Effect of early enteral nutrition and aggressive intravenous fluid resuscitation on clinical outcomes in pediatric severe acute pancreatitis

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Abstract

Background : Early enteral nutrition (EN) and aggressive intravenous fluid (IVF) resuscitation are recommended in adult patients with severe acute pancreatitis (SAP). Whether these recommendations influence the outcomes of pediatric SAP is unclear and need to be figured out.

Methods : We performed a retrospective review of pediatric patients with SAP admitted to Shengjing Hospital of China Medical University from January 1, 2012 to September 30, 2019. Data regarding demographic and baseline characteristics of SAP patients were collected. The outcomes studied were abdominal pain duration, time for recovery of food intake, length of stay (LOS), number of attacks, complication rate, and fatality rate.

Results : This study included 40 pediatric SAP patients. We divided all patients into the EN+IVF group, nil per os (NPO)+IVF group, and NPO+ no IVF group. There was no significant difference in demographic and baseline characteristics in the different groups. However, children who received EN and IVF treatment had the shortest abdominal pain duration, time for recovery of food intake, and LOS.

Conclusion : Our study found that early EN and aggressive IVF resuscitation improved the outcome of pediatric patients with SAP.

Background

Acute pancreatitis is one of the most common indications for inpatient hospital care in a gastroenterological emergency and sometimes life-threatening inflammatory disorders [1]. Epidemiological studies suggest that the incidence of acute pancreatitis in children has been increasing over the past decades and is estimated to be 3.6–13.2 cases per 100,000 every year [1], which is close to that for adult patients. The Atlanta classification for severity of acute pancreatitis delineates three severity subtypes of acute pancreatitis: mild, moderate and severe. Notably, approximately 15–20% of acute pancreatitis patients will develop the severe subtype [6, 7], which is called severe acute pancreatitis (SAP) and which has a much higher mortality compared to the mild or moderate subtype. Recently, advances in the diagnosis and management of SAP have been made in adult patients, but as for pediatric patients, a “special” and “different” group compared with adults, a standardized management protocol is lacking. Therefore, it is necessary to develop a management protocol for SAP in children to decrease mortality and improve the prognosis.

In adult SAP patients, the evidence suggests that initial goal-directed therapy, nutritional support, and vigilance for pancreatic complications are the best approach [1]. Patients with SAP can develop hypovolemia and therefore have hypotension secondary to a systemic inflammatory response. Several liters of fluid resuscitation may be needed to preserve organ function [1]. Additionally, enteral nutritional (EN) support has been proven to benefit SAP patients, and it can improve outcomes and limit complications [1]. However, all the above recommendations are limited to adult SAP patients. Whether the same or similar conclusions could be drawn in pediatric SAP patients is still unclear, and more cohort

studies or clinical trials are needed to resolve this issue. One retrospective cohort study conducted by Szabo et al. [8] found that pediatric acute pancreatitis patients who received feeding within 48 h and greater than maintenance intravenous fluid (IVF) within 24 h had a shorter length of stay (LOS) and less intensive care unit admissions. Whether children with SAP, who belong to a special subtype of acute pancreatitis, could benefit from early EN and aggressive IVF resuscitation is still unknown and needs to be explored more. Notably, no recent study has compared the different treatments with outcomes in pediatric SAP patients.

Therefore, to determine whether the outcomes of SAP were different in children treated with early EN and aggressive IVF resuscitation compared with those who were not, we conducted this retrospective cohort study including pediatric SAP patients in our hospital admitted between 2012 and 2019.

Materials And Methods

Study population and data source

The study was approved by the Ethics Committee of Shengjing Hospital of China Medical University (No. 2020PS294k). A retrospective review of admissions of children with SAP from January 1, 2012 to September 30, 2019 at Shengjing Hospital of China Medical University was conducted. Identification of SAP cases was based on the major diagnosis in our Hospital Information System (HIS). The cohort was limited to those children who had elevated lipase and/or amylase level ≥ 3 times the upper limit of normal values, and who were admitted to the pediatric services of the Department of Pediatrics, Division of Gastroenterology or Pediatric Emergency services including outpatient and inpatient services. We also retrieved the patients who were admitted to the pediatric intensive care unit (PICU) during this period.

