Published in final edited form as:

J Pediatr Gastroenterol Nutr. 2011 May ; 52(5): 590–594. doi:10.1097/MPG.0b013e3181fe2d7a.

Cisapride Improves Enteral Tolerance in Pediatric Short Bowel Syndrome with Dysmotility

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Abstract

Background—Gastrointestinal (GI) dysmotility is common in pediatric short bowel syndrome (SBS), leading to prolonged parenteral nutrition (PN) dependence. There is limited literature regarding the safety and efficacy of cisapride for this indication.

Objectives—To describe the safety and efficacy of cisapride for enteral intolerance in pediatric SBS.

Study design—Open-labeled pilot study in a limited access program for cisapride. Indications were SBS with underlying dysmotility and difficulty advancing enteral feeds despite standard therapies and without evidence of anatomic obstruction. Patients received cisapride 0.1–0.2 mg/kg/dose for 3 to 4 doses per day. We collected electrocardiogram, nutrition and anthropometric data prospectively at study visits.

Results—10 patients mean (SD) age 30.3 (30.5) months were enrolled in our multidisciplinary pediatric intestinal rehabilitation program. Median (IQR) duration of follow-up was 8.7 (3.1–14.3) months. Median (IQR) residual bowel length was 102 (85–130) cm. Median (IQR) citrulline level was 14.5 (10.5–31.3) micromoles/L. Diagnoses included isolated gastroschisis (n=3), gastroschisis with intestinal atresia (n=4), necrotizing enterocolitis (n=2), and long-segment Hirschsprung's disease (n=1). 6 subjects had at least 1 prior bowel lengthening procedure. Median (IQR) change in percentage enteral energy intake was +19.9% (15.4–29.8%) during follow-up (p=0.01). 7 patients improved in enteral tolerance during treatment and 2 weaned completely from PN.

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Complications during therapy were prolonged QTc interval (n=2), gastrointestinal bleeding (n=2), D-lactic acidosis (n=1) and death due to presumed sepsis (n=1). Longitudinal analysis (GEE model) showed a strong positive association between cisapride duration and improved enteral tolerance. Mean percentage of enteral intake increased by 2.9% for every month on cisapride ($p<0.0001$).

Conclusions—Cisapride is a potentially useful therapy in pediatric SBS patients with GI dysmotility. We observed modest improvement in feeding tolerance where prior treatments failed. However, patients treated with cisapride require careful cardiac monitoring as QTc prolongation occurred in 20% of our cohort.

Keywords

cisapride; dysmotility; feeding intolerance; short bowel syndrome; gastroschisis; parenteral nutrition; QTc prolongation; intestinal failure

Introduction

Short bowel syndrome (SBS) is a devastating condition characterized by chronically impaired absorption by the small intestine.(1,2,3) The most common etiologies in children are necrotizing enterocolitis, intestinal atresia, volvulus and gastroschisis.(4,5,6) The incidence of SBS has been estimated at 24.5/100,000 live births.(7) Current treatment includes supportive care with long-term parental nutrition (PN) while enteral feeds are carefully advanced. Unfortunately, many patients require prolonged PN due to chronic diarrhea and nutrient malabsorption. Another common reason for prolonged PN is gastrointestinal (GI) dysmotility.(8) Symptoms can include vomiting, regurgitation, pain and bloating. Although long-term PN is a life-saving therapy, it is associated with multiple complications, including sepsis, liver disease, electrolyte instability, hyperglycemia, and metabolic bone disease. Therefore, a goal of therapy for SBS is to wean PN as quickly as feasible.

