Journal of Pediatric Surgery 56 (2021) 483–486

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Colorectal Conditions

Outcomes of preoperative anal dilatation for Hirschsprung disease☆

Zhixiong Lin, Yu Lin, Jianxi Bai, Dianming Wu, Yifan Fang *

Department of Pediatric Surgery, Fujian Maternity and Child Health Hospital, Fujian, China

ARTICLE INFO

Article history:
Received 20 March 2020
Received in revised form 18 April 2020
Accepted 1 May 2020

Key words:
Anal dilatations
Hirschsprung disease
Enterocolitis
Obstructive symptoms

ABSTRACT

Background/Purpose: There are some studies about the effect of postoperative anal dilatation on anastomotic stenosis and Hirschsprung-associated enterocolitis (HAEC), but we have not seen any report about preoperative anal dilatation. We hypothesized that preoperative anal dilatation could reduce the incidence of HAEC and facilitate the operation. We aim to compare the HAEC rates and postoperative complications between groups who either had or did not have anal dilatations (AD or NAD) prescribed before laparoscopic-assisted Soave pull-through procedures for Hirschsprung disease (HD); by this means, we will evaluate the benefit of dilatations before the surgery for HD.

Methods: A retrospective review of children with HD operated in our hospital between 2014 and 2018 was performed. Those with 21 trisomy, total colonic aganglionosis, multiple stage procedures, serious congenital malformations, and lost to follow-up were excluded. Patients were divided into preoperative anal dilatation group (AD group) and no preoperative anal dilatation group (NAD group). Routine anal dilatation was performed in both groups from 2 weeks after laparoscopic-assisted Soave pull-through. The anal dilatation was carried out daily with metal anal dilators with size appropriate to the age of the child. The size of the anal dilators was increased by 1 mm every 2 weeks for at least 3 months. Demographic data, operation time, pre- and postoperative HAEC rates and postoperative obstructive symptoms between groups were compared. Significance was considered at $P < 0.05$.

Results: There were 95 children (17 female and 78 male) included, 36 AD and 59 NAD. There was no significant difference in demographic data between the two groups. The incidence of HAEC between the groups was not different both preoperatively (14% vs. 24%, $P = 0.298$) and postoperatively (11% vs. 19%, $P = 0.171$). The postoperative obstructive symptoms rates were 19% versus 22% for the AD and NAD groups, respectively ($P = 0.802$). The operation time of group AD was significantly shorter than that of group NAD ($P = 0.008$). Preoperative anal dilatation could shorten the operation time in short and typical-segment (2.08 ± 0.39 vs. 2.67 ± 0.37, $P = 0.009$ and 3.05 ± 0.38 vs. 3.29 ± 0.46, $P = 0.042$), but has no significant effect on long-segment disease (3.85 ± 0.41 vs. 3.89 ± 0.30, $P = 0.839$).

Conclusion: We have not shown a reduced risk of developing HAEC or postoperative obstructive symptoms if anal dilatations are prescribed before surgery. However, it may decrease the difficulties of surgeries, so the operative time is shortened.

Level of evidence: Prognosis study.

Level: II.

Hirschsprung disease(HD) is a congenital disorder characterized by the absence of enteric neurons in the distal colon, which is a common cause of neonatal intestinal obstruction [1,2]. Once HD is diagnosed, most children need surgical treatment in infancy [3]. Current treatment is surgical resection of the intestinal where the enteric neurons is missing and to reconstruct the digestive tract. Hirschsprung-associated enterocolitis (HAEC) is a common complication of HD, which can occur not only preoperatively but also postoperatively, and is the leading cause of death in children with HD [4,5]. The specific pathogenesis of HAEC is still unknown [6]. Fecal deposition, the gut microbiota altered and colonic mucosal barrier integrity caused by postoperative outflow obstruction (mainly anal stenosis and constipation) are believed to be closely related to the occurrence of HAEC [7,8]. Therefore, in order to avoid postoperative anal stenosis and its secondary cause of HAEC, surgeons recommend routine anal dilatation from two weeks post pull-through [9].

Abbreviations: HAEC, Hirschsprung-associated enterocolitis; HD, Hirschsprung disease; AD, preoperative anal dilatation; NAD, no preoperative anal dilatation; ARMs, anorectal malformations.

☆ Declarations of interest: none.