Inclusion criteria were: (1) admitted to one of the aforementioned services (Department of Pediatrics Division of Gastroenterology, Pediatric Emergency, and PICU); (2) elevated lipase and/or amylase level ≥ 3 times the upper limit of normal values; (3) imaging including computed tomography scan or magnetic resonance imaging to support the SAP diagnosis; (4) SAP as the primary disease; (5) 0–13 years old at the time of admission, which is also the criterion for admission to Department of Pediatrics in our hospital. Exclusion criteria were: (1) SAP secondary to other diseases such as trauma, sepsis, respiratory disorders, multiorgan failure, etc.; (2) incomplete personal information or management process; (3) patients' withdrawal from hospital.

Data Collection

Demographic and baseline data were collected for each patient. The personal information we focused on included sex, age, and weight, and the physiological conditions of interest were blood pressure, heart rate, temperature, and neurological signs. We also collected information on the etiology of SAP. Data on several blood biochemical tests, namely amylase, lipase, white blood cell count, hematocrit (HCT), C-reactive protein (CRP), serum creatinine and blood urea nitrogen, were collected as well. To compare the

outcome and prognosis in different groups, we divided all patients into three groups: EN + IVF group, nil per os (NPO) + IVF group, and NPO + no IVF group. EN refers to the patients who received EN within 48 h after admission. IVF refers to the patients who received early fluid resuscitation within 24 h after admission. In each group, we collected data regarding the treatment process such as use of proton pump inhibitor, octreotide, and somatostatin, as well as other advanced management including ventilator support and blood purification therapy. To evaluate outcome and prognosis, data on abdominal pain duration, time for recovery of food intake, length of intravenous nutrition, number of attacks, LOS, complication rate, and case fatality rate were collected.

Statistical Analyses

The statistical analysis of the data was performed using SPSS version 23.0 (IBM Corporation, Armonk, NY, USA). Continuous variables are expressed as mean with SD and median with range and interquartile range (IQR). For continuous variables in which we could get values including the minimum and maximum, we used one-way ANOVA to compare means. For categorical variables, Fisher's exact test was used to compare the rate in the different groups. When we compared the different clinical outcomes in different treatment groups (e.g., EN + IVF vs NPO + IVF, EN + IVF vs NPO + no IVF, and NPO + IVF vs NPO + no IVF), we used multiple comparison with the least significant difference test to determine if there was a statistical difference between the different groups. In our study, two-tailed P values less than 0.05 were considered statistically significant.

Results

Demographic and baseline characteristics of SAP patients

A total of 40 children were included in our study. We first summarized the demographics and baseline clinical variables of these patients in the different groups (Table 1). The groups were not significantly different in patients' characteristics, i.e., sex, age and weight on admission. Among all included cases, most of them were idiopathic SAP, while only a few SAP cases were due to pathogen infection, gallstone, trauma, or anatomic reason. Patients had comparable laboratory values on admission and other clinical variables measured. Although all patients had elevated amylase and/or lipase level, there was no statistical significance between the EN + IVF, NPO + IVF, and NPO + no IVF groups. Additionally, there were no obvious differences in the different groups regarding blood biochemical tests, including HCT, CRP, serum creatinine, and blood urea nitrogen. The white blood cell count in EN + IVF group tended to be lower than in the other groups, but there was no statistical significance. As for other physiological conditions including blood pressure, heart rate, and temperature, there was also no apparent difference between the different groups.

Table 1

Demographic and baseline characteristics of patients on presentation with SAP within each treatment group

