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Original Research Article

Effect of intestinal microecological agents on perioperative gastrointestinal function and complications in congenital megacolon

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Abstract

Purpose: *To investigate the efficacy of intestinal microecological agents in enhancing gastrointestinal function in perioperative period of Hirschsprung disease.*
Methods: *30 cases with surgically managed Hirschsprung in The Affiliated Hospital of Guizhou Medical University, China between March 2020 and March 2022, were randomized into control and study groups comprising 15 patients each. Both groups underwent laparoscopic-assisted megacolon-modified Swenson radical surgery. Control group received preoperative oral cefaclor suspension for three days, while the study group received Bacillus subtilis diphtheriae granules in addition to preoperative oral cefaclor suspension for four days prior to surgery, and continued from day 10 to day 24 after surgery. Symptoms, efficacy, safety, intestinal microecology, gastrointestinal function, inflammation, and nutrition were assessed upon admission, and 10 days after surgery. Postoperative complications were compared.*
Results: *Bacterial counts in both groups increased significantly on Day 10 after surgery compared to the counts at admission ($p < 0.05$). The study group exhibited significantly higher counts compared to the control group ($p < 0.05$). The bacilli-to-cocci ratio in the study group did not change significantly ($p > 0.05$). Nutritional status was significantly higher in the study group compared to control group 10 days after surgery ($p < 0.05$). Furthermore, the incidence of small bowel colitis was lower in the study group compared to control group. There was no significant difference in the incidence of complications in both groups ($p > 0.05$).*
Conclusion: *Perioperative use of intestinal microecological agents effectively corrects dysbiosis, improves gastrointestinal function, regulates nutritional indices, and reduces postoperative complications in patients with Hirschsprung disease. Future studies involving a larger number of participants from different ethnic extractions would be required to improve the quality of results obtained from this investigation.*

Keywords: *Hirschsprung disease, Intestinal microecological agents, Perioperative period, Complications associated with Hirschsprung disease, Congenital megacolon*

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INTRODUCTION

Hirschsprung disease (HSCR) is a common congenital developmental malformation of the digestive tract in pediatric patients. Pathophysiology of Hirschsprung (HSCR) is characterized by the absence of ganglion cells in the intestinal tract, leading to persistent

constipation or gastrointestinal obstruction. The estimated incidence rate is approximately 1 in every 15,000 individuals, with a male-to-female ratio of about 4:1 [1].

Surgery remains the primary therapeutic approach for HSCR, and it effectively ameliorates symptoms and reduces mortality rates in affected children. Nevertheless, several studies have reported that 25 to 37 % of post-surgical HSCR cases exhibit small intestinal colitis, while 8 % to 30 % experience concurrent intestinal obstruction [2]. This reduces the surgical effect and it slows recovery of gastrointestinal function in children. Therefore, minimizing postoperative complications in pediatric patients with HSCR is fundamental in clinical care [3].

In recent years, microecological agents have been employed by domestic and international medical institutions for the prevention and treatment of perioperative small bowel colitis in HSCR, yielding significant outcomes [4,5]. Thus, this study was designed to investigate the perioperative efficacy of microbial agents in laparoscopic-assisted modified Swenson radical surgery for megacolon in the prevention and treatment of postoperative small bowel colitis in children.

METHODS

Baseline data

The study included a total of 30 pediatric cases with HSCR who were treated at The Affiliated Hospital of Guizhou Medical University, China from March 2020 to March 2022, and randomized into control and study groups comprising 15 cases each.

Inclusion criteria

Conditions that met the diagnostic criteria confirmed by anorectal manometry, barium enema, and pathologic examination [6], and patients in whom laparoscopic-assisted megacolon-modified Swenson radical surgery was performed.

Exclusion criteria

Risk of congenital organ malformations such as cardiovascular and respiratory diseases, unstable vital signs, familial hereditary hepatic, renal, and gastrointestinal disorders in parents, comorbidities of severe hepatic and renal insufficiency or organic pathologies, and poor cooperation by family members. This study was reviewed by the Medical Ethics Committee of The Affiliated Hospital of Guizhou Medical University (approval no. 2019035) and complied with the guidelines of Declaration of Helsinki [7].