* Corresponding author at: Department of Pediatric Surgery, Fujian Maternity and Child Health Hospital, No.18 Daoshan Road, Fuzhou, Fujian 350001, China. Tel.: +86 137 0507 8937.

E-mail address: Fyf0599@163.com (Y. Fang).

https://doi.org/10.1016/j.jpedsurg.2020.05.008

Most anastomotic strictures can be relieved by anal dilatation to avoid operation [10]. In theory, it is feasible to reduce the incidence of anastomotic stenosis and even HAEC by anal dilatation post pull-through for HD. However, Aworanti et al. observed that routine anal dilatation post pull-through did not reduce the incidence of postoperative anastomotic stenosis and HAEC compared with patients without anal dilatation, so the role of postoperative anal dilatation was doubted [11]. If anal dilatation is performed before operation, can it affect the incidence of postoperative anastomotic stenosis and HAEC? At present, there is no research report on preoperative anal dilatation. It is assumed that preoperative anal dilatation can increase the diameter of anal canal, stimulate defecation, reduce fecal accumulation, and thus reduce the occurrence of HAEC. It can even avoid overpulling the internal anal sphincter during the operation, so as to reduce the difficulty of operation and postoperative anal edema. In this study, we will evaluate the role of preoperative anal dilatation in laparoscopic-assisted Soave pull-through by retrospectively comparing the incidence of HAEC and obstructive symptoms in children with or without preoperative anal dilatation.

1. Material and methods

1.1. Patient samples

A retrospective review was carried out of inpatient surgical records to identify children aged from 3 to 12 months and undergoing laparoscopic-assisted Soave pull-through procedures for HD between January 2014 and December 2018. All patients were followed up for at least 12 months. Patients who were diagnosed with total colonic aganglionosis, those with multiple stage procedures, 21 trisomy and other serious congenital malformations, and those lost to follow-up were excluded. The data collected included patient sex, age, type of HD, weight at birth and surgery, operation time, hospitalization time, incidence of HAEC before and after operation and other postoperative complications (such as obstruction symptoms, anastomotic stenosis, anastomotic leakage, perianal dermatitis). Demographics, perioperative data and postoperative complications were obtained from the relevant records and the cohorts identified. Children were divided into preoperative anal dilatation group (AD group) and those who did not (NAD group), the grouping was based on the individual practice of the surgeon. The study protocol was approved by the ethics committee at Fujian Maternity and Children Health Hospital before beginning the study.

1.2. Anal dilatation

The patient was diagnosed as HD by contrast enema, anorectal manometry and intestinal biopsy. During the hospitalization, the parents learned the technique of anal dilatation and then discharged. AD group parents selected anal dilators (a metal anal dilator similar to Hegar dilator) appropriate for the child's anal size and began to carry out anal dilatation after discharge. Generally, the daily anal dilatation was started from No. 6 or 7 (6 mm or 7 mm, 1 mm is a unit in size) anal dilators. After sufficient lubrication, the anal dilators were inserted about 9 to 11 cm deep into the rectum and lasted about 15 to 20 min; the size of the anal dilators was increased every two weeks for at least 3 months. The size of anal dilator used based on age of the baby and the schedule for advancing in size can be seen in Table 4. There were no children that had anal dilatation in NAD group and routine anal dilatation was performed in both groups from 2 weeks after laparoscopic-assisted Soave pull-through.

1.3. Type of HD, HAEC and postoperative obstructive symptoms

Short-segment Hirschsprung disease is defined as aganglionosis limited to the proximal rectum. Typical-segment is defined as aganglionosis extending from anus to the rectosigmoid junction, or into the distal sigmoid. Long-segment is defined as aganglionosis extending from anus to the level of descending colon, or into the transverse colon. Hirschsprung-associated enterocolitis (HAEC) was defined using the Delphi scoring system, which included clinical history, physical examination, laboratory findings and radiologic examination [12]. Postoperative obstructive symptoms include abdominal distension, bloating, borborygmi, vomiting, or ongoing severe constipation [13].

1.4. Statistical analysis

The data were analyzed using the SPSS 20.0 statistical software. Characteristics were compared between the two groups using Student's t-test for continuous variables and the chi-square test for categorical variables. When the expected counts were less than 5, Fisher's exact test was used. A P-value <0.05 was considered statistically significant difference.

2. Results

A total of 95 children were identified through the inclusion criteria. There were 36 (9 female and 27 male) in AD group and 59 (8 female and 51 male) in NAD group. The demographics of the patients included in the study can be seen in Table 1.