In SBS patients with possible GI dysmotility, management begins with evaluating for anatomic obstruction. Other strategies include maximizing anti-acid medications, using continuous intra-gastric tube feeding, placement of a feeding tube distal to the pylorus, treatment of underlying enteropathies including bacterial overgrowth, as well as use of prokinetic medications, such as metoclopramide and cisapride. Clinicians prescribing either of these pro-kinetic medications must do so with great caution and diligence. In February 2009, the US Food and Drug Administration (FDA) issued a black-box warning regarding the risk of tardive dyskinesia with chronic use of metoclopramide.(9) Therefore, clinicians are often reticent about using this medication for a prolonged duration. In 1993, the FDA approved the administration of cisapride (brand name Propulsid) for adults with gastroesophageal reflux disease. Cisapride improves motility by enhancing acetylcholine release at the myenteric plexus. It has been used for treating functional dyspepsia, gastroparesis, chronic constipation and chronic intestinal pseudo-obstruction. In an animal model using rabbit Purkinje fibers, cisapride prolongs the repolarization phase at plasma concentrations expected from therapeutic doses (10). There were reports of an association with its use and prolonged QTc interval leading to Torsade's de Pointes, heart block and death, especially in elderly patients, but also in children. These events initially prompted the manufacturer to discourage physicians from prescribing concurrent medications that increase serum cisapride levels by inhibiting hepatic cytochrome p-450 3A4, such as macrolide antibiotics, antifungals and cimetidine. In 2000, cisapride was removed from the market after reports of at least 341 cardiac dysrhythmias including eighty deaths.(11)

Under the US Limited-Access Program for Cisapride developed through Janssen Pharmaceutica Inc (Titusville, N.J) and the FDA, we obtained approval for the administration of cisapride in children with refractory GI dysmotility, including those with pediatric SBS. A literature search revealed only a single case report describing its use in SBS.(12) This patient cohort would seem to be at especially high risk of dysrhythmias while using cisapride due to frequent electrolyte instability. Here we report our two years experience using cisapride for enteral intolerance in pediatric SBS.

Methods

All subjects included in the present study were followed at the Center for Advanced Intestinal Rehabilitation at Children's Hospital Boston between January 2007 and January 2009. This multi-disciplinary program involves intestinal failure specialists in pediatric gastroenterology, surgery, nutrition, nursing, pharmacy and social work.(13) All subjects were enrolled in the Limited Access Program for Cisapride after obtaining parental informed consent. The protocol was approved by the institutional review board at Children's Hospital Boston.

All study subjects had SBS using the standard functional definition of PN dependence for congenital or acquired disease of the gastrointestinal tract for at least ninety days.(1) At the time of enrollment, all subjects were making little or no progress in advancing enteral feeds and had failed standard medical and surgical therapies to treat feeding intolerance. Feeding intolerance was defined as vomiting, regurgitation, pain and bloating directly associated with enteral feeds. We excluded subjects with a history of cardiac disease, prolonged baseline QTc interval, family history of prolonged QTc, electrolyte abnormalities, serious uncontrolled illness, as well as concomitant use of cardiotoxic medications or medications interfering with cisapride metabolism. History of PN exposure was collected from medical records. As outlined in the Limited Access Program, prior to treatment with cisapride, all participants underwent laboratory tests (complete blood counts, electrolytes, and liver panel), 12-lead electrocardiograms (ECG) for QTc interval and contrast radiographic studies for anatomic obstruction. If these results were normal and the patient fulfilled inclusion criteria, we prescribed cisapride at 0.1 mg/kg/dose for four doses per day. An ECG was obtained four to six days after starting cisapride. If ECG remained normal and response to therapy was not observed, we then increased the dose to 0.2 mg/kg/dose or maximum 10 mg/dose four times per day at next clinic visit. Again, an ECG was obtained four to six days after starting a new cisapride dose. As outlined by the protocol, patients had scheduled study visits every two months for clinical assessments including anthropometrics; ECGs and serum chemistry panels were checked every four months. Subjects were instructed to discontinue cisapride temporarily for prolonged QTc interval (defined as >450 msec), electrolyte abnormalities or general anesthesia. Dieticians used recommended daily allowance (RDA) to devise energy intake recommendations, and titrated PN prescriptions for appropriate weight gain according to CDC growth charts. Whenever possible, enteral nutrition was advanced as much as tolerated according to our standard feeding algorithm. (14)

Data collected included patient characteristics, medical and surgical history, and anthropometric data. Our study team recorded adverse effects prospectively. Height and weight z-scores were calculated using CDC 2000 growth charts. The percentage of enteral energy intake was calculated as the amount of dietary energy intake derived by oral and/or enteral routes divided by the total energy intake (oral, enteral plus parenteral routes) multiplied by 100. Primary end-points were defined as change in percentage of enteral energy intake, and change in QTc interval from baseline. We used Wilcoxon signed-rank test to compare change in percentage enteral intake and parenteral energy intake between

baseline and follow-up. Secondary end-points were defined as changes in weight and height z-scores, as well as death and any other adverse outcomes. We used a longitudinal regression model to balance effects seen amongst subjects contributing varying lengths of follow-up. We accounted for within-subject correlation in the outcomes by using general estimating equation (GEE) technique. Analysis was performed using SAS 9.2 (Cary, NC).

