ORIGINAL RESEARCH

Enhanced Recovery After Surgery Management for Neonatal Congenital Malformations to Accelerate the Postoperative Recovery of Children

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ABSTRACT

Objective • The purpose of this study was to investigate the clinical benefits of implementing enhanced recovery after surgery (ERAS) protocols in managing congenital malformations in newborns.

Methods • Sixty infants diagnosed with congenital malformations admitted to the Anqing Municipal Hospital between October 2020 and April 2022 were selected for this study. They were randomly assigned to either the observation group, receiving ERAS management, or the control group, receiving routine management, or the control group, receiving routine management. Each group consisted of 30 patients. Outcome measures included operative duration, intraoperative bleeding volume, intravenous nutrition maintenance duration, length of hospital stay, and hospital costs, complications, and readmission.

Results • The duration of the procedure did not show any notable variances, and there were no reports of bleeding during or after surgery in relation to the operative time, intraoperative bleeding, postoperative complications, or readmission. The implementation of ERAS management resulted in notably shorter periods of intravenous nutrition maintenance and hospitalization and reduced costs compared to standard management. Furthermore, ERAS management resulted in significantly lower scores on the Modified Faces, Legs, Activity, Cry, and Consolability Scale at 2, 12, and 24 hours after surgery. However, this difference became insignificant after 48 hours. All study participants experienced elevated levels of cortisol and C-peptide following interventions, with lower levels observed in the observation group. Additionally, all study participants exhibited increased levels of susceptible C-reactive protein and interleukin (IL)-6 and decreased serum albumin levels after interventions, with lower serum IL-6 levels observed in the observation group.

Conclusion • Implementing ERAS management for neonatal congenital malformations is safe and feasible, and it can potentially accelerate postoperative recovery in children. It shows promise for wider clinical adoption. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

In China, an estimated 800 000-1 200 000 children are born with birth defects each year, which imposes a heavy economic and psychological burden on families and society.[1] Therefore, diagnosing and treating birth defects is crucial to reduce their incidence and improve the population's overall quality.

Newborns with severe structural abnormalities, such as diaphragmatic hernia, ventral fissure, and esophageal atresia, face a high risk of fatality, requiring immediate interventions after birth.[2] Prenatal diagnosis facilitates identification of these severe congenital malformations before delivery, allowing for early surgical intervention post-birth. Newborn malformations of vital organ structures are associated with various complications and enormous treatment costs, often leading to the abandonment of these children and a reduced chance of recovery.[3] Unfortunately, no reliable preventive measures are available to avoid congenital malformations due to the complex etiology.[4,5]

Enhanced recovery after surgery (ERAS) is a new approach to perioperative care to minimize stress and complications, reduce the length of hospital stays, and expedite patient recovery. ERAS is a product of a multidisciplinary team (MDT) concept that has been applied in several areas of adult surgery, but its application in neonatal surgery remains limited.[6,7] Therefore, this study explored the potential clinical value of ERAS in treating congenital malformations in newborns.

MATERIALS AND METHODS

Participants

The researchers recruited 60 children with congenital malformations admitted to the Anqing Municipal Hospital between October 2020 and April 2022. The children were divided into 2 groups: the observation group, which received ERAS management, and the control group, which received routine management. Each group consisted of 30 patients. The experiment was conducted with the approval of the hospital's ethics committee, and the children's families signed the informed consent form.

To be included in the study, patients had to meet the following criteria: (a) they underwent surgical treatment within 28 days, b) they did not have any dysfunction in essential organs, their case data was complete, and the guardians of the provided written informed consent. Patients were excluded from the study if they met any of the following criteria: (a) they ha severe dysfunction in important organs, (b) their family members chose to abandon treatment during the process, or (c) they were unavailable for follow-up after surgery.

Perioperative Management

Both groups underwent surgical procedures in the neonatal period to correct congenital deformities. An identical team of neonatal surgeons performed the surgeries. Below, the researchers present a more comprehensive description of the surgical procedures and techniques used to treat congenital deformities. The specific surgical procedures were customized to target the particular type of congenital abnormalities observed in the children. These encompassed corrective surgeries for cardiac anomalies, neural tube defects, gastrointestinal abnormalities, or other congenital conditions.

The observation group received ERAS management,[8] which included various perioperative strategies and multiple steps to optimize recovery. Preoperative education involves explaining ERAS to the patient's families and providing information on implementing procedures, goals, and postoperative care skills of ERAS.