The groups were similar in their gender ($P = 0.177$) and the type of HD distribution ($P = 0.395$). The weight at birth (median 3.22 kg AD vs. 3.00 kg NAD; $P = 0.329$), weight at surgery (median 7.65 kg AD vs. 8.15 kg NAD; $P = 0.318$), age at surgery (median age 7.75 months AD vs. 6.50 months NAD; $P = 0.305$) and length of stay (median 17 days AD vs. 17 days NAD; $P = 0.623$) were also similar between the two groups. Compared with the NAD group, the AD group had significantly shorter operation time (median 3.15 h vs. 3.33 h, $P = 0.008$). Preoperative anal dilatation could shorten the operation time in short and typical-segment (2.08 ± 0.39 vs. 2.67 ± 0.37, $P = 0.009$ and 3.05 ± 0.38 vs. 3.29 ± 0.46, $P = 0.042$), but has no significant effect on long-segment disease (3.85 ± 0.41 vs. 3.89 ± 0.30, $P = 0.839$; Table 2). (See Table 3.)

The overall incidence of HAEC was 20% and 16% before and after operation, respectively, and the recurrence rate was 4%. When the HAEC rates were compared, five children (14%) in the AD group and fourteen children (24%) in the NAD had HAEC before operation (P = 0.298). There were four (11%) and eleven (19%) children who developed

Table 1
Clinical characteristics of preoperative anal dilatation and no anal dilatation groups.

Characteristics	Total	AD	NAD	P[a]
Total	$N = 95$	$N = 36$	$N = 59$	
Male n (%)	78 (82)	27 (33)	51 (67)	0.177
Female n (%)	17 (18)	9 (43)	8 (59)	
Type of HD				0.395[b]
Short segment type n (%)	16 (17)	7 (30)	9 (70)	
Typical-segment type n (%)	62 (67)	24 (38)	38 (62)	
Long-segment type n (%)	17 (16)	5 (26)	12 (74)	
Weight at birth (kg)	3.00 (1.90–4.25)	3.22 (1.90–4.25)	3.00 (2.35–4.20)	0.329
Age at surgery (month)	6.37 (3.00–12.00)	5.75 (3.00–12.00)	6.50 (3.34–12.00)	0.305
Weight at surgery (kg)	8.00 (3.50–12.00)	7.65 (4.80–12.00)	8.15 (3.50–12.00)	0.318
Length of stay (d)	17 (10–43)	17 (10–33)	17 (10–43)	0.623
Operating time (h)	3.25 (1.50–4.30)	3.15 (1.50–4.30)	3.33 (2.00–4.22)	0.008

Abbreviations: HD, Hirschsprung disease; AD, preoperative anal dilatations; NAD, no preoperative anal dilatations.
Note: Ages, weights, length of stay and operating times are expressed as medians with range.
[a] Fisher exact test for nominal categories and t test for continuous variables.
[b] Mann–Whitney test for nominal categories.

Table 2
Comparison of operating time at each type of HD between the AD and NAD groups.

Type of HD	AD	NAD	P^a
Short-segment type	2.08 ± 0.39	2.67 ± 0.37	0.009
Typical-segment type	3.05 ± 0.38	3.29 ± 0.46	0.042
Long-segment type	3.85 ± 0.41	3.89 ± 0.30	0.839

[a] T test for continuous variables.

HAEC postoperatively (P = 0.171), and the HAEC recurred in two (3%) and four (7%) children in AD and NAD group (P = 0.647), respectively. There was no difference between the groups in the incidence of HAEC whether preoperative or postoperative. The results of statistics comparing the incidence of HAEC and postoperative complications in the AD and NAD groups can be seen in Table 2.

There were 20 patients (21%) with obstructive symptoms, but there was no significant difference between the two groups (19% vs. 22%; $P = 0.802$). Anastomotic stenosis occurred in 4 cases (4%, 1 AD and 3 NAD) and the difference was not significant (3% vs.5%; $P = 1.000$). One patient in NAD group developed anastomotic leakage on the second day after operation, and was cured by conservative treatment without anastomotic stenosis, but HAEC occurred at the fourth month after operation. In the cases of anastomotic stenosis, one patient was cured by reoperation and botulinum toxin injection, respectively, and the other 2 cases were improved after anal dilatation.