Variables	Category	EN + IVF(A)	NPO + IVF(B)	NPO + no IVF (C)	*p* value
		N = 9	N = 25	N = 6	
Sex	F	2	14	4	0.159[b]
	M	7	11	2	
Age	N	9	25	6	0.474[a]
	Mean (SD)	9.33 (3.94)	8.46 (3.73)	10.50 (3.78)	
	Median	11.0	9.0	11.5	
	(Min, max)	(3.00, 13.00)	(1.08, 13.00)	(3.00, 13.00)	
	IQR	(5.00, 12.50)	(5.50, 12.00)	(9.00, 13.00)	
Weight	N	9	25	6	0.471[a]
	Mean (SD)	45.44 (23.98)	41.28 (21.22)	53.25 (19.38)	
	Median	47.00	40.00	58.25	
	(Min, max)	(16.00, 80.00)	(12.00, 74.80)	(16.00, 70.00)	
	IQR	(22.50, 68.50)	(21.90, 62.60)	(43.00, 66.25)	
Etiology	Viral	2 (22.22%)	8 (32.00%)	0 (0)	0.272[b]
	Mycoplasma	0 (0)	3 (12.00%)	1 (16.67%)	
	Idiopathic	7 (77.78%)	12 (48.00%)	3 (50.00%)	
	Gallstone	0 (0)	1 (4.00%)	0 (0)	
	Trauma	0 (0)	0 (0)	1 (16.67%)	
	Anatomic	0(0)	1 (4.00%)	1 (16.67%)	
Amylase	N	9	25	6	0.472[a]
	Mean (SD)	1045.47 (1352.05)	848.49 (638.03)	507.67 (408.84)	
	Median	691.00	639.00	449.00	

CRP C-reactive protein; *EN* Enteral nutrition; *HCT* Hematocrit; *IVF* Intravenous fluid; *NPO* nil per os; *SD* Standard deviation;

[a] One-way ANOVA test; [b] Fisher's exact test.

	(Min, max)	(250.00, 4609.00)	(140.00, 2428.00)	(118.00, 1252.00)	
	IQR	(427.50, 848,10)	(360.50, 1497.00)	(184.00, 742.00)	
Lipase	N	9	25	6	0.272[a]
	Mean (SD)	848.49 (638.03)	2206.78 (1637.13)	1288.55 (939.81)	
	Median	639.00	1592.00	1026.75	
	(Min, max)	(140.00, 2428.00)	(493.00, 5907.90)	(406.00, 2982.60)	
	IQR	(360.50, 1497.00)	(959.55, 3421.80)	(630.93, 1933.13)	
White blood count	N	9	25	6	0.306[a]
	Mean (SD)	13.93 (5.03)	18.16 (8.05)	18.65 (6.80)	
	Median	13.51	18.32	17.20	
	(Min, max)	(5.73, 21.40)	(4.40, 39.30)	(12.50, 27.80)	
	IQR	(10.91, 18.60)	(11.10, 23.00)	(12.65, 25.36)	
HCT	N	9	20	6	0.158[a]
	Mean (SD)	41.99 (3.54)	43.11 (5.77)	37.99 (7.20)	
	Median	41.10	42.20	38.75	
	(Min, max)	(36.42, 46.60)	(34.41, 56.00)	(29.45, 48.00)	
	IQR	(39.15, 45.57)	(38.55, 44.90)	(30.61, 43.50)	
CRP	N	9	24	6	0.141[a]
	Mean (SD)	10.52 (7.07)	80.88 (106.27)	64.08 (65.56)	
	Median	39.10	32.50	32.70	
	(Min, max)	(2.34, 21.00)	(1.85, 376.00)	(8.75, 165.00)	
	IQR	(3.53, 17.00)	(5.75, 120.65)	(15.16, 137.25)	
Serum creatinine	N	9	20	6	0.372[a]

CRP C-reactive protein; *EN* Enteral nutrition; *HCT* Hematocrit; *IVF* Intravenous fluid; *NPO* nil per os; *SD* Standard deviation;

[a] One-way ANOVA test; [b] Fisher's exact test.

	Mean (SD)	37.28 (6.10)	66.02 (69.34)	88.65 (115.33)	
	Median	39.10	38.15	43.10	
	(Min, max)	(26.20, 43.30)	(22.60, 300.50)	(22.60, 320.60)	
	IQR	(32.15, 42.55)	(32.08, 56.43)	(24.33, 138.35)	
Blood urea nitrogen	N	9	20	6	0.077[a]
	Mean (SD)	3.82 (1.43)	6.45 (4.06)	9.89 (9.35)	
	Median	3.87	5.53	5.29	
	(Min, max)	(1.73, 6.24)	(2.31, 19.92)	(3.58, 27,17)	
	IQR	(2.44, 4.80)	(3.61, 7.91)	(3.75, 17.46)	
Blood pressure	Normal	0 (0)	5 (20.00%)	1 (16.67%)	0.449[b]
	Abnormal	9 (100%)	20 (80.00%)	5 (83.33%)	
Hear rate	Normal	1 (11.11%)	5 (20.00%)	0 (0)	0.693[b]
	Tachycardic	8 (88.89%)	20 (80.00%)	6 (100%)	
Temperature	Afebrile	8 (88.89%)	23 (92.00%)	5 (83.33%)	0.773[b]
	Febrile	1 (11.11%)	2 (8.00%)	1 (16.67%)	
Neurological sign	Normal	7 (77.78%)	22 (88.00%)	5 (83.33%)	0.822[b]
	Abnormal	2 (22.22%)	3 (12.00%)	1 (16.67%)	

