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Efficacy and safety of an abbreviated perioperative care bundle versus standard perioperative care in children undergoing elective bowel anastomoses: A randomized, noninferiority trial☆,☆☆

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ABSTRACT

Purpose: The aim was to evaluate if an abbreviated perioperative care bundle (APCB) is noninferior to the standard care, in terms of efficacy and safety, in pediatric patients undergoing bowel anastomoses.
Methods: A randomized, open, noninferiority trial with two parallel groups of equal size was carried out at the National Institute of Pediatrics in Mexico City, Mexico, from April 2016 to July 2018. The total number analyzed was 74 (37 per group).
The APCB comprised same day admission, avoidance of mechanical bowel preparation, optimized antibiotic prophylaxis, and early feeding. Statistical analysis was done with Fisher's exact test or Chi^2, and Student's T test.
Results: No significant differences were found for demographic variables and type of disease, either for the safety (anastomotic leakage, p 0.753; organ/space surgical site infection, p 0.500) or for some efficacy outcomes (ileus or bowel obstruction, p 0.693). Other efficacy outcomes were better in the study group, with shorter median times for feeding tolerance (19 h vs. 92 h, $p < 0.001$), for first bowel movement (15 h vs. 36 h, $p < 0.001$), and for discharge (1 vs. 6 days, $p < 0.001$).
Conclusion: The abbreviated care bundle was proven to be as safe but more efficacious than the standard care.
Level of evidence: I — randomized controlled trial with adequate statistical power.

An elective bowel anastomosis to restore continuity after temporary intestinal diversion is commonplace in pediatric surgery, in cases of anorectal malformations, Hirschsprung's disease, inflammatory bowel disease, traumatic pelvic or genital injuries, perineal burns, and rectal or perianal inflammatory processes in immunocompromised children [1–3]. Some patients with other reasons for segmental bowel resection with immediate reconstruction may be considered for a similar perioperative treatment protocol. There are controversies regarding the components of perioperative management, such as the use of mechanical bowel preparation, the timing and length of antibiotic prophylaxis, the suturing technique, and the timing for postoperative feedings [3–8]. Solid scientific evidence to support recommendations is scarce or lacking, and on the other hand there have been some studies about individual components of the perioperative protocol, but not about an integrated strategy or care bundle, i.e., a set of interventions that have proven effective independently, but when applied together could improve care even more, and should be implemented as standard practice [9]. Other named strategies are called “fast track” [10] or “enhanced recovery protocols” [11], but are not yet widespread routinely applied in children and adolescents, and if so, they have not been validated with properly designed clinical trials. The standard protocol for perioperative care at our institution in children and adolescents scheduled for surgery with an elective anastomosis included admission in advance, mechanical bowel preparation if the distal bowel (distal ileum or colon) was involved, and intravenous antibiotics 24 h before the operation and until full feedings were achieved (and thus anastomotic leak was ruled out). Postoperative fasting extended for a minimum of three days in all patients, even if bowel transit was evident before. Although the latter may seem excessive for some surgeons, that was the routine particularly at our institution, and it still occurs in many settings in our country.

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We recently questioned our practice and, since the available evidence was scarce, we decided to challenge it by means of a clinical trial including several components, in order to set a new paradigm.

1. Objectives and hypothesis

The purpose of this study was to conduct a randomized, noninferiority clinical trial designed with proper methodology to compare the efficacy and safety of an abbreviated perioperative care bundle that included same day admission, avoidance of mechanical bowel preparation (MBP), optimized antibiotic use, and early feeding (8 h postoperatively), versus the standard perioperative management, with admission in advance for routine mechanical bowel preparation, start of feedings 72 h postoperatively, and longer use of antibiotics (since the MBP until feeding tolerance). Our hypothesis was that the abbreviated perioperative care bundle would be at least as safe and efficacious than, or noninferior to, the standard perioperative care protocol, but some of its components may result in earlier discharge.