Results

The clinical characteristics of the ten subjects enrolled are presented in Table 1. The mean (SD) patient age at enrollment was 30.3 (30.5) months. The ages ranged from one month to seven years. There were a variety of underlying diagnoses leading to SBS, including gastroschisis with and without intestinal atresia, necrotizing enterocolitis, and long-segment Hirschsprung's disease. Only one female subject was enrolled. The median (IQR) PN exposure prior to starting cisapride was 23 months (5.6 months to 4.9 years). For all subjects, this length of PN use reflected nearly an entire lifetime with few interruptions. The median (IQR) duration of follow-up was 8.7 (3.1 – 14.3) months. The median (IQR) residual bowel length was 102 (85 – 130) cm. There were two subjects whose residual bowel lengths were unknown. Six subjects had previously undergone at least one bowel lengthening procedure, such as serial transverse enteroplasty procedure (STEP) or Bianchi procedure, including two subjects who had had both procedures. Four subjects were known to be missing the ileocecal valve. The median (IQR) plasma citrulline level was 14.5 (10.5 – 31.3) micromol/L. Five subjects had citrulline levels less than 15 micromol/L, which is prognostic of low likelihood of eventual PN independence.(15)

Figure 1 depicts the percentage of enteral energy intake after enrollment on study protocol. Enteral tolerance improved in seven of the ten subjects during treatment, including two subjects who weaned completely from PN. The median (IQR) percentage of enteral energy intake at baseline was 30.3% (4.4 – 52.8%). Feeding route at baseline was intragastric (60%), post-pyloric (30%), mixed oral and intragastric (10%). Comparing the parenteral energy intake at baseline and at last follow-up, the median (IQR) change was –20.8 (–61.0 to –14) kcal/kg/day ($p=0.01$). Comparing percentage enteral energy intake at baseline and at last study follow-up, the median (IQR) change was +19.9% (15.4 – 29.8%) ($p=0.01$). Comparing percentage enteral energy intake at baseline and at last follow-up using cisapride, the median (IQR) change was +18.9% (2.6–26.65%) ($p=0.03$). Using longitudinal regression analysis, we detected a strong positive association between duration of cisapride administration and improved enteral tolerance. The mean percentage of enteral energy intake increased by 2.9% for every month on cisapride ($p<0.0001$). Cisapride dose per day was not a significant predictor of enteral tolerance ($p=0.5$). Weight and height Z-scores did not significantly change according to treatment duration ($p=0.08$ and $p=0.25$ respectively). Median (IQR) weight gain was 7.7 (3.7–17.2) grams per day and height velocity was 0.15 (0.1 – 0.38) cm per week. Five of the ten subjects discontinued cisapride by the last follow-up.

All subjects had documented normal QTc intervals prior to treatment with cisapride. Prolonged QTc intervals developed in two subjects at 30 days and 11 months on treatment, neither of whom was symptomatic. As a result, one of these subjects permanently discontinued cisapride. The other subject restarted cisapride at a lower total daily dose after QTc returned to normal. The subject's ECG was repeated again while taking medication and it was normal. Among the whole cohort, we did not detect a relationship between length of QTc and total daily cisapride dose ($p=0.07$) or treatment duration ($p=0.36$). The mean change in QTc interval from baseline was –0.44 msec (95% CI: –1.23 to 0.40).

Other adverse events noted during the study included three subjects with GI bleeding, one subject with D-lactic acidosis and one death due to presumed sepsis. The data safety and monitoring board concluded that it was doubtful that cisapride was related to the death.

Discussion

In SBS, the most common obstacles to weaning PN and advancing enteral nutrition are diarrhea and nutrient malabsorption. GI dysmotility, however, is another problem that frequently leads to prolonged PN dependence. Unfortunately, there are few therapeutic medical modalities available, and US federal regulations and advisories have limited the availability of two such agents: metaclopramide and cisapride.