3. Discussion

With the development of minimally invasive surgical technology, laparoscopic-assisted Soave pull-through procedure has become the most widely used operation for its advantages of minimal invasiveness, quick recovery and low complications in HD patients [14–16]. However, the incidence of obstructive symptoms and HAEC did not decrease or even increase [17]. According to the literature, the incidence of postoperative obstruction symptoms is 8%–30% [13], the incidence of preoperative HAEC is 6%–60%, and the incidence of postoperative HAEC is 25%–37% [18]. The incidence of postoperative obstruction and preoperative HAEC was 20% and 18%, respectively, which was consistent with the previous study. The incidence of HAEC after operation was 17%, slightly lower than that reported in the literature, for long-segment disease, total colonic aganglionosis and trisomy 21 were excluded from the study.

HAEC is the leading cause of morbidity in HD children, when someone has vomiting, abdominal distention and septicemia post pull-through. It has been found that anastomotic stenosis and intestinal obstruction postprocedure are the risk factors for HAEC [8,19], and some pediatric surgeons believe that the occurrence of HAEC is closely related to postoperative obstruction symptoms (including anastomotic stenosis) [8,11,20]. It is proposed to avoid anastomotic stenosis by anal dilatation so as to decrease the incidence of HAEC. There is some dispute about routine anal dilatation after surgery [21,22]. Some scholars believe that anal dilatation can cause pain and discomfort, increase the psychological pressure of parents and children, and even lead to later psychological problems. Temple found that the effect of weekly anal dilatation by the surgeon is equal to that of daily anal dilatation by the parents, and daily anal dilation is not necessary [22,23]. There is only one study comparing the incidence of anastomotic stenosis with or without anal dilatation. Unfortunately, Aworanti found that postoperative routine anal dilatation did not significantly reduce the incidence of anal stenosis [11]. However, the number of patients included in their study was small, and the frequency of anal dilatation and the compliance of children were not clear. Compared with the control group, the anal dilatation group could prevent early symptomatic stenosis, and the incidence of anal stenosis and HAEC was lower in AD group. In another study, Rouzrokh accidentally found that 30 children who began anal dilatation two weeks after operation did not have anastomotic stenosis [9]. Concealed anal stenosis can be found by routine anal dilatation with examination at 6 weeks after operation and early treatment can improve prognosis [24]. So it's too early to deny the role of anal dilatation. Anal dilatation is simple and practicable, and it provided a good result in the treatment of constipation and anal stenosis and in preventing anal stenosis after repair of anorectal malformations (ARMs) [25–28]. A survey of 36 pediatric surgeons from 20 countries shows that 70% of surgeons began anal dilatation two weeks after operation, and 94% of surgeons prefer to use metal dilators [29]. Our method of anal dilatation is the same as that of most surgeons in the world. In our study, the incidence of postoperative obstruction symptoms and anastomotic stenosis in the two groups was similar, and the incidence of HAEC in AD group was lower than that in NAD group, but there was no statistical difference. It seems that preoperative anal dilatation has no effect on the incidence of HAEC. It is possible that other factors found in recent years could lead to HAEC, such as abnormal epithelial barrier function, an abnormal composition of intestinal microorganisms, and immune dysfunction [30–34] and even the interaction of the three factors [20]. To further clarify the pathogenesis of HAEC, we can formulate effective prevention and treatment strategies for HAEC in the future [30].

In present study, we found that the average operation time of the AD group was significantly shorter than that of NAD group. We speculated that preoperative anal dilatation could increase the diameter of anal canal, making it easy to pull the colon out through muscular sheath; it greatly reduced the difficulty of operation and shortened the operation time. The anal canal is narrow and internal sphincter is very weak in infants, making the pull-through procedure difficult. Vigorous anal dilation and excessive anal canal traction during operation can damage the internal sphincter and have adverse effects on the postoperative continence function [35]. Therefore, preoperative anal dilatation can avoid vigorous anal dilation and excessive anal canal traction during operation; it may alleviate anal edema and promote postoperative rehabilitation. But we did not find that the length of stay in AD group was significantly shorter than that in NAD group, and the postoperative complications (include obstruction symptoms, anastomotic stenosis, anastomotic leakage) were similar between the two groups.

This analysis was limited by its retrospective nature and the small population analyzed. The diagnosis of HAEC and postoperative complications was also somewhat subjective and depended on the clinical assessment of the patient by the surgeon. Furthermore, only episodes of enterocolitis that are serious to require admission and outpatient care will be identified, which may affect the true incidence of this complication.