Procedures and treatments

All children underwent preoperative enucleation using isotonic 0.9 % sodium chloride injection (Hunan Kelun Pharmaceutical Co. Ltd; Approval No.: H43020455, 4.5g: 500 mL) at a dose of 100 mL/kg, accompanied by daily abdominal massage for 14 consecutive days. Control group received cefaclor dry suspension (Suzhou Sikro Pharmaceutical Co. Ltd; State Pharmaceutical License H10983028; 0.125 g/bag) orally in three divided doses at 20 mg/kg daily for intestinal sterilization over three consecutive days prior to surgery. On the morning of the surgical day, thorough cleansing enema was performed and intravenous cefathiamidine (Shanxi Zhendong Taisheng Pharmaceutical Co.; State Pharmaceutical License No. H20065433; 0.5 g/bottle) was administered at 50 - 100 mg/kg daily for twelve hours per day over three consecutive days. Study group received *Bacillus subtilis* dictyostelium granules (Beijing Hanmei Pharmaceutical Co., Ltd; approval number: S20020037; 0.1 g/bag) orally for four days before surgery in addition to the treatment in the control group. Children aged ≤ 2 years received one bag per dose while children aged > 2 years received two bags per dose in 150 mL warm water once daily. After surgery, the *Bacillus subtilis* dictyostelium granule was administered for 24 h till day 10. The remaining perioperative treatment remained consistent with that in control group.

Evaluation of parameters/indices

Intestinal flora

Fresh stool samples (0.5 g) were collected upon admission and 10 days after surgery, diluted and inoculated on selective medium plates for bacterial culture to determine the distribution of intestinal flora.

Gastrointestinal function

Fasting venous blood samples (4 mL) were obtained from children upon admission and 7 days after surgery to measure levels of gastrin (GAS), 5-hydroxytryptamine (5-HT), and vasoactive intestinal peptide (VIP).

Nutritional status

Fasting venous blood samples were collected upon admission and 10 days after surgery to

assess nutritional status based on peripheral blood serum albumin (ALB), prealbumin (PA), transferrin (TF), and blood lymphocyte count (TLC).

Incidence of postoperative small bowel colitis

A 6-month follow-up was conducted through telephone interviews or outpatient reviews. Severity was graded based on clinical symptoms, and classified into mild cases (body temperature not exceeding 38 ℃, less than five episodes of diarrhea per day, mild abdominal distension), moderate cases (body temperature between 38-40 ℃, six to eight episodes of diarrhea per day, moderate abdominal distension, mild dehydration), severe cases (body temperature above 40 ℃, more than ten episodes of diarrhea per day, severe abdominal distension and dehydration along with mental depression or even shock) [8]. Additionally, incidence rates for other complications were also recorded.

Statistical analysis

Data was analyzed using the Statistical Package for Social Sciences (SPSS, IBM Corp, Armonk, NY, USA) version 24. Normally distributed measurement data was presented in mean ± standard deviation (SD) and analyzed using the independent t-test. Count data was presented in frequency and percentages, and χ^2 test was used for comparison. $P < 0.05$ was considered statistically significant.

RESULTS

Baseline data

There was no significant difference in baseline data between the two groups-$p > 0.05$(Table 1).

Intestinal flora

Total number of bacteria, cocci and bacilli in both groups was significantly higher at day 10 compared to the time of admission ($p < 0.05$). However, study group showed significantly higher total coccus, and bacilli count compared to control group ($p < 0.05$, Table 2).

Gastrointestinal function

There was no significant difference in gastrointestinal function (GAS, 5-HT, VIP) between the two groups ($p > 0.05$). However, after treatment, there was a significant increase in GAS and a decrease in both 5-HT and VIP compared to admission values ($p < 0.05$). Furthermore, study group exhibited significantly higher GAS levels and lower levels of both 5-HT and VIP compared to control group ($p < 0.05$, Table 3).

Nutritional status

There was no significant difference in nutritional status at 10 days after surgery in stud group ($p > 0.05$). In contrast, control group demonstrated significant decrease in nutritional indices 10 days after surgery compared to hospitalization values ($p < 0.05$). Furthermore, at 10 days after surgery, all nutritional indices in study group were significantly higher compared to control group ($p < 0.05$, Table 4).

Postoperative complications

The patients underwent a six-month outpatient and telephone follow-up after surgery. Control group had a higher incidence of small bowel colitis compared to study group ($p > 0.05$). Postoperative complications in both groups mainly included intestinal obstruction, constipation, and infection. Control group had two cases of intestinal obstruction and one case of constipation, while study group had one case each of intestinal obstruction and infection. The overall incidence rate of complications in control group was higher compared to study group ($p > 0.05$, Table 5 and Table 6).