2. Methods

This was a randomized controlled, noninferiority trial, comparing two different perioperative strategies in children undergoing an elective bowel anastomosis, assigned to two parallel groups. The participants were patients with a temporary intestinal diversion scheduled for an elective ostomy closure or for an operation requiring segmental bowel resection with immediate reconstruction, at the Colorectal Clinic of the Department of General Pediatric Surgery, National Institute of Pediatrics, in Mexico City, Mexico. Patients of any gender, from 0 to 17 years old, with parental consent would be eligible for the study during the recruitment period, from April 2016 through July 2018. The exclusion criteria were the need for more than one anastomosis, a history of more than one laparotomy, or comorbidities such as immunodeficiency, renal failure, and electrolyte imbalance. As part of the preoperative evaluation, in all patients with intestinal diversion the patency of the distal bowel was verified with a contrast study. If they had a program of rectal dilations, the adequate passage of the correct size Hegar dilator was verified. The operative and anesthetic protocol was equal for both groups: all the operations were performed or supervised by the same surgeon, and every patient received both general and regional anesthesia, a caudal block in patients younger than two years and an epidural block for other ages. For every patient the anastomoses were constructed manually with a single layer of interrupted sutures with 3-0 or 4-0 polyglactin. Although we occasionally use mechanical sutures in our everyday surgical practice, for standardization we decided to do all the anastomoses handsewn for both groups. No peritoneal drains were used, and the incision was irrigated with normal saline solution after fascial closure. For postoperative analgesia the patients received acetaminophen, 15 mg/kg, and if necessary, ketorolac 0.7 mg/kg was added. Routine gastric decompression was not a part of postoperative care in either group. Patients in whom the operative findings changed the course of treatment were eliminated. In those who had the planned intervention but developed postoperative complications like bowel obstruction, or anastomotic leak, the strategy was modified as needed, but were considered for the analysis in the originally assigned group. The postoperative in-hospital surveillance and the follow up at the clinic were under the supervision of the same surgeon. The timeframe for the study was from April 2016 to August 2018, including a follow up period of at least 30 days postoperatively for all patients.

2.1. Interventions

In the experimental group (Group 1), the patients came in as same day admission, with a fasting period of 6 to 8 h depending on the age. Oral antibiotics were not used for prophylaxis, and intravenous antibiotics were administered 30 min before the incision (ceftriaxone 50 mg/kg/dose and metronidazole 10 mg/kg/dose). Anesthesia, surgical technique, and postoperative analgesia were as described above. Oral feedings were initiated with clear liquids 8 h after surgery, and if tolerated, they were advanced to regular diet for their age for the next feeding, which could be breast milk for infants younger than 6 months of age. Two additional doses of intravenous antibiotics were administrated before the removal of the catheter from the peripheral vein. The conditions for discharge included tolerance of ≥80% of the regular diet, adequate peristalsis (assessed by audible and regular bowel sounds on auscultation), pain control, adequate mobility and absence of fever. The follow up was by means of a phone call 72 h after discharge, and at the clinic on the 7th +/−2 and 30th +/−2 postoperative days.

In the standard group (Group 2), the patients were admitted 24 to 48 h in advance, and they received mechanical bowel preparation (MBP) with polyethylene glycol (1 pack of 105 g diluted in 1 l of water) at a dose of 100 ml/kg PO or with a nasogastric tube if needed, and irrigations with 0.9% normal saline solution, either through the proximal and distal stoma, or through the proximal stoma and the rectum if they had a Hartmann's procedure. Oral antibiotics were not used for prophylaxis, and IV antibiotics were initiated at the time of MBP, with ceftriaxone 50 mg/kg/dose BID and metronidazole 10 mg/kg/dose TID, and it was continued until the patient had tolerance ≥80% of the regular diet. Anesthesia, surgical technique, and postoperative analgesia were as described above. In the postoperative period, feedings were started 72 h after surgery with clear liquids PO, and if there was adequate tolerance, they were advanced to regular diet for their age. The conditions for discharge were the same as for Group 1. Follow up visits at the clinic were scheduled for postoperative days 7th +/−2 and 30th +/−2.

For both groups, all the surgical procedures were performed by general pediatric surgery residents, under direct supervision of the first author, who is a general pediatric surgeon, with further training in pediatric colorectal surgery, certified by the Mexican Board of Pediatric Surgery, and with 8 years of experience. Four senior residents participated as operating surgeons, all of them with previous experience with bowel anastomoses, and each one performed between 17 and 19 operations for this study.