Table 3
Results of statistics comparing the incidence of HAEC and postoperative complications in the AD and NAD groups.

Characteristics	Total ($n = 95$)	AD ($n = 36$)	NAD ($n = 59$)	P^a
HAEC *n* (%)				
Preoperative	19 (20)	5 (14)	14 (24)	0.298
Postoperative	15 (16)	4 (11)	11 (19)	0.171
Recurrent	4 (4)	1 (3)	4 (7)	0.647
Postoperative obstructive symptoms *n* (%)	20 (21)	7 (19)	13 (22)	0.802
Anastomosis stricture *n* (%)	4 (4)	1 (3)	3 (5)	1.000
Anastomosis leak *n* (%)	1 (1)	0 (0)	1 (2)	1.000

[a] Fisher exact test for nominal categories.

Table 4
Age of starting anal dilatation and the corresponding size of anal dilator.

Age (month)	<1	1–2	2–3	3–4	4–5	5–6	>6
Anal dilator (mm)	6	7	8	9	10	11	12
Size advancing schedule	increasing 1 mm per 2 weeks.						

Note: 1 mm is a unit in size of anal dilator, and the maximum anal dilator we use before operation is 18 mm.

4. Conclusion

To our knowledge, this is the first report about the effect of preoperative anal dilatation on the incidence of HAEC and complications post pull-through. Unfortunately, we have not shown preoperative anal dilatation reducing HAEC and obstruction symptom rates. However, this retrospective analysis suggests that operative time was significantly shorter in those with preoperative anal dilatation as compared with those without in short and typical segment children, and it may reduce the operation difficulty. In view of the limitations of this study, the role of preoperative anal dilatation needs to be proved by a prospective randomized study in the future.

Acknowledgment

The authors would like to thank all participants who contributed to the study.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

