants were not allowed to change the volume of PN until study completion. On visit 1, eligible participants were randomized (as described previously). Participants were instructed in the process of self-administration of the study drug and were given box 1 with study drug or placebo for 6 days.

On visit 2 (study day 7) participants arrived in the Clinical Research Unit after having fasted for at least 8 hours. Women of childbearing potential provided a urine sample for a point-of-care pregnancy test, which had to be negative before proceeding with the scintigraphy test. Subjects then received their seventh dose of placebo or teduglutide (1 dose, 1 hour before breakfast). We then proceeded to measure, over the next 8 hours, GI transit by scintigraphy, intestinal permeability by oral ingestion of mannitol and lactulose, and urine and stool collection (for stool and urine weight). At the end of visit 2, participants received the alternate treatment arm (box 2 with 6 daily doses) to take home and to be started after a washout period. The planned washout period was for at least 7 days, but due to scheduling reasons, all participants had 14 days of washout, except for 1 (10 days). On visit 3 (study day 21 for all except 1 [day 17]), participants returned to the Clinical Research Unit and followed the same approach to the assessments as on visit 2.

**Adverse Events**

Participants were asked to keep track of any symptoms suggestive of adverse events in their daily stool diary. Participants were contacted by phone on days 2 and 5 during each phase of the study medications to address any adverse events. Participants were encouraged to contact the study staff at any time to report any adverse events during the study period.

**Measurement of GI Transit**

We used a previously validated scintigraphic method, which is used extensively in our laboratory, to measure gastric and small bowel transit. All participants received a standard 550-kcal meal (chicken meal) at 4 hours after a 99mTc-egg breakfast meal.
We took into account any small intestine or colon resection to conduct the appropriate measurements. Given the variation in the anatomy of the participants and the likelihood of prior ileal and/or ileo-colonic junction resection, we used only 99mTc for transit measurements. Radioisotope content in stomach and whole abdomen was corrected for decay and tissue attenuation or depth. Static, upright, anterior, and posterior images were obtained immediately following consumption of the radiolabeled meal. An irregular region of interest (ROI) was drawn around the anterior and posterior images of the entire stomach to determine the amount of activity within the ROI, which was used to determine the geometric mean for correction of tissue attenuation. This geometric mean value was then used as the 100% reference for each subsequent scan.

Prior to the 6- and 8-hour scans, participants were instructed to empty their ileostomy bags to prevent interference with the abdominal imaging. The 6- and 8-hour transit determinations were analyzed by an irregular ROI drawn around the entire abdomen where radioisotope could be detected by scintigraphy. The values of each anterior and posterior scan were used to determine the geometric mean for correction for tissue attenuation and then corrected for 6- and 8-hour isotope decay.

**Data Analysis of GI Transit**

The primary efficacy outcome measures for transit were gastric emptying half-time (T1/2) following the 99mTc-egg meal and overall gut transit. Given the variable extent of the residual length of the small intestine and colon, we assessed the proportion emptied from the body at 6 hours as an overall estimate of whole gut transit. The 6- and 8-hour transit determinations were analyzed by an irregular ROI drawn around the entire abdomen where radioisotope could be detected by scintigraphy. The values of each anterior and posterior scan were used to determine the geometric mean for correction for tissue attenuation and then corrected for 6- and 8-hour isotope decay.

**Measurement of Small Intestinal and Colonic Permeability**

We appraised small intestinal and colonic permeability by measuring the urinary excretion of mannitol and lactulose. The chemical analysis was a refinement of the method of Lostia et al with 1 improvement: we used high-speed liquid chromatography (HPLC) tandem mass spectrometry to increase assay accuracy and test sensitivity. Following administration of sugars (mannitol 200 mg and lactulose 1 g in 30 mL of water administered with the radiolabeled test meal), we collected urine during 0–2 and 2–8 hours. A baseline urine sample was also collected prior to ingestion of the sugars.