2.2. Outcomes

The outcomes were divided in two sets, one for efficacy and the other for safety. The main variables for efficacy were 1) time for tolerance of ≥80% of the regular diet (in hours); 2) time for the first postoperative fecal evacuation (in hours); 3) absence of intestinal dysfunction, either ileus or mechanical bowel obstruction (registered through the presence of abdominal distention with or without abdominal pain, gastric or biliary vomiting, need for nasogastric decompression, and inability to pass gas or stool). A secondary efficacy outcome was the length of hospital stay. The variables for security were: 1) dehiscence or leakage of the intestinal anastomosis, 2) organ/space surgical site infection, 3) superficial or deep surgical site infection (SSI).

2.3. Sample size

The sample size was calculated for equivalence studies [12], to consider the treatment of the experimental group (group 1) not inferior to the treatment of the standard group (group 2), with a threshold δ of 0.1; since the anastomotic leak or dehiscence was considered the most serious potential complication, with a reported incidence of 3%, and calculating 5% of losses to follow up, the size obtained was $n = 37$ participants per group.

2.4. Randomization, allocation, and blinding

Randomization was done with a table of random numbers, in blocks of four. One of the researchers generated the allocation sequence, with sealed envelopes, and this was hidden until the patient was recruited

by the principal investigator at the clinic, when the envelope was opened. The participants, parents and healthcare professionals involved in the perioperative care were not blinded, but those assessing the outcomes did not know the intervention assigned.

2.5. Statistical methods

Statistical analysis was done with the Statistical Program for the Social Sciences version 22 (IBM SPSS version 22, 2013, IBM Corporation, Armonk, NY, 2013), with descriptive statistics, Fisher's exact test (FE) or Chi^2 for analysis of the categorical variables, and Student's T test for numerical variables. To analyze the age distribution, we used the Mann–Whitney U test, and the Kruskal–Wallis test for the etiology of the underlying disease.

2.6. Trial registration

This protocol was authorized by the Institutional Review Board with the number 0010/2016.

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3. Results

3.1. Recruitment

The protocol was started in April 2016, and by July 2018 the sample size was completed. One hundred and one patients were evaluated for eligibility, but 25 were excluded (6 patients had anemia, 1 had an impaired glomerular filtration rate, and 13 had more than one laparotomy; another 5 children with logistics problems for follow up owing to living in a remote zone).

A total number of $N = 76$ children were randomized, and 38 were assigned per group, as depicted in Fig. 1.

The information regarding the basal characteristics of both groups, showing that both were equivalent, is summarized in Table 1. The age was analyzed with the Mann Whitney U test, and there was no difference, with p 0.267. Regarding the type of disease, the Kruskal–Wallis test had a result of p 0.07. For the number of stomas, the Chi^2 had a result of p 0.151, and the same test was used for the anatomical site, with a result of p 0.747.

3.2. Outcomes

From the 76 patients allocated, the total number of analyzed patients was 74, with 37 per group, since two were eliminated. One patient in