CRP C-reactive protein; *EN* Enteral nutrition; *HCT* Hematocrit; *IVF* Intravenous fluid; *NPO* nil per os; *SD* Standard deviation;

[a] One-way ANOVA test; [b] Fisher's exact test.

Comparison Of Treatments And Outcomes In The Different Groups

To see whether different treatments contributed to different outcomes, we further evaluated management and prognosis in the different groups (Table 2). The treatment for most SAP patients in each group included the use of a proton pump inhibitor, octreotide, and somatostatin. There were no statistically significant differences regarding ventilator support and blood purification therapy in these three groups. Therefore, we found that medical treatment was similar in the different groups.

Table 2

Comparison of treatments and outcomes and process among treatment groups

Response variables	Category	EN + IVF (A)	NPO + IVF(B)	NPO + no IVF (C)	*p* value	Significantly different pairs
		N = 9	N = 25	N = 6		
Proton pump inhibitor	use	9 (100%)	24 (96.00%)	6 (100%)	1.000[b]	-
	not use	0 (0)	1 (4.00%)	0 (0)		
Octreotide	use	8 (88.89%)	20 (80.00%)	5 (83.33%)	1.000[b]	-
	not use	1 (11.11%)	5 (20.00%)	1 (16.67%)		
Somatostatin	use	4 (44.44%)	15 (60.00%)	6 (100%)	0.080[b]	-
	not use	5 (55.56%)	10 (40.00%)	0 (0)		
Ventilator support	N	9	25	6	0.486[a]	
	Mean (SD)	0 (0)	0.792 (2.19)	1.00 (1.55)		-
	Median	0.00	0.00	0.00		
	(Min, max)	(0, 0)	(0.00, 8.00)	(0.00, 3.00)		
	IQR	(0, 0)	(0, 0)	(0.00, 3.00)		
Blood purification therapy	N	9	25	6	0.278[a]	
	Mean (SD)	0 (0)	1.15 (2.40)	0.33 (0.82)		-
	Median	0.00	0.00	0.00		
	(Min, max)	(0.00, 8.00)	(0.00, 10.00)	(0.00, 2.00)		

ACS Abdominal compartment syndrome; *EN* Enteral nutrition; *IQR* Interquartile range; *IVF* Intravenous fluid; *LOS* Length of stay; *NPO* nil per os; *SD* Standard deviation

[a] one-way ANOVA test; [b] Fisher's exact test.

Response variables	Category	EN + IVF (A)	NPO + IVF(B)	NPO + no IVF (C)	*p* value	Significantly different pairs
		N = 9	N = 25	N = 6		
	IQR	(0, 0)	(0.00, 1.35)	(0.00, 5.00)		
Length of abdominal pain	N	7	23	5	0.000[a]	AC (0.000), BC (0.000)
	Mean (SD)	5.00 (5.07)	5.65 (4.45)	22.98 (16.62)		
	Median	3.00	5.00	28.00		
	(Min, max)	(2.00, 16.00)	(0.00, 18.00)	(0.00, 39.90)		
	IQR	(2.00, 6.00)	(3.00, 7.00)	(6.00, 37.45)		
Length of NPO	N	9	25	6	0.000[a]	AC (0.000), BC (0.001)
	Mean (SD)	2.11 (0.78)	6.08 (4.18)	15.33 (13.00)		
	Median	2.00	5.00	12.00		
	(Min, max)	(1.00, 3.00)	(1.00, 18.00)	(3.00, 39.00)		
	IQR	(1.50, 3.00)	(3.00, 10.00)	(5.25, 24.75)		
Length of intravenous nutrition	N	9	25	6	0.003[a]	AC (0.001), BC (0.002)
	Mean (SD)	2.11 (4.76)	4.72 (6.20)	15.33 (12.45)		
	Median	0.00	0.00	13.00		
	(Min, max)	(0.00, 14.00)	(0.00, 19.00)	(0.00, 34,00)		
	IQR	(0.00, 2.50)	(0.00, 10.50)	(5.25, 27.25)		