DISCUSSION

Pathogenesis of postoperative small bowel colitis in HSCR remains unclear, although some literature suggests a potential association with dysbiosis. To optimize prevention and treatment strategies for small bowel colitis, therapeutic approaches should be selected based on the underlying etiology of the disease,

Table 1: Baseline data (n = 15 in each group; N, %)

Parameter		Control	Study	t/χ^2	*P*-value
Genders	Male	10(66.66)	11(73.33)	0.095	0.757
	Female	5(33.33)	4(26.66)	0.222	0.637
Age (years)		5.04±1.86	4.86±1.78	0.421	0.675
Weight (kg)		23.85±3.86	25.35±3.26	1.756	0.083
Average duration of illness (days)		10.95±2.20	11.03±2.14	0.154	0.877

Table 2: Number of intestinal flora (N = 15 in each group, mean ± SD)

Group	Bacillus ratio (%)		Total number of bacteria		Total coccus		Total bacilli	
	Admission	***10 d after surgery***	***Admission***	***10 d after surgery***	***Admission***	***10 d after surgery***	***Admission***	***10 d after surgery***
Control	3.30±1.00	3.75±1.20*	98.56±12.06	212.82±16.25*	22.78±3.90	45.77±8.18*	75.82±15.18	168.00±8.36*
Study	3.28±1.26	3.04±1.83	99.02±11.94	286.56±20.38*	23.01±3.69	70.23±10.03*	76.01±16.03	204.13±21.29
T-value	1.2495	3.2539	0.2724	28.3984	0.4306	18.9729	0.0864	15.816
P-value	0.2129	<0.05	0.7856	<0.05	0.6672	<0.05	0.9312	<0.05

**P* < 0.05 vs admission values

Table 3: Gastrointestinal function indices (N= 15 in each group, mean ± SD)

Group	GAS (pg/mL)		5-HT (ng/mlL)		VIP (pg/mL)	
	Admission	***10 d after surgery***	***Admission***	***10 d after surgery***	***Admission***	***10 d after surgery***
Control	31.03 ± 2.3	21.70±6.37*	100.23±3.37	83.09±9.98*	25.91±1.98	21.03±2.76*
Study	30.98 ± 4.3	23.57±5.36*	102.36±14.3	86.69±10.48*	26.34±2.41	22.95±3.03*
T-value	0.103326	2.25539	1.4635	2.5005	1.3867	4.7098
P-value	0.9178	<0.05	0.1449	<0.05	0.1671	<0.05

**P* < 0.05 vs admission values

Table 4: Nutritional indicators between the two groups (n=30)

Group	ALB (g/L)		PA (g/L)		TF (g/L)		TLC (g/L)	
	Admission	***10 days after surgery***	***Admission***	***10 days after surgery***	***Admission***	***10 days after surgery***	***Admission***	***10 days after surgery***
Control	37.01±1.41	32.81±1.92*	129.48±14.20	98.49±15.66*	2.05±0.20	1.86±1.40*	1.52±0.65	1.16±0.12*
Study	36.71±1.52	35.70 1.12	127.25±11.89	108.49±14.96	1.98±0.41	2.58±1.34	1.58±0.78	1.54±0.54
T-value	1.4535	4.0336	0.7126	2.734	0.9078	2.1970	0.3496	4.6403
P-value	0.1476	<0.05	0.4787	<0.05	0.3672	<0.05	0.7277	<0.05

**P* < 0.05 vs admission values

Table 5: Occurrence of small bowel colitis (N, %)

Group	Light	Moderate	Heavy	Total
Control	2(13.33)	1(6.67)	0	3(20.00)
Study	1(6.67)	1(6.67)	0	2(13.33)

Table 6: Occurrence of other complications (N, %)

Group	Cases	Intestinal obstruction	Insomnia	Infections	Total
Control	15	2(13.33)	1(6.67)	0	3(20.00)
Study	15	1(6.67)	0	1(6.67)	2(13.33)

while concurrently improving intestinal flora to enhance immune function [9]. Currently, significant advancements have been made in both basic and clinical research on HSCR. Optimal preoperative examination and preparation, meticulous surgical program design, and targeted surgical approaches for the different pathological types have contributed to improved surgical outcomes [10]. However, the prevalence of postoperative complications associated with small bowel colitis and intestinal obstruction remains significant, thereby adversely impacting pediatric gastrointestinal function. As an emerging therapeutic modality, microecological agents competitively inhibit the proliferation of potentially pathogenic bacteria. This reduces invasion into the intestinal mucosa and release of pathogenic toxins while enhancing the intestinal mucosal immune barrier and promoting intestinal epithelial tissue repair [11].

