Human Breastmilk Feeding in Necrotising Enterocolitis Patients With Surgical Treatment A Retrospective Chart Review Study

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Abstract

Background

One of the surgical treatments for necrotising enterocolitis (NEC) is to resect the necrotic bowel and defunction the gut by stoma, which can come with severe complications impacting infant growth. Human breastmilk feeding has been proved to prevent NEC, world-widely. This study is to identify whether human breastmilk could reduce the incidence of stoma related complications in NEC patients after primary surgery.

Methods

A retrospective chart review was done on patients who had intestine resection and stoma for NEC in the period from 2015-1-1 to 2021-4-30 at Anhui Provincial Children's Hospital (APCH). Demographics, feeding methods (human milk feeding versus formula milk feeding) and stoma related complications were collected, and the factors, potentially associated with stoma related complications, were analysed.

Results

A total of 58 patients, including 35 males and 23 females, had stoma for NEC. The mean gestational age was 34 weeks (28 to 40). The mean body weight at surgery was 2.83kg (1.03 to 4.80). Before surgery, 38 patients had perforation. Additionally, 46 patients had ileostomy; 12 had colostomy. After primary operation, 40 of them were fed with human breastmilk while 18 of them were fed with formula milk. 26 of 58 patients had stoma related complications, including fluid/electronic imbalance, stoma prolapse, and stoma stenosis. Feeding methods and gestational age were found significantly related to stoma related complications via a binary logistical multivariable analysis.

Conclusions

In this study, the most frequent stoma related complication was fluid/electronic imbalance. Younger gestational age was identified as a risk factor associated with stoma related complications; human breastmilk feeding can benefit patients against these complications.

Introduction

Necrotising enterocolitis (NEC) is one of the most common serious gastrointestinal disease in neonatal, especially in preterm [1]. The treatments of NEC patients are including non-surgical and surgical ones, based on the BELL's criteria [2]. Specific surgical treatment has not been changed much since 1907. Primary anastomosis is identified to be an optional approach to extreme low birth weight infants [3]. Additionally, the traditional surgical approach is to resect the necrotic bowel and defunction the gut by stoma [4]. However, the stoma related complications, including fluid/electronic imbalance, prolapse, retraction, and skin excoriation/wound breakdown, could cause negative influence on patient recovery or even poor outcomes. Among them, fluid loss is particularly troublesome and has significant impact in

infants' growth [4]. Moreover, the related metabolic and functional problems can cause earlier surgery than planned stoma reverse and harm further development of patients [5]. Recently, human breastmilk has been proved to have a preventive effect against NEC, especially in low-birth-weight infants [6–8]. However, clinical research, which is about the human breastmilk preventive effect against surgical stoma related complications on NEC patients, is still lacking. The purpose of this study is to identify whether human breastmilk could benefit NEC patients against surgical stoma related complication via a chart review.

Methods

A retrospective chart review was done on patients who were surgically treated for NEC in the period from 2015-1-1 to 2021-4-30 at Anhui Provincial Children's Hospital (APCH). APCH is a tertiary paediatric hospital in Anhui Province, East China.

Exclusion criteria: no suspicion of NEC during surgery, focal intestinal perforation, no intestinal resection, no stoma formation, no NEC on histological examination, and uncomplete medical record.

Demographics and stoma related complications were collected via reading the medical records. Stoma related complications were defined as the complications occurring between primary and stoma reversal surgery.

NEC was defined as gangrene of intestinal segment with or without perforation and confirmed by histology. Postoperative complications were identified according to the Clavien-Dindo Classification (CDC) [9].

Two paediatric surgery specialists performed all the surgeries. The standard for resection and stoma formation was a proximal stoma placed in the lower left or right abdominal quadrant with at least 3 cm distance from the abdominal incision. The stoma was fixed by three-point sutures after eversion of the mucosal side, and attempting for a stoma height of approximately 1 cm. The standard for stoma reversal was after 3 months depending on the patient's clinical condition.

Continuous data were expressed as mean and range. Categorical data were expressed as percent (%). The binary logistical multivariable analysis was used to identify the risk factors of stoma related complications on NEC patients after primary operation. Statistical analysis was performed on an Apple MacBook laptop by using Statistical Product and Service Solutions (SPSS) software, version 26. P values < 0.05 were considered as significant.

Results

Demographic data

100 patients were operated for NEC, and 60 of them had stoma. 2 patients were excluded due to incomplete medical record. The demographic data of the rest 58 patients were summarised (Table 1). 35 were male patients and 23 were female patients. The mean age at surgery of the included patients was 47 days. The mean gestational age (GA) was 34 weeks, which 29 of them were mature infants, 9 of them were late premature ($34 \text{ weeks} \leq \text{GA} < 37 \text{ weeks}$), and 20 were early premature ($\text{GA} < 34 \text{ weeks}$). The mean body weight of patients at NEC was 2.83 kilogram (kg). Before surgery, 38 patients had intestinal perforation. The mean time between primary surgery and stoma reversal was 134 days. After primary surgery, the numbers of infant fed with human milk and formula milk were 40 and 18, respectively. Furthermore, 10 patients had a reoperation prior to their planned stoma reversal operation ($\text{CDC} > 3\text{b}$).