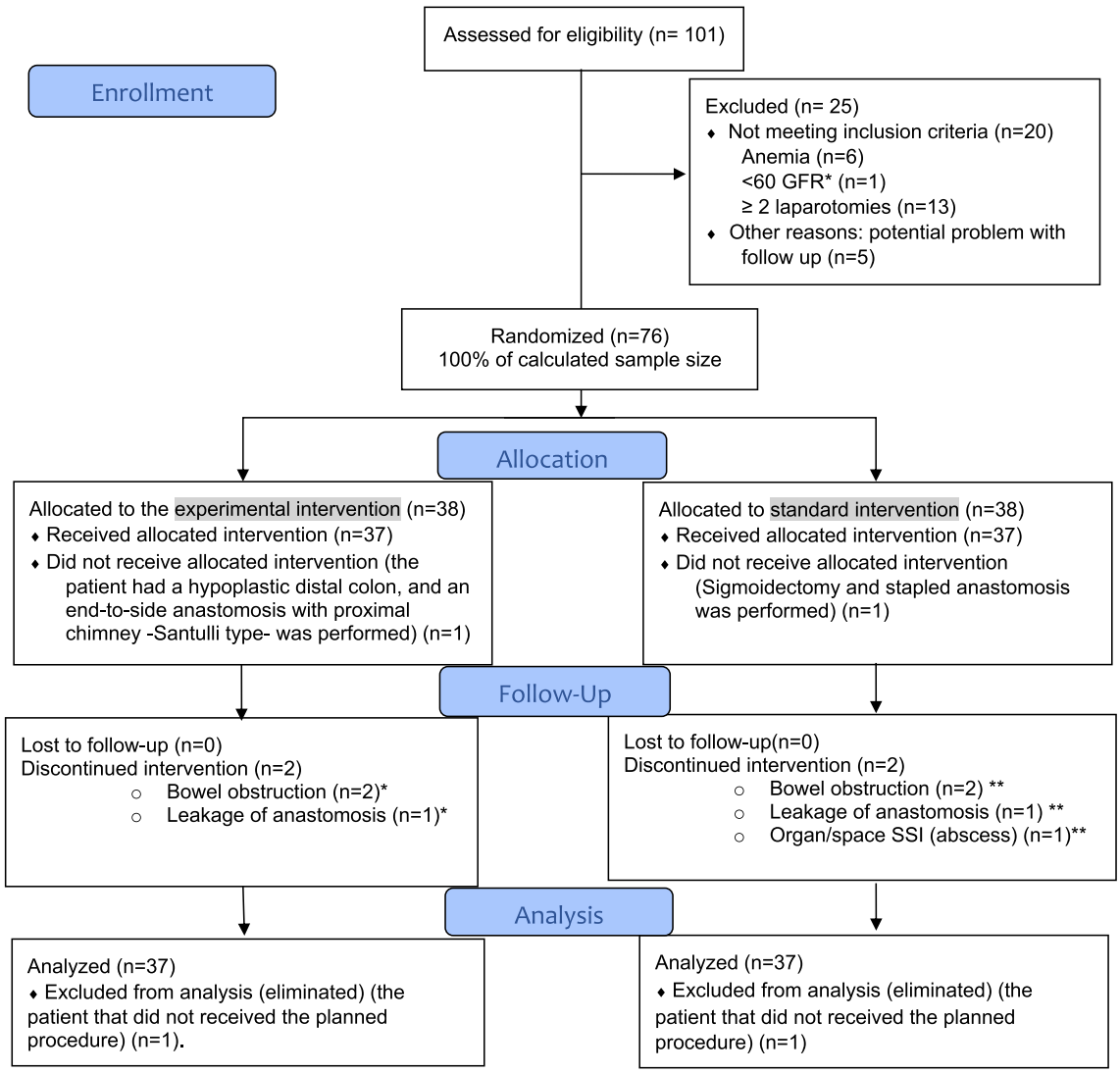

Fig. 1. Flow diagram according to CONSORT (Consolidated Standards of Reporting Trials). *In the experimental intervention group, one of the patients with bowel obstruction required reintervention; he was found to have an anastomotic leak. ** in the standard intervention group, one of the patients that developed bowel obstruction required reintervention; he was found to have an anastomotic leak with an organ/space surgical site infection (intrabdominal abscess).

Table 1
Results of the demographic variables.

Variable	Group 1 (Intervention)	Group 2 (Standard)	Statistical significance
Age (months)	Median 10 (range 5–137)	Median 13 (range 2–168)	p 0.267
Underlying disease			p 0.070
-ARM	27	19	
-HD	4	10	
-Neonatal obstruction	3	1	
-Appendicitis (ileostomy)	3	0	
-Other	1	8	
Types of stoma			p 0.151
-1	5	2	
-2	32	31	
-None	0	4	
Involved anatomical site			p 0.747
-Ileum	3	3	
-Ileum–colon	3	4	
-transverse colon	3	3	
-descending colon	0	2	
-sigmoid	27	25	

ARM: anorectal malformation. HD: Hirschsprung's disease.
Note: One patient from each group was eliminated; in group 1 it was a patient with a history of neonatal obstruction that had a Santulli procedure, and in group 2 it was one patient with ARM and megasigmoid that had a more complex procedure (see text below).

each group did not receive the assigned intervention, because the operative findings mandated a different procedure and not just a regular end-to-end anastomosis. In one of them, from group 1, the distal colon was hypoplastic with a disproportion ratio of 8:1, so it was decided to perform an end-to-side anastomosis with a proximal chimney (Santulli procedure); in the other patient, a case from group 2, he was found to have a significant sigmoid dilation, a sigmoidectomy was done, and a stapled anastomosis was constructed for reconnection.