In our open labeled pilot study among pediatric patients with nearly lifelong PN dependency, we observed a median increment of percentage enteral nutrition of 19.9% (IQR, 15.4 – 29.8%) over the course of follow-up ($p=0.01$). Nearly all the improvement in enteral tolerance occurred while using cisapride. Two of ten subjects weaned completely from parenteral nutrition support, and seven of ten had some improvement in enteral tolerance. There was no evidence of growth faltering while PN was weaned in this cohort, as weight gain and height velocity was maintained, as were weight and height z-scores, before and after the course of cisapride. Therefore, decreasing parenteral nutrition support reflected real improvement in enteral tolerance.

There are few studies of therapies for enteral intolerance in SBS. Modi et al. reviewed nutritional outcomes of the STEP registry of 38 patients. (16) The percentage of enteral energy intake at baseline and length of follow-up were similar to our study. However, enteral intake improved by 36% following STEP compared with 19.9% in the present study. The STEP and cisapride have both been used in short bowel syndrome. However, the STEP is a surgical intervention that lengthens and tapers the bowel, thereby improving intestinal function and motility. Cisapride, on the other hand, is a medical treatment that treats only GI motility and has no direct effect on intestinal structure. The majority of our subjects had a history of autologous bowel reconstructive surgery, such as the STEP, and still remained PN dependent.

We observed QTc prolongation in two subjects (20%); both subjects were clinically asymptomatic. The QTc prolongation was discovered as a result of routine ECG screening. The incidence of QTc prolongation is similar to previous reports in the literature. Khongphatthanayothin et al. reported an incidence of QTc prolongation (defined as >440 msec) of 13% in a prospective study of 101 children treated with cisapride. (17) The incidence was only 6% in children without any identifying risk factors, such as drug interaction, heart disease, renal or liver dysfunction, electrolyte abnormalities or prematurity. Hill et al. found an incidence of QTc prolongation (defined as >450 msec) of 31% in a prospective study of thirty-five children treated with cisapride. (18)

Of note, the majority of our SBS subjects had dysmotility due to gastroschisis. In this condition, prenatal amniotic fluid exposure to the serosal surface of the GI tract causes inflammation and bowel wall thickening, leading to post-natal disordered motility. A rat model of gastroschisis suggests that the damage leads to delayed neuronal differentiation and abnormal myenteric plexus organization. (19) In infants with gastroschisis, esophageal motor abnormalities and gastrointestinal dysmotility are common. (20,21,22) Erythromycin is not effective in improving enteral tolerance after primary repair. (23) In contrast to other prokinetics like erythromycin, metoclopramide and octreotide, cisapride improves ileal contractility in newborn and adult rabbits. (24) Our findings suggest that cisapride may be useful in humans with gastroschisis as well.

Our study had several limitations. First, the manner in which the manufacturer made the study drug available dictated an open-label design. A randomized placebo-controlled study of cisapride in SBS would have been preferable but logistically infeasible. In addition, extensive data on enteral feeding advancement prior to cisapride treatment was not available for all patients, limiting the control data to the period of time immediately prior to cisapride initiation. However, all patients had refractory feeding intolerance as reflected by nearly lifelong PN dependence (n=10), history of autologous bowel reconstructive surgery (n=6), and low plasma citrulline levels (median = 14.5 micromol/L). Taken together, these factors substantiate the severity of intestinal failure in the cohort. A third limitation is the lack of formal manometry testing to corroborate the diagnosis of GI dysmotility. The clinical features of these patients seem sufficient to attribute their symptoms to motility disorders, after anatomic obstruction had been extensively evaluated. In the future, manometry might be helpful in defining which patients might benefit from cisapride treatment, similar to its role in studying erythromycin.(25)

In summary, in ten subjects with SBS and GI dysmotility, cisapride use was associated with a median increment of percentage enteral nutrition of approximately 20%, with 7 patients exhibiting some degree of improvement and two patients weaning completely from PN. QT_C prolongation occurred in 20% of subjects, which is similar to the reported incidence in other conditions. At the time of study enrollment, these subjects were making little or no progress in advancing enteral feeds and had failed all standard medical therapies to treat feeding intolerance with nearly lifelong PN exposure. Among those who tolerated the drug, cisapride use was associated with a modest but statistically significant improvement in enteral tolerance; the mean percentage of enteral energy intake increased by 2.9% for every month on cisapride (p<0.0001). It is important to continue investigating pro-kinetic medications for SBS, as the incidence of gastroschisis continues to increase steadily.(26) Future studies should seek to identify clinical and manometric findings to select patients most likely to benefit from cisapride or other pro-kinetic medical therapy.