**Statistical Methods**

Descriptive statistics are presented as counts or percentages for discrete variables and as median (interquartile range [IQR]), mean ± standard deviation (SD), or standard error of the mean (SEM) for quantitative variables. Participants’ baseline demographics and clinical characteristics were compared between groups at the time of randomization with either the t test or χ2 test, as appropriate.

Table 1 shows the a priori power calculation, which was based on a recently completed study in 23 patients with irritable bowel syndrome (IBS)–diarrhea who were treated with a gluten-free diet as the intervention. Prediet data vs response to a gluten-free diet (“placebo”) was used to estimate the standard deviation within subject deltas. According to this power calculation, we anticipated that, with 8 patients involved in a crossover study, there would be adequate power to detect a clinically meaningful difference, such as an 18.5-minute difference in gastric emptying T1/2.

Within-participant treatment effects (placebo [PLA] vs teduglutide [TED]) were compared using a paired t test or signed rank test as warranted. All tests were 2-tailed, using an α level of .05 (ie, P < .05 was considered statistically significant). Analyses were done using SAS version 9.3 (SAS Institute, Cary, NC).

**Results**

**Study Enrollment and Participant Demographics**

Eighteen patients with SBS who were closely followed by the Mayo Clinic HPN Program were deemed potentially eligible.
and invited to participate in the study. Of these, 8 responded to the invitation and were screened, enrolled, and completed the study. The demographic characteristics and baseline clinical parameters of the study cohort are reported in Table 2. Importantly, no significant differences between groups at baseline were encountered (data not shown).

**Effect of Teduglutide on Gastric Emptying and Overall Gut Transit**

No treatment effect on gastric emptying T\textsubscript{1/2} was observed (106 ± 20 min PLA vs 113 ± 16 min TED, \(P = .74\)). Overall gut transit, expressed as percent emptied at 6 hours, was 62.4% ± 15.2% during PLA treatment and 53.4 ± 15% with TED (\(P = .075\)).

**Effect of TED on Urinary Mannitol Excretion**

TED numerically increased urine mannitol excretion, both during 0- to 2-hour (mean ± SEM, 11.3 ± 2.2 mg PLA vs 16.2 ± 3.6 mg TED, \(P = .20\)) and during 0- to 8-hour (32.7 ± 5.9 mg PLA vs 48.8 ± 8.9 mg TED, \(P = .17\)) collections compared with placebo, suggesting increased monosaccharide uptake.

**Effect of TED on Urinary Lactulose Excretion and Lactulose/Mannitol Ratio**

There were no relevant differences in urine lactulose excretion at 0–2 hours (0.38 ± 0.14 mg PLA vs 0.42 ± 0.14 mg TED) or in lactulose/mannitol ratio (0.021 ± 0.005 PLA vs 0.024 ± 0.005 TED), suggesting there was no acute effect of TED on mucosal permeability.

**Effect of TED on Urine Volume and Stool Weight During First 8 Hours**

TED compared with placebo numerically improved fluid balance by reducing stool weight at 0–8 hours (106 ± 43 g PLA vs 77 ± 18 g TED, \(P = .42\)). Teduglutide also numerically increased urine volume at 0–8 hours (365.7 ± 57.3 mL PLA vs 408.9 ± 52.2 mL TED; \(P = .34\)).

**Adverse Events**

Overall, TED was well tolerated. Only 3 participants reported transient side effects. The first participant described moderate abdominal discomfort on days 1 and 2 of placebo treatment, resolving by day 4. The second participant reported mild and self-limiting headache and nausea on day 4 of TED treatment and progressive increase in the size of her stoma since day 1 that required modification of her stoma appliance. The third participant reported a mild increase in stoma size by day 5 of teduglutide treatment. Both participants completed the study and reported a normalization of stoma size after discontinuation of the drug or placebo.

**Discussion**

In this pilot, 1-week crossover study of 8 participants with SBS dependent on HPN, TED demonstrated potential beneficial effects, including numerically enhanced fluid balance, monosaccharide absorption, and retardation of overall gut transit, with no effects on gastric emptying or intestinal mucosal permeability.