[1] Langer JC. Hirschsprung disease. Pediatr Rev. 2013;25:368–74.
[2] Ambartsumyan L, Smith C, Kapur RP. Diagnosis of Hirschsprung disease. Pediatr Dev Pathol. 2019. https://doi.org/10.1177/1093526619892351.
[3] Das K, Mohanty S. Hirschsprung disease—current diagnosis and management. Indian J Pediatr. 2017;84:618–23.
[4] Löf Granström MA, Wester T. Mortality in Swedish patients with Hirschsprung disease. Pediatr Surg Int. 2017;33:1177–81.
[5] Prato AP, Rossi V, Avanzini S, et al. Hirschsprung's disease: what about mortality? Pediatr Surg Int. 2011;27:473–8.
[6] Heuckeroth Robert O. Hirschsprung disease — integrating basic science and clinical medicine to improve outcomes. Nat Rev Gastroenterol Hepatol. 2018;15:152–67.
[7] Murphy F, Puri P. New insights into the pathogenesis of Hirschsprung's associated enterocolitis. Pediatr Surg Int. 2005;21:773–9.
[8] Annie Le-Nguyen, Franziska, et al.. Factors influencing the incidence of Hirschsprung associated enterocolitis (HAEC). J Pediatr Surg. 2019;54:959–63.
[9] Rouzrokh M, Khaleghnejad AT, Mohejerzadeh L, et al. What is the most common complication after one-stage transanal pull-through in infants with Hirschsprung's disease? Pediatr Surg Int. 2010;26:967–70.
[10] Teitelbaum DH, Coran AG. Reoperative surgery for Hirschsprung's disease. Semin Pediatr Surg. 2003;12:124–31.
[11] Kampe S, Rocha M, Darwiche K, et al. Are routine dilatations necessary post pull-through surgery for Hirschsprung disease? Eur J Pediatr Surg. 2013;23:383–8.
[12] Pastor AC, Osman F, Teitelbaum DH, et al. Development of a standardized definition for Hirschsprung's-associated enterocolitis: a Delphi analysis. J Pediatr Surg. 2009;44:251–6.
[13] Gosain A, Frykman PK, Cowles RA, et al. Guidelines for the diagnosis and management of Hirschsprung-associated enterocolitis. Pediatr Surg Int. 2017;33:517–21.
[14] Zhu T, Sun X, Wei M, et al. Optimal time for single-stage pull-through colectomy in infants with short-segment Hirschsprung disease. Int J Colorectal Dis. 2019;34:255–9.
[15] Tomuschat C, Zimmer J, Puri P. Laparoscopic-assisted pull-through operation for Hirschsprung's disease: a systematic review and meta-analysis. Pediatr Surg Int. 2016;32:751–7.
[16] Iacusso C, Leonelli L, Valfre L, et al. Minimally invasive techniques for Hirschsprung disease. J Laparoendosc Adv Surg Tech A. 2019;29:1605–8.
[17] Huang EY, Tolley EA, Blakely ML, et al. Changes in hospital utilization and management of Hirschsprung disease: analysis using the Kids' Inpatient Database. Ann Surg. 2013;257:371–5.
[18] Langer JC, Rollins MD, Levitt M, et al. Guidelines for the management of postoperative obstructive symptoms in children with Hirschsprung disease. Pediatr Surg Int. 2017;33:523–6.
[19] Hackam DJ, Filler RM, Pearl RH. Enterocolitis after the surgical treatment of Hirschsprung's disease: risk factors and financial impact. J Pediatr Surg. 1998;33:830–3.
[20] Jiao CL, Chen XY, Feng JX. Novel insights into the pathogenesis of Hirschsprung's-associated enterocolitis. Chin Med J-Peking. 2016;129:1491–7.
[21] Temple SJ, Shawyer A, Langer JC. Is daily dilatation by parents necessary after surgery for Hirschsprung disease and anorectal malformations? J Pediatr Surg. 2012;47:209–12.
[22] Peña A, Elicevik M, Levitt MA. Reoperations in Hirschsprung disease. J Pediatr Surg. 2007;42:1008–14.
[23] Diseth TH. Dissociation following traumatic medical treatment procedures in childhood: a longitudinal follow-up. Dev Psychopathol. 2006;18:233–51.
[24] Obermayr F, Szavay P, Beschorner R, et al. Outcome of transanal endorectal pull-through in patients with Hirschsprung's disease. Eur J Pediatr Surg. 2009;19:220–3.
[25] Keshtgar AS, Ward HC, Clayden GS, et al. Role of anal dilatation in treatment of idiopathic constipation in children: long-term follow-up of a double-blind randomized controlled study. Pediatr Surg Int. 2005;21:100–5.
[26] Kashkooli SB, Samanta S, Rouhani M, et al. Bougie dilators: simple, safe and cost-effective treatment for Crohn's-related fibrotic anal strictures. Can J Surg. 2015;58:347–8.
[27] Jumbi T, Kuria K, Osawa F, et al. The effectiveness of digital anal dilatation in preventing anal strictures after anorectal malformation repair. J Pediatr Surg. 2019;54:2178–81.
[28] Mueller CM, Beaunoyer M, St-Vil D. Topical mitomycin-C for the treatment of anal stricture. J Pediatr Surg. 2010;45:241–4.
[29] Brisighelli G, Morandi A, Di Cesare A, et al. The practice of anal dilations following anorectal reconstruction in patients with anorectal malformations: an international survey. Eur J Pediatr Surg. 2016;26:500–7.
[30] Gosain A. Established and emerging concepts in Hirschsprung's-associated enterocolitis. Pediatr Surg Int. 2016;32:313–20.
[31] Nakamura H, Lim T, Puri P. Probiotics for the prevention of Hirschsprung-associated enterocolitis: a systematic review and meta-analysis. Pediatr Surg Int. 2018;34:189–93.
[32] Li Y, Poroyko V, Yan Z, et al. Characterization of intestinal microbiomes of hirschsprung's disease patients with or without enterocolitis using Illumina-MiSeq high-throughput sequencing. PLoS One. 2016;11:e0162079.
[33] Singer G, Kashofer K, Castellani C, et al. Hirschsprung's associated enterocolitis (HAEC) personalized treatment with probiotics based on gene sequencing analysis of the fecal microbiome. Case Rep Pediatr. 2018;3292309. https://doi.org/10.1155/2018/3292309.
[34] Tang W, Su Y, Yuan C, et al. Prospective study reveals a microbiome signature that predicts the occurrence of post-operative enterocolitis in Hirschsprung disease (HSCR) patients. Gut Microbes. 2020:1–13.
[35] Sun X, Wang R, Zhang L, et al. Efficacy of pelvic floor muscle training for the treatment of fecal incontinence after Soave procedure for Hirschsprung disease. Eur J Pediatr Surg. 2012;22:300–4.