The results for the efficacy variables were as follows: the median time for tolerance of ≥80% of the regular feedings was of 19 h (range 7–138 h), and a mean of 21.7 h (SD 21.88, with CI 95% 14.69 to 29.71) in the experimental group versus 92 h in the experimental group, and the Student's T test had a p value of <0.001, with a 95% confidence interval (CI) of −92.48 to −63.62. The median time for the first bowel movement was of 15 h (range 4 to 52), and a mean 16.8 h (SD 11.62, 95% CI 12.81 to 21.02) in the experimental group versus 34 h (range 6 to 74) and a mean of 35.7 (SD 17.52, 95% CI 29.86 to 41.55) in the experimental group, with a Student's T test p value of <0.001, with a 95% CI of −25.92 to −12.01. Bowel dysfunction occurred in 4 patients, 2 in each group, with a Fisher's exact test p value of 0.693; one subject in each group developed postoperative ileus, which resolved even without gastric decompression, and 1 patient in each group coursed with mechanical bowel obstruction that initially required a nasogastric tube, Fisher's exact test of p 0.753, and later on required reintervention, with a Fisher's exact test result of p 0.753. The length of stay was considered a secondary outcome for efficacy, and it was a mean of 1 day (SD 1.28) and median of 1 day (range 1–7) for the abbreviated protocol versus a mean of 6.57 days (SD 3.07) and a median of 6 days (range 1–22) for the standard one, with a Student's test p value of <0.001, with a 95% CI of −6.23 to −4.04. Regarding the safety outcome variables, the two patients that required reintervention were found to have an anastomotic leak, one from each group, with a 2.7% rate and a Fisher's exact test of p 0.753. One of these patients, from the standard group, developed an organ-space surgical site infection, an intraperitoneal abscess, which represents a rate of 1.35%, and a Fisher's exact test of p 0.500. There were no other cases of surgical site infection, either superficial or deep. See Table 2. There were no readmissions after discharge for this study.

4. Discussion

Over the last two decades significant changes have occurred in the perioperative management of adult patients undergoing elective colorectal surgery, but similar changes have not yet been defined as new guidelines in pediatric patients undergoing operative colorectal procedures. In this study we aimed to incorporate different simultaneous interventions in an integrated manner. There have been studies about the use or avoidance of mechanical bowel preparation, the stewardship of prophylactic antibiotics, the use of routine nasogastric decompression, and the timing for the start of feedings, and based on those we considered that a clinical trial was the best study design to compare this composite strategy against the usual perioperative protocol at our institution, measuring not only the effectiveness but also the safety of the intervention. In order to measure the impact of several actions in a single trial, we decided to use the concept of "care bundle". This concept was developed at the turn of the century by a joint initiative by the Institute of Health Improvement (IHI) and the Voluntary Hospital Association (VHA) to improve quality in the setting of Intensive Care Units, with two initial "bundles", the IHI Ventilator Bundle and the IHI Central Line Bundle, integrating evidence based individual strategies into an "all-or-nothing" model [9]. Our original idea was that if our trial proved the proposed care bundle to be at least noninferior to the standard practice, we would recommend its implementation in the routine practice for perioperative care in elective bowel anastomoses with that "all-or-nothing" approach.

Within this composite strategy, our main concern was to demonstrate that the mechanical bowel preparation could be obviated in patients undergoing elective anastomoses. Regarding the bowel preparation, there are two issues, one is the mechanical bowel preparation with orally administered solutions in order to clear the bowel from

Table 2
Outcomes.

Variable	Group 1 (Intervention)	Group 2 (Standard)	Statistical significance
Time to tolerance of ≥80% of regular diet, postoperatively	Median 19 h (range 7 to 138) Mean 21.7 h (SD 21.88, with 95% CI 14.69 to 29.71)	Median 92 h (range 52 to 264) Mean 99.8 h (SD 38.27, with 95% CI 87.03 to 112.54)	p < 0.001 95% CI −92.48 to −63.62
Time to first postoperative bowel movement	Median 15.0 h (range 4 to 52) Mean 16.8 h (SD 11.62, 95% CI 12.81 to 21.02)	Median 34 h (range 6 to 74) Mean 35.7 (SD 17.52, 95% CI 29.86 to 41.55)	p < 0.001 95% CI −25.93 to −12.01
Postoperative bowel dysfunction	2 (5.4%)	2 (5.4%)	p 0.693
NG tube needed	1 (2.7%)	1 (2.7%)	p 0.753 (Chi^2)
Anastomotic leak (reintervention)	1 (2.7%)	1 (2.7%)	p 0.753
SSI, superficial	0	0	
SSI, deep	0	0	
SSI, space (intraabdominal abscess)	0	1	p 0.500 (Chi^2)
Length of stay (days)	Mean 1, SD 1.28 Median 1 (range 1–7)	Mean 6.57, SD 3.07 Median 6 (range 1–22)	p < 0.001 CI −6.23 to −4.03 (Student's T)