The improved fluid balance seen in this study, as reflected by the decrease in stool weight by approximately 30% and the increase in urine volume by approximately 15%, is consistent with a previous rigorous clinical study by Jeppesen et al,\textsuperscript{17} in which TED reduced wet weight excretion and improved wet weight absorption in patients with SBS with and without a colon. Subsequent studies corroborated TED enhancement of intestinal fluid absorption and reducing PN and/or IV fluid requirements.\textsuperscript{19,32,33}

The increase in absorption of fluids might be related to the intestinotrophic properties of the GLP-2 agonist by increasing the height of intestinal villi and depth of their associated crypts, as well as a decrease in apoptosis.\textsuperscript{5,6} Such intestinotrophic effects may also have contributed to the increase in nipple stoma size and reduction of stoma output that has been documented to occur even as soon as 72 hours from commencing GLP-2.\textsuperscript{16} This is consistent with our study, since 2 participants

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**Table 2. Patient Demographics and Clinical Characteristics.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study Cohort (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/Female, No.</td>
<td>4/4</td>
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<tr>
<td>White race, No. (%)</td>
<td>8 (100)</td>
</tr>
<tr>
<td>Age, y</td>
<td>54 ± 13</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>25 ± 4</td>
</tr>
<tr>
<td>Residual small bowel and colon</td>
<td></td>
</tr>
<tr>
<td>Overall residual SB</td>
<td>63 ± 12</td>
</tr>
<tr>
<td>Patient 1</td>
<td>100 cm SB, no colon</td>
</tr>
<tr>
<td>Patient 2</td>
<td>25 cm SB, one-third colon</td>
</tr>
<tr>
<td>Patient 3</td>
<td>35 cm SB, no colon</td>
</tr>
<tr>
<td>Patient 4</td>
<td>45 cm SB, no colon</td>
</tr>
<tr>
<td>Patient 5</td>
<td>150 cm SB, no colon</td>
</tr>
<tr>
<td>Patient 6</td>
<td>95 cm SB, colon present</td>
</tr>
<tr>
<td>Patient 7</td>
<td>80 cm SB, no colon</td>
</tr>
<tr>
<td>Patient 8</td>
<td>60 cm SB, one-half colon</td>
</tr>
<tr>
<td>Time on PN, y</td>
<td>2.95 (IQR, 2.4–13.2; range, 2.4–27.3)</td>
</tr>
<tr>
<td>Etiology of short bowel syndrome, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Crohn’s diseas-related complications</td>
<td>4 (50)</td>
</tr>
<tr>
<td>Adhesive SB obstruction with perforation</td>
<td>1 (20)</td>
</tr>
<tr>
<td>Desmoid tumor</td>
<td>1 (20)</td>
</tr>
<tr>
<td>Intestinal ischemia</td>
<td>1 (20)</td>
</tr>
<tr>
<td>Trauma</td>
<td>1 (20)</td>
</tr>
</tbody>
</table>

BMI, body mass index; IQR, interquartile range; PN, parenteral nutrition; SB, small bowel; SD, standard deviation.

aData presented as mean ± SD, unless otherwise specified.
with end-jejunostomy experienced an increase in stoma size within a few days of starting therapy. Overall, it is possible that TED’s intestinotrophic and hormonal mediated effects, such as retardation of intestinal transit and decreased intestinal secretions, may explain the acute effects on fluid balance within days of administration. TED’s profile of clinical benefits appears promising for patients with SBS whose goal is to improve quality of life by increasing the absorptive potential of the remnant intestine and, thus, decreasing or eliminating the use of PN.34

Few studies have evaluated the effect of GLP-2 on intestinal permeability in animals. GLP-2 was shown to enhance transepithelial resistance in the normal gut after induction of experimental gut injury.9,35,36 In a mouse model, treatment with a GLP-2 analogue increased the length and weight of the small bowel and significantly improved jejunal transepithelial resistance, suggesting that GLP-2 reduces intestinal permeability.17

In patients with SBS, D-xylose was used to test intestinal carbohydrate absorption, and results suggested that TED increased D-xylose plasma absorption at 2 hours without affecting D-xylose urinary excretion over 5 hours.17 The current data suggest that there was increased mannitol (monosaccharide) absorption (and urinary excretion) with no change in intestinal permeability, as measured by the lactulose/mannitol ratio. Mannitol is a monosaccharide that is hypothesized to diffuse across the tip of the small intestinal villi, along concentration gradients through the relatively permeable tight junctions in the residual small intestine, where channels allow permeability of these small molecules.