ACS Abdominal compartment syndrome; *EN* Enteral nutrition; *IQR* Interquartile range; *IVF* Intravenous fluid; *LOS* Length of stay; *NPO* nil per os; *SD* Standard deviation

[a] one-way ANOVA test; [b] Fisher's exact test.

Response variables	Category	EN + IVF (A)	NPO + IVF(B)	NPO + no IVF (C)	*p* value	Significantly different pairs
		N = 9	N = 25	N = 6		
Attack number of times	no replase	6 (66.67%)	22 (88.00%)	5 (83.33%)	0.353[b]	-
	replase	3 (33.33%)	3 (12.00%)	1 (16.67%)		
LOS in d	N	9	25	6	0.043[a]	AC (0.028), BC (0.016)
	Mean (SD)	14.31 (4.19)	14.99 (12.04)	27.17 (10.79)		
	(Min, max)	(9.00. 22.50)	(0.70, 59.50)	(25.30, 40.60)		
Complication rate		5 (55.56%)	13 (52.00%)	6 (100%)	0.097[b]	-
	ACS	0 (0)	1 (4.00%)	0 (0)		
	Diabetes mellitus	0 (0)	1 (4.00%)	0 (0)		
	Pancreatic pseudocyst	1 (11.11%)	4 (16.00%)	1 (16.67%)		
	Abnormal liver function	1 (11.11%)	7 (28.00%)	2 (33.33%)		
	Myocardial damage	1 (11.11%)	6 (24.00%)	1 (16.67%)		
	Lung edema/pleural effusion	3 (33.33%)	7 (28.00%)	2 (33.33%)		
	Kidney damage	0 (0)	4 (16.00%)	2 (33.33%)		
Case fatality rate		0 (0)	2 (8.00%)	1 (16.67%)	0.494[b]	-

ACS Abdominal compartment syndrome; *EN* Enteral nutrition; *IQR* Interquartile range; *IVF* Intravenous fluid; *LOS* Length of stay; *NPO* nil per os; *SD* Standard deviation

[a] one-way ANOVA test; [b] Fisher's exact test.

Furthermore, we compared outcome and prognosis in the different groups. Notably, abdominal pain duration in the EN + IVF group was 3 days compared with 5 days in the NPO + IVF group ($P < 0.001$) and 28 days in the NPO + no IVF group ($P < 0.001$). In addition, time for recovery of food intake was 2 days in the EN + IVF group, which was the shortest compared with 5 days in the NPO + IVF group ($P < 0.001$) and 12 days in the NPO + no IVF group ($P < 0.001$). This suggested that EN combined with IVF therapy could help reduce the period for recovery of food intake, which could be beneficial for recovery of the function of the digestive system. Notably, as for LOS, patients in the EN + IVF group had the shortest in-hospital period: 14.31 days in the EN + IVF group compared with 14.99 days in the NPO + IVF group ($P < 0.05$) and 27.17 days in the NPO + no IVF group ($P < 0.05$). However, there was no evident difference between the three groups regarding complication rate and case fatality rate.

Discussion

Our study demonstrated that early EN and IVF had a good impact on the outcomes of pediatric SAP patients. EN combined with IVF treatment in these patients may reduce abdominal pain duration, time for recovery of food intake and LOS better than with NPO + IVF and NPO + no IVF. Our study found that EN and IVF could play important roles and should be recommended in the management of children with SAP.