Type of stoma, complication, and risk factor of stoma

Among the 58 patients, ileostomy and colostomy were performed in 46 and 12 infants, respectively. 29 complications were found in 26 patients, which were 19 cases of fluid/electronic imbalance, 5 cases of stoma prolapse, and 5 cases of stoma stenosis (Table 2). The gender, type of stoma, feeding methods, GA, body weight at primary surgery, and perforation before surgery were analysed in a binary logistical multivariable analysis for their relationship to stoma related complications. The results showed the feeding methods and GA were significantly associated with stoma related complications ($P = 0.008$ and $P = 0.0403$, respectively) (Table 3).

Discussion

In this study, we found the most frequent stoma related complication was fluid/electronic imbalance, which was normally caused by postoperative diarrhea. Diarrhea in NEC patients is associated with antibiotics use and enterostomy effluent [10]. Antibiotic-associated diarrhea (AAD) can vary nuisance loose to watery stool, even severe diarrhea, which relates to antibiotics destroying normal intestinal microbial flora [11, 12]. Lactoferrin, a human breastmilk protein, has both anti-bacterial and anti-inflammatory effect. Moreover, this protein dose not impact normal gut microbiota in intestine [13]. In 1978, Chandra and colleague performed a cohort study in 70 infants, which 35 were fed with human breastmilk and 35 were fed with formula milk. The results showed a human breastmilk can significantly protect infants against diarrhea [14]. In 2018, Doherty and colleague published a meta-analysis, which demonstrated human breastmilk feeding can reduce diarrhea incidence in infancy [15]. Enterostomy includes ileostomy and colostomy. Kennedy and colleagues reported the patients with ileostomy had higher risk of fluid/electronic imbalance than the ones with colostomy in their study [16]. However, in our study, no significant difference of complication rate was found between the two groups ($P = 0.0631$); instead, the formula milk feeding patients had the higher. According to this conflict, more studies should be exploited about reintroduction of feeding and relevant complications on infants with enterostomy, especially for NEC patients.

The other two stoma related complications, found in this study, were prolapse and stenosis. Stoma prolapse is a full-thickness telescope of the bowel, which locates out of a stoma. Five prolapse cases were found in this study and all of them had a reoperation, and three of them were because of increased

intra-abdominal pressure associated with diarrhea. According to previous publication, the risk factors of prolapse formation are obesity, abdominal wall laxity, a large fascial opening, and other conditions which could increase intra-abdominal pressure [17]. In 2018, Wolf and colleagues published a retrospective 10-year cohort study. They reported 51 patients had primary enterostomy and stoma formation for NEC; 22 prolapse cases were observed among them [18]. Compared to their findings, the prolapse rate in our study was lower. This is because a lower incidence of diarrhea was found in the human breastmilk feeding patients, which reduced the chance of increasing intra-abdominal pressure in our patients.

Stoma stenosis can occur in any postoperative period. The most common symptom is a noise from stoma when the flatus passes through, and stoma stenosis is rare to present as an acute intestinal obstruction [19]. Therefore, most of stenotic stoma cases are not problematic and can be treated by local procedure. In our study, the five stomas stenosis cases were managed by serial gentle dilation and none of them required a reoperation. However, in 2019, Baelum and colleagues published a chart review study about enterostomy complications in NEC patients, and the results showed the most frequent stoma related complication in the reoperation group was stenosis [20].

To determine the risk factors of stoma related complications in NEC patients after primary operation. We performed a binary logistical multivariable analysis in this study, and the results showed two risk factors, GA (OR: 0.793) and formula milk feeding (OR: 8.345), were associated. It also demonstrated that younger GA and formula milk feeding after primary surgery could increase the risk of stoma relevant complications. In 2009, Aguayo and colleagues published a similar retrospective study. 73 NEC patients were included and younger GA and low preoperative body weight were identified to increase risk of stoma related complications [21]. However, more researches are still needed in the field, especially a multicentre perspective study.

Conclusions And Limitations

We found the most frequent stoma related complication was fluid/electronic imbalance; younger gestational age was identified as a risk factor associated with stoma related complications; human breastmilk feeding could benefit patients against these complications. There are several limitations in this study: firstly, we did not do multivariable analysis on the relationship between each stoma related complication and their potential risk factors, due to the small number of patients; secondly, we did not perform a long-term follow-up after stoma reversal surgery, due to hard to connect with these patients' family. Therefore, we suggest a further multicentre study with a long-term follow-up in the future.

Abbreviations

NEC

Necrotising enterocolitis; CDC:Clavien-Dindo Classification; GA:Gestational age; AHCP:Anhui Provincial Children's Hospital; AAD:antibiotic-associated diarrhea; OR:odds ratio

Declarations

Conflicts of Interests

The authors declare no conflicts of interests.

Funding

This study has not received any fund.

Ethics Approval

This study was approved by the institutional Review Board/Ethics Committee of Anhui Provincial Children's Hospital. This study was limited to registry data without direct contact with patients.

Consent to publication

Not applicable

Authors' contributions

Dr Jing Shan and Dr Yao Shen conceptualised and designed the study, screened charts, extracted the data, analysed and interpreted the data, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr Rongqiang Yang, Dr Danqun Jin and Dr Yang Shen conceptualised and designed the study, analysed and interpreted the data, and critically reviewed and revised the manuscript for important intellectual content.

Dr Hao Ding, Dr Wei Zuo and Dr Yuanyuan Xu conceptualised and designed the study, critically reviewed and revised the manuscript for important intellectual content.

Dr Xiaole Li conceptualised and designed the study, analysed and interpreted the data, and critically reviewed and revised the manuscript for important intellectual content.

Availability of data and materials

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

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Tables

Due to technical limitations, table 1,2,3 is only available as a download in the Supplemental Files section.

Supplementary Files

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- [Table1.jpg](#)
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