Acknowledgments

We thank the entire CAIR team for their expert care of these patients.

This work is supported by NIH grants: T32DK007477-25 (Dr. Raphael), K24DK082792A (Dr. Nurko), 1K24HD058795 (Dr. Duggan)

References

1. O'Keefe SJ, Buchman AL, Fishbein TM, Jeejeebhoy KN, Jeppesen PB, Shaffer J. Short bowel syndrome and intestinal failure: consensus definitions and overview. *Clin Gastroenterol Hepatol*. 2006; 4(1):6–10. [PubMed: 16431298]
2. Duro D, Kamin D, Duggan C. Overview of pediatric short bowel syndrome. *JPGN*. 2008; 47(1):S33–S36. [PubMed: 18667916]
3. Goulet OSF. Short bowel syndrome and intestinal transplantation in children. *Curr Opin Clin Nutr Metab Care*. 2006; 9(3):304–313. [PubMed: 16607133]
4. Olieman JFTD, Penning C. Growth and nutritional aspects of infantile short bowel syndrome for the past 2 decades. *J Pediatr Surg*. 2008; 43(11):2061–2069. [PubMed: 18970941]
5. Vargas JHAM, Berquist WE. Long-term home parenteral nutrition in pediatrics: ten years of experience in 102 patients. *J Pediatr Gastroenterol Nutr*. 1987; 6(1):24–32. [PubMed: 3098947]
6. Cole CRHN, Higgins RD, Ziegler TR, Stoll BJ. Eunice Kennedy Shriver NICHD Neonatal Research Network. Very low birth weight preterm infants with surgical short bowel syndrome: incidence, morbidity and mortality, and growth outcomes at 18 to 22 months. *Pediatrics*. 2008; 122(3):e573–e582. [PubMed: 18762491]