CI: confidence interval. SD: standard deviation. NG: nasogastric. SSI: surgical site infection.

stool, and the other is the use of oral antibiotics to decrease the bacterial counts. Mechanical bowel preparation has been used for decades now, but it has been challenged in studies done in the adult population since the previous decade. The preparation solutions may contain polyethylene glycol (PEG), sodium phosphate, sodium picosulfate or magnesium nitrate; additionally, enemas or irrigations with normal saline given per rectum or through the stomata can be used. The reasoning for the use of MBP has been to decrease the risk of surgical site infections and anastomotic leaks, and to a lesser extent to provide a cleaner surgical field that could facilitate the operative technique; nevertheless, this postulates lack solid foundations since they were based mostly on expert opinions [13]. The evidence from adult studies in patients undergoing colorectal surgery has failed to prove a protective effect from MBP. A Cochrane systematic review in 2003 reported an increase risk of anastomotic leak associated with the use of MBP, with an OR of 2.03, and a 95% CI 1.276–3.26, and $p = 0.03$ [14]. The Canadian Society of Colorectal Surgeons in 2010 issued a Clinical Practice Guideline foregoing the use of MBP, owing to this risk [13]. The mechanical bowel preparation causes histological changes in the thickness of the superficial mucosa, with decreased number of epithelial cells, edema of the lamina propria, and infiltration of the submucosa with lymphocytes and neutrophils. It is not clear if these changes could lead to bacterial translocation, and to an increased rate of anastomotic leaks [15]. Even though the use of MBP has been almost abolished in adult colorectal surgery, the pediatric surgeons have not changed that practice in a widespread manner yet. Feng et al conducted a survey among members of the American Pediatric Surgical Association, and found the following rates of perioperative protocols: MBP alone 31.1%, diet modification only 26.8%, MBP with oral antibiotics 19.6%, no preparation or diet modification 12.2%, and oral antibiotics alone (5.4%) [16]. Another survey by Feng et al proposed the idea that more than a problem of equipoise, the lack of use of oral antibiotics for bowel preparation was because of a knowledge gap in the pediatric surgical community about the existing evidence for it [17]. Another study by the same group of researchers, included more than 5000 patients treated at 42 hospitals across the United States; 49% were preadmitted, and 54.3% of them received MBP (with polyethylene glycol) alone, 18.8% received MBP with oral antibiotics, 4.2% oral antibiotics alone, 22.7% neither MBP nor oral antibiotics, and 2.2% an electrolyte laxative solution. Although they did not analyze postoperative outcomes in this paper, from a literature review they called "evidence-based bowel preparation treatment" the administration of oral antibiotics, either with or without MBP [18]. Ares et al published a retrospective review of more than 1500 patients undergoing elective colon surgery, and found a shorter length of stay but an increased rate of complications in those patients with no bowel preparation when compared to those undergoing MBP and MBP with oral antibiotics, and they suggested that a three-armed controlled trial was needed [19]. Besides all those scientific facts, for practical purposes, most patients find MBP unpleasant [13], and in children a nasogastric tube may be required because of poor tolerance, and although outpatient MBP has been advocated, it is customary in many centers to admit the pediatric patients for it. The use of oral antibiotics as adjuvant to preoperative care for ostomy closure was studied by Beckler et al in a retrospective 10-year review, and they did not find a significant decrease in the surgical site infection rate in those patients receiving oral antibiotics in addition to MBP and intravenous antibiotics before an elective procedure [20]. The study by Rosenfeld compared pediatric patients undergoing colostomy closure, with or without MBP, without significant differences in surgical complications, with similar postoperative length of stay in both groups, but with earlier preoperative admission in those receiving MBP [2]. Oral antibiotics were not evaluated in this trial either. In other words, this trial found that foregoing the MBP was not inferior, but it missed the chance to prove it more effective in terms of timing for feedings and length of stay.