Previous studies have shown conflicting data regarding the effects of TED on GI transit, with some studies showing decreased transit,16,20,21 while others demonstrated no difference.22–24 These conflicting results are possibly related to different methods of measurement. For example, in 1 study, emptying of liquids was measured by antral ultrasonography,21 while others have assessed gastric emptying and small bowel transit of a solid meal with radioscintigraphy.16 Furthermore, other studies have appraised gastric emptying of liquids22 or solids through a stable isotope gastric emptying test23 or by measurement of the emptying of a radiolabeled omelet meal using scintigraphy.24 We observed no TED effects on gastric emptying of solids in the patients with SBS, consistent with previous data seen in healthy adults.22 However, we did observe a trend toward significance (P = .075) in retardation of transit in the TED treatment arm of the study, as measured by the proportion of the meal excreted at 6 hours. This occurred in the absence of an effect on gastric emptying and suggests that the retardation of transit must have occurred in the residual small bowel or colon. These differences in transit may facilitate absorption of water from the residual small intestine and colon and may have contributed to the numerical but nonsignificant increase in urine volume and decrease in stool weight over the 8-hour studies.

It is possible that GLP-2 is not as effective as glucagon-like peptide 1 (GLP-1) in decreasing gastric emptying of solids. Both GLP-1 and GLP-2 are intestinotropic hormones released by the L cells in the small intestine after consumption of nutrients. Slowing of GI transit, as well as increasing nutrient absorption, may both enhance intestinal rehabilitation. It is possible that the use of both hormones in patients with SBS might constitute a synergistic approach to enhance intestinal adaptation; this warrants further research.38

Our study has limitations. It is a pilot study with a relatively small sample size and short period of administration of TED; for example, it is conceivable that the duration of treatment may not have been sufficient to demonstrate effects on small intestinal permeability. Nonetheless, benefits from benefits from GLP-2 administration have been seen in as short as a treatment period of 35 days of therapy.16 In addition, we believe that the crossover design and the rigor of the previously validated measurements are strengths. Although we used washout periods of 14 days (with only 1 participant having a washout period of 10 days), there is still potential of a carryover effect in the crossover study. We also did not evaluate important long-term outcomes such as weight gain, hunger, or satiety, in view of the relatively short duration of the study. Other studies that seek to explore the long-term effects of TED should include such outcome measures. Nonetheless, our study provides impetus to further study GLP-2 and other potential interrelated key hormones such as GLP-1, peptide YY, and neurotensin that may play a role in intestinal adaptation and rehabilitation in patients with SBS. The present study also appraised the magnitude of the variance in responses to plan definitive studies based on prespecified effect sizes and statistical power to understand the mechanism of action of TED and provide evidence of pharmacodynamics efficacy. For example, based on the observed SD of 15% for overall gut transit, the inclusion of 20 patients in a future crossover study would have sufficient power to identify a 10% difference in overall gut transit (which was the magnitude of difference observed in the current study) and a 2.4-mg difference in mannitol excretion in the first 2 hours (approximately 17%) between the 2 treatment arms. We conclude that, in this pilot, crossover trial of 7-day teduglutide treatment, there were beneficial effects in patients with SBS on HPN, primarily with regard to improved fluid balance and monosaccharide absorption, as well as retarded overall gut transit, without effects on gastric emptying or mucosal permeability. Larger, long-term studies of TED in SBS are, therefore, warranted.

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Statement of Authorship
J. Iturrino, M. Camilleri, and A. R. Zinsmeister contributed to the conception or design of the research; J. Iturrino, M. Camilleri, A. Acosta, and A. R. Zinsmeister contributed to the acquisition,
References


