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ORIGINAL ARTICLE

Risk factors for the development of post-operative enterocolitis in short segment Hirschsprung's disease

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Abstract

Aim of the study The objective of this study is to identify risk factors associated with the development of post-operative enterocolitis (HAEC), in short segment Hirschsprung's disease (HSCR-S).

Methods A retrospective study was carried out for post-operative patients with HSCR-S from 1997 to 2017. HSCR-S was defined as the most proximal extension of aganglionosis limited to the sigmoid colon. An episode of HAEC was defined as the presence of (1) vomiting or explosive diarrhea; (2) abdominal distension; (3) fever and (4) leukocytosis. Risk factors for the development of HACE were determined using multivariate logistic regression.

Main results The medical records of 96 patients were reviewed. The overall incidence of HAEC was 20.8% ($n=20$) and 65.0% ($n=13$) of HAEC occurred within the first year of operation. After a univariate logistic regression analysis, three risk factors for HAEC were identified: (1) presence of other major anomalies [OR: 1.43 (1.12–2.32), $p=0.041$]; (2) creation of pre-operative defunctioning stoma [OR: 2.28 (1.47–3.23), $p=0.035$]; (3) extension of aganglionosis to the sigmoid colon [OR: 1.89 (1.05–3.19), $p=0.049$]. After multivariate logistic regression analysis, a significant association was demonstrated for creation of pre-operative defunctioning stoma [OR: 1.81 (1.08–3.22), $p=0.045$] and extension of aganglionosis to the sigmoid colon [OR: 1.91 (1.37–2.98), $p=0.038$].

Conclusions The requirement of pre-operative defunctioning stoma and a more proximal extension of aganglionosis are risk factors for the development of post-operative HAEC in HSCR-S. Patients with these risk factors should be closely followed up especially during the first year after the operation.

Keywords Hirschsprung's disease · Enterocolitis · Dysbiosis · Defunctioning stoma

Introduction

Hirschsprung's disease (HSCR) is a congenital disorder characterized by the absence of ganglion cells in distal hindgut with a variable proximal extension. It is a common cause of intestinal obstruction in the newborn and infant. Despite the significant advancement in the surgical management of HSCR, the post-operative bowel function remains suboptimal in some patients. Hirschsprung's associated enterocolitis (HAEC) is a serious and life-threatening condition which can occur in up to 60% of HSCR patients [1]. Classical manifestations of HAEC include abdominal distension, vomiting, fever and the passage of foul smelling or bloody stool. Early HAEC can be managed conservatively with bowel resting, rectal irrigation and antibiotics, but diverting colostomy is occasionally required in severe cases. The underlying pathophysiology of HAEC is largely unknown although the changes in the intestinal barrier and mucosal immunity as well as dysbiosis of the gut flora have been proposed [2]. While a higher incidence of HAEC is found in patients with long segment disease, there are paucity of data about its occurrence in short segment disease which is the most common form of HSCR [3]. The objective of this study is to evaluate the incidence and risk factors associated with the development of post-operative HAEC with focus on short segment Hirschsprung's disease (HSCR-S).

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Material and method

We conducted a retrospective study of all post-operative patients with HSCR-S who received surgery in our hospital from 1997 to 2017. The diagnosis of HSCR was made according to the results of rectal biopsy confirming the absence of ganglion cell. HSCR-S was defined as the most proximal extension of aganglionosis limited to the sigmoid colon after histopathological analysis of the resected specimen. An episode of HAEC was defined according to physical examination and blood parameters including the presence of (1) vomiting or explosive diarrhea; (2) abdominal distension; (3) fever (core body temp ≥ 38.5 °C) and (4) leukocytosis (WBC > 4.0×10^9/L). These four clinical features have been shown to be consistently present in patients with HAEC [4, 5]. Risk factors were analyzed for their associations with the occurrence of post-operative enterocolitis in HSCR-S. Patients referred from other centres for post-operative management and those with incomplete follow up data were excluded from this study.

Data were quoted as median (range). Statistical analysis was performed using standard statistical package (IBM Statistical Package for Social Science, version 20.0). Univariate and multivariate analyses were performed to evaluate the odds ratio (OR) of each variable and a ratio > 1 was considered as a risk factor for the development of HAEC. A p value of < 0.05 was regarded as significant. This retrospective study has been approved by the appropriate ethics committee and was performed in accordance with the ethical standards laid down in the Declaration of Helsinki.