In our study we did not find a significant difference between both groups regarding anastomotic leaks, surgical site infection, or the need for reoperation, so we considered it noninferior. Although we do not have a publication regarding our surgical site infection rate, from the internal reports of our Department of Hospital Epidemiology we knew it was less than 5%. This may be owing to the fact we follow a strict protocol that precludes unwarranted variations. The responsible use of antibiotics for prophylaxis in surgery is a mainstay of modern care, so we included this as a component of our "all or nothing" strategy to change our practice regarding the use of intravenous antibiotics, and followed the current guidelines from the Centers for Disease Control [21]. Although there are recommendations for the use of oral antibiotics as an adjunct to prophylaxis, we decided not to include that variable in this study; nevertheless, we did not observe a significant infection rate. Now that we plan to implement our abbreviated preoperative care bundle as a routine, there will be room to plan a new study comparing it against the same protocol with the addition of oral antibiotics.

Up to seven years ago, the protocol for elective bowel anastomoses at our institution included postoperative gastric decompression with a nasogastric tube, and fasting for five days in most instances, and parenteral nutrition was administered often. Since then we avoided routine gastric decompression, and we shortened the postoperative fasting period to three days. Postoperative early feeding has been advocated in recent publications [3,5–8], but the timing to start clear liquids or diet was 24 h, and the time for full feedings has not been drastically reduced, and neither was the length of stay. We decided to include this issue in our abbreviated protocol, and our findings were even better than we expected, allowing for a significantly earlier discharge. Fast-track or abbreviated perioperative management that results in an enhanced recovery has been on the scene since 1990s, and this has been led by the ERAS® (Enhanced Recovery After Surgery) protocols, but the definition and implementation of a pediatric version are still in process. Approximations to it include reviews [22], surveys [23], matched comparisons to adult controls in pediatric patients undergoing bowel surgery [24], the proposal of an adapted pediatric Enhanced Recovery Protocols by a group of experts [25], and trials [26,27]. The survey by Short et al showed an interest among the pediatric surgery community in the United States, and a relatively low proportion of surgeons were already using some of the strategies included in ERAS®, but found that 7 of the 21 items were not considered applicable to children [23]. The literature review by Schinnick et al. identified only five studies with an Enhanced Recovery Protocol somehow following the ERAS® protocol, but none of them followed a prospective comparative randomized trial design [22]. The study by West et al compared children undergoing surgery for inflammatory bowel disease to similar adult patients, and found that if an adapted ERAS® protocol would have been followed, the time for feedings, for mobilization, and the length of stay, would all have been shorter [24]. Although our abbreviated care bundle could be considered an Enhanced Recovery Protocol, it does not qualify to be labeled as an "ERAS-type" one. The main reason for it, is that ERAS® studies are not designed to evaluate a new strategy as a clinical trial, but to integrate already proven ones [28], and our composite strategy was not considered already proven to be superior or not even noninferior, and we also considered that several of the ERAS® guidelines were not applicable. Also, there is the issue of copyright, since the ERAS Society requires affiliation, and we are not in such position.

To conclude, our abbreviated perioperative care bundle was proven to be as safe but more efficacious than standard care. In terms of the time-sensitive outcomes, such as the time for the start and tolerance of oral feedings, the time for postoperative stooling, and the length of stay, the abbreviated care bundle was proven to be superior. A limitation to consider for this study would be that the statistical and clinical differences may be magnified since in the group with mechanical bowel preparation feedings were withheld until day three, instead of starting them after the first bowel movement. As explained before, this was planned this way because the purpose was to contrast the protocol set at our institution against the proposed bundle of care. The strength of this study is that it was a well-designed clinical trial, with

a calculated sample size, with an intention to treat analysis, and without losses to follow-up. We did not consider costs in this analysis, but we can assume that reducing the use of antibiotics, intravenous fluids, and the length of stay, will result in significant savings for the institution.

We will implement this care bundle as our routine, and it will eventually provide more data. We will apply it uniformly to patients that have an elective bowel anastomosis, either hand-sewn of stapled. We consider our results valid and therefore generalizable, and we firmly believe that it will prove to be both safe and effective in "real life" environments.

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