There are several important studies suggesting that early EN in adults with SAP can lead to better outcomes [9–11], and this has been confirmed by a meta-analysis including five randomized controlled trials with 202 patients showing a reduced risk of infectious complications, pancreatic infections and mortality [12]. Similarly, another meta-analysis that included eight trials with 348 participants also found that EN was superior to parenteral nutrition in terms of complications and mortality [13]. EN may support the gut-mucosal barrier and reduce bacterial translocation, and thereby reduce the risk of infected peripancreatic necrosis and other serious acute pancreatitis outcomes [1]. Daily caloric requirements can be calculated on the basis of the patient's weight and severity of illness, with the goal of improving serum nutritional parameters including prealbumin and albumin levels [1]. Although our study demonstrated the decrease in abdominal pain duration, time for recovery of food intake, and LOS of patients in the EN + IVF group compared with patients in the NPO + IVF group, we did not find any difference in complication rate and case fatality rate. The main reason might have been the limited number of cases in our study. Further studies should include more cases to determine the influence of early EN on complications and mortality.

Early resuscitation is also recommended in adult SAP patients considering that they could develop hypovolemia and have hypotension secondary to a systemic inflammatory response. Various fluid preparations are available for resuscitation such as lactated Ringer's solution or hydroxyethyl starch solution. In adult patients with SAP, several trials have evaluated the influence of these two solutions on outcomes [11, 14, 15], but not all trials have drawn the same conclusion. Although the different types of fluid do not seem to affect the outcome and prognosis in adult patients with SAP, the consensus guidelines from the International Association of Pancreatology and American Pancreatic Association recommend lactated Ringer's solution as the first choice for initial phase of resuscitation [16]. However, a consensus is still lacking for pediatric patients with SAP. Our study successfully demonstrated that early

fluid resuscitation is better in decreasing abdominal pain duration, time for recovery of food intake, and LOS compared with no IVF. But future studies are also needed to explore which fluid type is more suitable for children with SAP. Moreover, in adult SAP patients, goal-directed IVF therapy with 5–10 ml/kg/h should be used initially until resuscitation goals are reached, but the dose of fluid resuscitation in pediatric patients with SAP is still unclear and needs to be standardized.

Our study has several strengths. Only a few studies have reported an association between early EN as well as IVF and outcome or prognosis in pediatric patients with acute pancreatitis [8]. To the best of our knowledge, there has been no pediatric study focusing on the role of EN and IVF in the outcome and prognosis of SAP. Our study is the first one to explore the influence of EN and IVF on the outcome and prognosis of children with SAP. In addition, we used several response variables including abdominal pain duration, time for recovery of food intake, and LOS to evaluate the outcomes, which are more objective and comprehensive.

Despite the clear strengths of our study, some limitations should be acknowledged. First, our study was a retrospective study. Besides the limitation from the retrospective nature of the analysis, we only retrieved the patients' information in our HIS. The lack of follow-up could have lost sight of long-term complications. Secondly, because the complete HIS of our hospital has been developed since 2012, it is hard for us to get the full information regarding the demographic characteristics and treatment details of patients before 2012. Therefore, our study only included 40 children patients with SAP after January 1, 2012. The limited number of patients may underestimate the benefit of EN and IVF. In the future, we will collect more SAP cases and perform a prospective cohort study to evaluate the influence of EN and IVF on outcomes in pediatric patients with SAP.

Conclusions

In conclusion, our study assessed the outcomes of different treatment modalities. Our results showed that compared with NPO + IVF and NPO + no IVF, EN combined with IVF decreased abdominal pain duration, time for recovery of food intake, and LOS in children with SAP. However, there was no evident difference regarding complication and mortality rates in the different treatment groups. It is essential to conduct further prospective cohort studies with more cases to determine the influence of EN and IVF on complications and mortality. Also, multicenter, large-scale clinical trials are needed to define the important factors to be considered for early EN and IVF in pediatric SAP. It is necessary to develop standardized management for pediatric patients with SAP in the future.

Abbreviations

ACS: Abdominal compartment syndrome; CRP: C-reactive protein; EN: Enteral nutrition; HCT: Hematocrit; HIS: Hospital information system; IQR: Interquartile range; IVF: Intravenous fluid; LOS: Length of stay; NPO: nil per os; PICU: Pediatric intensive care unit; SAP: Severe acute pancreatitis; SD: Standard deviation.

Declarations

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None.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by JX and JL. The first draft of the manuscript was written by JX and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

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

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Ethical approval for the study (reference number 2020PS294K) was granted by the Institutional Research Ethics Committee of Shengjing hospital, China Medical University. Since this is a retrospective anonymized study, the informed consent of the children's caregiver was not requested.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

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