Preoperative and postoperative pain management was a significant consideration in patient health care. The patient was to receive 2 mL of 24% sucrose and a pacifier 2 minutes before invasive procedures. Before establishing intravenous access, a thick layer of compound lidocaine cream (approximately 2mm thick) was applied to the puncture site and covered with a protective cap. Intraoperative pain management involved using sufentanil analgesia and performing a transverse abdominis plane block with 2% ropivacaine (4mL/kg).

Respiratory management involved maintaining a small tidal volume of 6 ~ 8 mL/kg. After the surgery, extubation was performed in the post-anesthesia recovery room, and the child was transferred back to neonatal surgery after achieving an Aldrete score of > 9. Fluid management involved a restriction infusion rate of 6~8 mL/(kg·h) pumping. They maintained body temperature through continuous heating of a water bath, adjusting room temperature, using a special cotton pad to wrap the newborn's limbs, employing disinfectant, and ensuring that input liquid was warmed to 37°C. If necessary, an intraoperative heater and warm air were to be used to guarantee that the oropharyngeal temperature during surgery was maintained at 35.5~36.5°C.

After surgery, the patients received postoperative nutritional support by administering nasal feeding through a gastric tube. This process began within 24 hours after surgery, and the gastric tube was withdrawn before each nasal feeding. Initially, a 5% glucose solution was pumped at a constant rate of 2mL per kg every 3 hours for 2 hours. On the second day, whole milk is pumped in at the same steady rate for 2 hours, followed by an increase of 2mL per kg every 3 hours each day until the sixth day when the gastric tube is removed, and oral feeding is initiated.

A collaborative discussion involving multiple disciplines involved deciding when to perform the surgery and which surgical method to use. Measures were taken to keep the patient warm during the operation to prevent intraoperative hypothermia. The surgical plan was designed to minimize the length of the surgery and anesthesia, decrease the time the patient needed to have a catheter after the surgery, enable early feeding through the mouth, and provide suitable analgesia and sedation. The control group followed traditional perioperative management practices.

Outcome Measures

Perioperative Indicators. For both groups, the researchers recorded the duration of the operation, the amount of bleeding during surgery, how long intravenous nutrition was maintained, the length of hospital stay, the cost of hospitalization, the rate of postoperative complications, and the readmission rate within 30 days after discharge.

Post-Operative Pain. The pain level of children in both groups was assessed using the Modified Faces, Legs, Activity, Cry, and Consolability Scale (FLACC) at 2, 12, 24, and 48 hours after the operation. The scale ranged from 0-1 for no pain, 1-3 for mild pain, 4-6 for moderate pain, and 7-10 for severe pain. A higher score indicated a more severe level of pain.

Stress Response. The stress response of the 2 groups of children was evaluated by comparing the levels of cortisol and C-peptide before and after surgery. Blood samples were taken from the children one day before the operation and 24 hours after and then centrifuged at high speed to separate the supernatant. The levels of serum cortisol and C-peptide were measured using radioimmunoprecipitation.

Inflammation and Nutrition Status. To compare the inflammation response between 2 groups of children, the high-sensitivity C-reactive protein (hs-CRP) and interleukin (IL)-6 levels were recorded before and after surgery. Additionally, the nutritional status of the children was evaluated by measuring their albumin levels. Venous blood samples (4ml) were collected from the children 2 days before surgery and 24 hours after surgery. The samples were then centrifuged at high speed to obtain the supernatant. The levels of IL-6 in the serum were measured using electrochemiluminescence, while the levels of hs-CRP in the plasma were measured using immunoturbidimetry. The serum albumin levels were measured using the bromocresol green test.

Statistical Analysis

The data from the study was analyzed using SPSS 20.0 software for organization and statistical analysis. Measurement data were expressed as mean ± standard deviation (Mean±SD) and examined using the t-test. Count data were expressed as n (%) and analyzed using the chi-square test. Any differences with a significance level of $P < .05$ were considered statistically significant.

RESULTS

Patient Characteristics

The 2 groups did not differ in the basic clinical profiles ($P > .05$) (Table 1).

Disease Composition

The observation group consisted of 4 instances of abdominal cleft, 2 cases of sacrococcygeal teratoma, 6 instances of esophageal atresia, 6 instances of diaphragmatic hernia, and 12 instances of intestinal atresia. On the other hand, the control group had 3 cases of abdominal cleft, 1 instance of sacrococcygeal teratoma, 5 instances of esophageal atresia, 5 cases of diaphragmatic hernia, and 16 instances of intestinal atresia. The variation in the distribution of diseases between the 2 groups did reach the level of statistical standard ($P > .05$) (Table 2).

Perioperative Indicators

Neither group recorded any deaths during surgery or after. There were no notable variances in operating time and intraoperative bleeding ($P > .05$). Implementing the ERAS protocol resulted in a significantly shorter duration of intravenous nutrition maintenance, reduced hospital stay, and lower costs compared to the standard management approach ($P < .05$) (Table 3).