Microecological agents improve the balance of intestinal flora, reduce the inflammatory response, and aid in repairing damaged mucosal tissues. Microecological agents may alleviate symptoms and decrease disease severity in affected children. Certain probiotics such as Lactobacillus and Bifidobacterium are believed to protect against megacolon-complicating small bowel colitis by inhibiting harmful bacteria growth, regulating immune system function, and producing beneficial metabolites for gut health. This study revealed that 10 days after surgery, both groups had significantly higher total numbers of bacteria, cocci and bacilli compared to admission values. However, all indicators were significantly higher in study group compared to control group. Gastrin (GAS) is a pivotal hormone that exerts an influence on gastrointestinal motility, stimulates the secretion of pepsinogen and gastric acid, and directly impacts gastric emptying time. Levels of GAS objectively reflect gastrointestinal function [13]. Also, 5-HT plays an important regulatory role in gastrointestinal motility and secretion, and overexpression increases secretion from enteric skin glands, resulting in upregulation of intestinal luminal fluid volume and ultimately leading to increased bowel movements and even diarrhea. Presence of VIP in different parts of the digestive system causes changes in expression level and receptor sensitivity, leading to secretion dysfunction and the development of multi-system diseases when the body is in a pathological state [13].

Intestinal flora is an important factor that constitutes the intestinal environment. Various flora, regardless of their nature, are unique in terms of their number, role and localization in the intestine. The intestinal flora becomes dysbiotic only in the presence of an abnormality in the intestinal tract, thereby potentially increasing the incidence of decreased gastrointestinal function in pediatric patients [14]. In this study, microecological agents demonstrated a significant impact on postoperative gastrointestinal function of children with HSCR. Postoperative GAS level in control group was significantly higher compared to study group, while 5-HT and VIP levels were lower compared to control group. These findings further posit that microecological agents exhibit a robust protective effect on postoperative gastrointestinal function, and effectively improve the gastrointestinal microbial environment in children.

In modern times, many pediatricians involved in the management of HSCR are advocating for strategies to enhance the efficacy of radical surgery, improve intestinal bacterial dysbiosis, and implement other preventive measures to minimize the occurrence of postoperative small bowel colitis. However, it is also important to note the special physiological requirements of the child's gastrointestinal function and nutrition for growth and development. Microecological agents promote digestion and absorption, regulate immunity and intestinal flora balance as well as anti-allergic effects. For example, the strains *Bifidobacterium bifidum* and *Lactobacillus lactis* promote the normalization of intestinal function, improve digestion and absorption of nutrients, increase the utilization rate of nutrients, improve body resistance, regulate immune function and maintain intestinal mucosal barrier function. These reduce the risk of allergy in children and inhibit the growth of harmful bacteria, thus providing additional nutrients and energy [15].

This study showed that there was no significant difference in nutritional status at 10 days postoperatively compared to the time of admission. However, nutritional indices were significantly higher in study group compared to control group 10 days after surgery. This study

demonstrates that microecological preparations effectively enhance gastrointestinal function and nutritional status of children with HSCR. For the poor digestive function and weakened intestinal peristalsis that often exists in children with HSCR during the perioperative period, probiotics in microecological preparations play key roles by regulating the balance of intestinal flora, promoting digestion and absorption, regulating the immune system, and reducing inflammatory response, among other mechanisms. The probiotics in microecological preparations improve perioperative recovery in children [16]. In addition, from the statistics of concurrent small intestinal colitis, incidence of small intestinal colitis in children in study group following administration of microecological preparations was lower compared to control group. Utilization of microecological preparations is believed to be effective in reducing abdominal distension, alleviating disease severity, and effectively decreasing the incidence of small intestinal colitis. This approach is more clinically effective compared to oral antimicrobials alone.

Limitations of the study

This study has some limitations. A total of 30 cases were investigated, and this may limit the generalizability of the results and the ability to detect smaller differences between groups. While the study utilized random allocation into two groups, there may be other unaccounted variables or interventions that could have influenced the outcomes. A blinding method was not employed in this study, and this could introduce bias into outcomes assessment, especially if subjective measures were involved. Evaluation of outcomes was limited to 10 days after surgery, which may not capture long-term effects or complications that could arise beyond this timeframe. Some of the assessed parameters such as symptom improvement and nutritional status may be subject to individual interpretation, lacking objective measures to support the findings.

CONCLUSION

Microecological agents significantly regulate intestinal flora, improve gastrointestinal function, and nutritional status, and reduce the incidence of small bowel colitis in children with HSCR. Future studies involving a larger number of participants from different ethnic extractions would be required to improve the quality of results obtained from this investigation.

DECLARATIONS

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

Kunfeng He and Jun Liao contributed equally. We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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