Results

During the study period, there were 172 patients with HSCR operated in our hospital of which 118 patients suffered from the short form of the disease. 22 patients with incomplete medical record or follow up status were excluded. Among the 96 patients who were included in this study, there were 75 male and 21 female patients. The median age at diagnosis and definitive operation were 2.8 months (range: 0.5–46 months) and 3.2 months (range: 0.5–60 months) respectively. The median follow up-period was 102.8 months (range: 12–244 months). Nine patients (9.3%) suffered from Down's syndrome and 21 patients had other concomitant major anomalies. Ten patients (10.4%) suffered from pre-operative enterocolitis and 22 patients (23.9%) required a defunctioning stoma before the definitive surgery. There were 31 patients (32.2%) with aganglionosis extending above the rectum to the sigmoid colon. 44 patients (45.8%) underwent a trans-abdominal Duhamel surgery as the definitive pullthrough operation while 52 patients (54.2%) underwent the transanal endorectal procedure. 12 patients (12.5%) suffered from post-operative anastomotic stricture. The demographic data of the patients are summarized in Table 1.

The overall incidence of post-operative HAEC was 20.8% ($n = 20$) and 65.0% ($n = 13$) of the HAEC episodes occurred within the first year of operation. 60% of the HAEC episodes could be treated by non-operative management. After univariate analysis, three risk factors for HAEC were identified: (1) presence of other major anomalies [OR: 1.43 (1.12–2.32), $p = 0.041$]; (2) creation of pre-operative defunctioning stoma [OR: 2.28 (1.47–3.23), $p = 0.035$]; (3) extension of aganglionosis above the rectum to the sigmoid colon [OR: 1.89 (1.05–3.19), $p = 0.049$]. After multivariate logistic regression analysis, a significant association for the development of post-operative HAEC was demonstrated for creation of pre-operative defunctioning stoma [OR: 1.81 (1.08–3.22), $p = 0.045$] and extension of aganglionosis above the rectum to the sigmoid colon [OR: 1.91 (1.37–2.98), $p = 0.038$]. The results of risk factor analysis are summarized in Table 2.

Discussion

Although the advancement in the surgical management has improved the overall prognosis of HSCR, HAEC is still a challenging condition that would adversely affect the outcome [6]. The incidence of HAEC appears unchanged and the exact pathogenesis remains largely unknown. It is an important subject to investigate as the most common cause for prolonged hospitalization in HSCR is HAEC related [7]. From previous studies, long-segment disease has been shown to be associated with an increased risk of post-operative HAEC due to its effect on intestinal motility and immunity [3, 8]. However, short segment disease is more commonly encountered in clinical practice and HAEC can also occur in HSCR-S. As a result, the actual number of HAEC patients with short segment disease may exceed those with underlying long segment disease to become the major disease burden. Therefore, a study of HAEC in short segment disease is warranted.

From the above findings, more than half of the HAEC episodes occurred within the first year of operation and therefore a frequent follow up in the early post-operative period is recommended. The caretakers should be given adequate instructions regarding the early symptoms of HAEC which can mimic simple gastroenteritis. These two conditions are sometimes indistinguishable. If in doubt, HSCR patients presenting with non-specific gastrointestinal symptoms should be promptly referred to the centre with attending paediatric surgeons for further management. Due to the increased risk of HAEC in the early post-operative period, some authors

Table 1 Demographics of the participants in the current study (n = 96, study period 1997 to 2017)

Variables	*N* = 96 *n* (%) or median (range)
Follow up period (months)	(12–244)
Sex	
Male	75 (78.1%)
Female	21 (21.9%)
Age at diagnosis (months)	2.8 (0.5–46)
Age at definitive operation	3.2 (0.5–60)
Down's syndrome	9 (9.3%)
Association with major anomalies	21 (21.9%)
Cardiac	14 (14.6%)
Neurological	8 (8.3%)
Genito-urinary	6 (6.3%)
Gastrointestinal	5 (5.2%)
Endocrine	6 (6.3%)
Others	10 (10.4%)
Occurrence of pre-operative enterocolitis	10 (10.4%)
Creation of pre-operative defunctioning stoma	22 (23.9%)
Extension of aganglionosis above the rectum to the sigmoid colon	31 (32.2%)
Surgical approach	
Transabdominal Duhamel	44 (45.8%)
Transanal endorectal	52 (54.2%)
Occurrence of post-operative HAEC	20 (20.8%)
Occurrence of post-operative anastomotic stricture	12 (12.5%)

Table 2 Univariate and multivariate analysis of various risk factors associated with the development of post-operative HAEC in HSCR-S