7. Wales PW, de Silva N, Kim J, Lecce L, To T, Moore A. Neonatal short bowel syndrome: population-based estimates of incidence and mortality rates. *J Pediatr Surg.* 2004; 39(5):690–695. [PubMed: 15137001]
8. Phillips JD, Raval MV, Redden C, Weiner TM. Gastroschisis, atresia, dysmotility: surgical treatment strategies for a distinct clinical entity. *J Pediatr Surg.* 2008; 43(12):2208–2212. [PubMed: 19040936]
9. Puiseux FL, Adamantidis MM, Dumontier BM, Dupuis BA. Cisapride-induced prolongation of cardiac action potential and early afterdepolarizations in rabbit Purkinje fibers. *British J of Pharm.* 1996; 117(7):1377–1379.
10. Kenney C, Hunter C, Davidson A, Jankovic J. Metoclopramide, an increasingly recognized cause of tardive dyskinesia. *J Clin Pharmacol.* 2008; 48(3):379–384. [PubMed: 18223146]
11. FDA. Withdrawal of Troglitazone and Cisapride. *JAMA.* 2000; 283(17):2228. [PubMed: 10807369]
12. Puntis JW, Booth IW, Buick R. Cisapride in neonatal short gut. *Lancet.* 1986; 2(8498):108–109. [PubMed: 2873371]
13. Modi BP, Langer M, Ching YA, Valim C, Waterford SD, Iglesias J, Duro D, Lo C, Jaksic T, Duggan C. Improved survival in a multidisciplinary short bowel syndrome program. *J Pediatr Surg.* 2008; 43(1):20–24. [PubMed: 18206449]
14. Utter, S.; Duggan, C. Short bowel syndrome. In: Hendricks, K.; Duggan, C., editors. *Manual of Pediatric Nutrition.* (4th ed). Hamilton, ON: BC Decker; 2005. p. 718-735.
15. Fitzgibbons S, Ching YA, Valim C, Zhou J, Iglesias J, Duggan C, Jaksic T. Relationship between serum citrulline levels and progression to parenteral nutrition independence in children with short bowel syndrome. *J Pediatr Surg.* 2009; 44(5):928–932. [PubMed: 19433172]
16. Modi BP, Javid PJ, Jaksic T, et al. First report of the international serial transverse enteroplasty data registry: indications, efficacy, and complications. *J Am Coll Surg.* 2007; 204(3):365–371. [PubMed: 17324769]
17. Khongphatthanayothin A, Lane J, Thomas D, Yen L, Chang D, Bubolz B. Effects of cisapride on QT interval in children. *Pediatrics.* 1998; 133(1):51–56.
18. Hill SL, Evangelista JK, Pizzi AM, Mobassaleh M, Fulton DR, Berul CI. Proarrhythmia associated with cisapride in children. *Pediatrics.* 1998; 101(6):1053–1056. [PubMed: 9606235]
19. Vannucchi MG, Midrio P, Flake AW, Faussone-Pellegrini MS. Neuronal differentiation and myenteric plexus organization are delayed in gastroschisis: an immunohistochemical study in rat model. *Neuroscience Letters.* 2003; 339(1):77–81. [PubMed: 12618304]
20. Jadcherla SR, Gupta A, Stoner E, Fernandez S, Caniano D, Rudolph CD. Neuromotor markers of esophageal motility in feeding intolerant infants with gastroschisis. *JPGN.* 2008; 47(2):158–164. [PubMed: 18664867]
21. Oyachi N, Lakshmanan J, Ross MG, Atkinson JB. Fetal gastrointestinal motility in a rabbit model of gastroschisis. *J Pediatr Surg.* 2004; 39(3):366–370. [PubMed: 15017553]
22. Cheng G, Langham MR, Sninsky CA, Talbert JL, Hocking MP. Gastrointestinal myoelectric activity in a child with gastroschisis and ileal atresia. *J Pediatr Surg.* 1997; 32(6):923–927. [PubMed: 9200103]
23. Curry JL, Lander AD, Stringer MD. A multicenter, randomized, double-blind, placebo-controlled trial of prokinetic agent erythromycin in the postoperative recovery of infants with gastroschisis. *J Pediatr Surg.* 2004; 39(4):565–569. [PubMed: 15065029]
24. Langer JC, Bramlett G. Effect of prokinetic agents on ileal contractility in a rabbit model of gastroschisis. *J Pediatr Surg.* 1997; 32(4):605–608. [PubMed: 9126764]
25. Jadcherla SR, Berseth CL. Effect of erythromycin on gastroduodenal contractile activity in developing neonates. *JPGN.* 2002; 34(1):16–22. [PubMed: 11753158]
26. Keys C, Drewett M, Burge DM. Gastroschisis: the cost of an epidemic. *J Pediatr Surg.* 2008; 43(4):654–657. [PubMed: 18405711]

Figure 1. Percentage of enteral energy intake of 10 subjects with short bowel syndrome treated with cisapride. Mean percentage of enteral intake increased by 2.9% for every month on cisapride ($p < 0.0001$). Fit line represents the fitted line for regression model.

Table 1

Characteristics of 10 subjects with short bowel syndrome treated with cisapride

Subject	Primary Diagnosis	Age	Gender	Residual bowel length (cm)	Ileocecal Valve Present	Citrulline level (micromole /L)	Treatment Duration (months)	Baseline parenteral energy intake (kcal/kg/day)	Follow-up parenteral energy intake (kcal/kg/day)
1	Gastroschisis and intestinal atresia	1 mo.	Male	95	Yes	12	2	84	0
2	Gastroschisis	7 yrs.	Male	200 [‡]	Yes	24	11	29	0
3	Necrotizing enterocolitis	5 yrs.	Male	104 [‡]	Yes	55	8	78	34
4	Gastroschisis and intestinal atresia	2 yrs.	Female	113 [‡]	No	11	11	76	59
5	Gastroschisis and intestinal atresia	13 mo.	Male	180 [‡]	No	53	12	87	33
6	Gastroschisis	4 mo.	Male	100	Yes	9	12	149	54
7	Gastroschisis	2 yrs.	Male	51 [‡]	No	11	16	64	37
8	Hirschsprung's disease	5 mo.	Male	Unknown	No	8	4	93	75
9	Gastroschisis and intestinal atresia	16 mo.	Male	56 [‡]	Yes	23	3	68	66
10	Necrotizing enterocolitis	3 yrs.	Male	Unknown	Unknown	17	17	41	20

[‡]history of autologous bowel reconstructive surgery, such as STEP, Bianchi procedure or both.