Variable	Univariate		Multivariate	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Male gender	1.10 (0.78–1.67)	0.212	–	–
Diagnosis at neonatal period	0.89 (0.45–1.34)	0.351	–	–
Association with Down's syndrome	1.89 (0.92–2.56)	0.643	–	–
Presence of other major anomalies	1.43 (1.12–2.32)	0.041	1.10(0.77–1.54)	0.065
Family history of HSCR	0.75 (0.32–1.92)	0.689	–	–
Extension of aganglionosis above the rectum to the sigmoid colon	1.89 (1.05–3.19)	0.049	1.91 (1.37–2.98)	0.038
Creation of pre-operative defunctioning stoma	2.28 (1.47–3.23)	0.035	1.81 (1.08–3.22)	0.045
Occurrence of pre-operative enterocolitis	1.99 (0.78–4.02)	0.152	–	–
Trans-abdominal surgery	2.04 (0.88–3.93)	0.097	–	–
Post-operative anastomotic stricture	1.59 (0.86–3.67)	0.124	–	–

have advocated the use of prophylactic oral flagyl and probiotics although further prospective studies would be required to address the efficacy of this practice [9, 10].

Regarding the risk factors for the development of HAEC, a history of pre-operative stoma creation and the extension of aganglionosis to the sigmoid colon were shown to be significant risk factors in the current study. The presence of either or both of these two conditions may suggest the disease is more severe than usual. This finding also concurs with our previous study which demonstrated that patients with disease involvement proximal to the rectum would have a worse functional outcome [11]. A higher incidence of HAEC was found in this group of patients. Adding together, we believe that the overall outcome of HSCR patients with aganglionosis extending to the sigmoid colon maybe closer to those with long segment disease. In the recent 10–15 years, the surgical approach has moved towards one-stage procedure. A pre-operative stoma is usually reserved for those with complicated disease when bowel decompression could not be achieved

by rectal washout. A recent study in the gut microbes has shown that dysbiosis and impaired intestinal renewal could happen in the defunctioned bowel [12]. We postulated that the creation of a defunctioning stoma may have a similar effect on the gut microbiome and immunity leading to the increased chance of HAEC. However, a study on the microbe of defunctioned bowel in HSCR patient would be required to test this hypothesis. Based on this, extra effort including rectal irrigation by an experienced surgeon or early operation should be considered to avoid the creation of pre-operative stoma.

On the other hand, the associations of some commonly quoted risk factors for HAEC were not obvious in this study. For instance, the association of Down's syndrome with HAEC due to intrinsic immune deficiency has been reported in other studies but this could not be demonstrated here [13]. As only HSCR-S was studied, the incidence of Down's syndrome is low and this may explain why the association was not apparent in this study. Similar explanation can be applied during the analysis of pre-operative enterocolitis. Anastomotic stricture has been shown to be a risk factor for HAEC in many other studies and successful treatment of this complication can alleviate recurrent HAEC [14, 15]. In our centre, all the patients received weekly to monthly follow up with digital rectal examination by the surgeons within the first year of operation. Most anastomotic stricture was detected early and anal dilatation would be commenced once this complication was found. The low actual incidence and prompt management of anastomotic stricture may account for the insignificant association found in the current study.

The debate on whether transabdominal Duhamel surgery or transanal endorectal surgery would lead to a higher incidence of HACE has continued since early 2000s. Conflicting evidence have been reported from different studies but one of the most recent studies by Parahita et al., suggested that the incidence of HAEC is higher after the Duhamel procedure [8, 16]. Our findings did not support either approach. However, transanal endorectal surgery has gradually replaced Duhamel operation in recent years due to other reasons such as technical difficulty and patient recovery.

This study was limited by its retrospective nature and has been subjected to different con-founding variables such as the variation of operative technique among different surgeons. However, as this was a single centre study and all the surgeons followed the same operative principle, the technical variation should be minimal. Inevitably, the post-operative management protocol has undergone some changes over the study period that might have influenced the analysis. Although some of the analyses did not reach a statistical significant level in this study, we believe they are still clinically significant. These risk factors should be carefully monitored and should not to be ignored during the follow up of HSCR patients.

Conclusions

The incidence of HAEC in short segment disease is comparable to long segment disease and commonly occurs within the first year of operation. In addition to the other known risk factors, the requirement of pre-operative defunctioning stoma and the extension of aganglionosis above the rectum to the sigmoid colon have been shown to be significant risk factors for the development of post-operative HAEC in HSCR-S. Patients with these risk factors should be closely followed up especially in the early post-operative period. Preventive and treatment strategies should focus on avoiding the creation of pre-operative stoma and the consideration of prophylactic medication in HSCR-S patients with 'longer' segment of HSCR-S.

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Compliance with ethical standards

Conflict of interest The author(s) declare that they have no conflict of interests.

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