Postoperative Complications and Readmission

After their surgeries, both groups of children were monitored for 3 months. The observation group had 3 cases of complications: one incidence of incisional infection after sacrococcygeal teratoma, one case of pulmonary infection after intestinal atresia, and one case of gastroesophageal reflux after esophageal atresia. In the control group, there were also 3 cases of complications: one case of adhesive intestinal obstruction after multiple intestinal atresia, one case of inflammatory intestinal obstruction after abdominal cleft, one case of anastomotic leak after esophageal atresia, and one case of gastroesophageal reflux after diaphragmatic hernia. These complications were successfully treated with symptomatic measures, and the patients were discharged. However, one patient from the control group experienced intestinal atresia, developed intestinal obstruction after discharge, and had to be readmitted to the hospital. The patient was eventually healed through fasting and intravenous nutritional management (Table 4).

Table 1. Patient Characteristics

Group	n	Sex (Male/Female)	Gestational age (weeks)	Birth weight (kg)
Observation group	30	19/11	38.40±1.59	2.91±0.35
Control group	30	20/10	38.28±1.34	2.89±0.41
t/χ^2	-	0.073	1.374	0.663
P value	-	0.787	0.093	0.271

Table 2. Disease Composition (n)

Group	Observation group	Control group	χ^2	*P* value
n	30	30	1.229	.873
Abdominal cleft	4	3		
Sacrococcygeal teratoma	2	1		
Esophageal atresia	6	5		
Diaphragmatic hernia	6	5		
Intestinal atresia	12	16		

Table 3. Perioperative Indicators (±s)

Group	Observation group	Control group	*t*	*P* value
n	30	30		
Operative time (min)	127.6±23.7	131.5±30.4	0.568	.401
Intraoperative bleeding (ml)	9.75±3.98	11.23±4.15	0.028	.992
Intravenous nutrition (d)	7.87±1.24	10.45±1.98	13.84	<.001
Hospital stays (d)	18.15±3.78	23.54±5.70	6.896	<.001
Hospitalization costs (Thousand yuan)	32.8±5.7	40.3±6.5	5.075	<.001

Table 4. Postoperative Complications and Readmission (n)

Group	n	Postoperative complications	Readmission
Observation group	30	3	0
Control group	30	4	1
χ^2	-	0.162	1.017
P value	-	.688	.313

Table 5. Postoperative Pain (±s)

Group	n	2h	12h	24h	48h
Observation group	30	2.83±0.84	2.33±0.85	1.52±0.79	1.26±0.64
Control group	30	4.22±1.51	3.47±1.26	2.48±1.18	1.34±0.72
t	-	4.406	4.108	3.703	0.455
P value	-	<.001	<.001	<.001	.651

Table 6. Stress Response (±s)

Group		Observation group	Control group	*t*	*P* value
n		30	30		-
Cortisol (ng/mL)	Preoperative	154.26±21.21	149.36±26.87	0.784	.436
	Postoperative	271.11±48.16	302.25±56.39	3.039	.004
C-peptide (mg/mL)	Preoperative	0.77±0.23	0.74±0.19	0.551	.584
	Postoperative	1.19±0.31	1.24±0.29	2.901	.005

Postoperative Pain

The utilization of ERAS management led to a notable decrease in Modified FLACC scores compared to routine management at 2, 12, and 24 hours following surgery ($P < .05$). However, this discrepancy became insignificant after 48 hours ($P > .05$) (Table 5).

Stress Response

All patients showed markedly increased levels of cortisol and C-peptide after interventions, with lower levels observed in the observation group ($P < .05$) (Table 6). The observation

Table 7. Blood Indicators for Stress Response (±s)

Group		Observation group	Control group	*t*	*P* value
n		30	30	-	-
hs-CRP (mg/L)	Preoperative	1.86±5.19	1.94±4.26	0.065	.948
	Postoperative	5.32±4.77	4.52±3.94	2.833	.06
IL-6 (pg/mL)	Preoperative	6.14±1.82	5.93±1.58	0.477	.635
	Postoperative	15.62±9.57	32.45±17.38	4.646	<.001
Albumin (g/L)	Preoperative	34.35±2.29	33.42±3.25	1.281	.205
	Postoperative	26.45±2.24	25.86±3.41	0.792	.431

group showed lower cortisol and C-peptide levels, indicating the potential benefit of ERAS management in reducing the surgical stress response and promoting recovery.

Inflammation and Nutrition Status

After the interventions, it was observed that all study participants showed significant increases in hs-CRP and IL-6 levels while experiencing reduced serum albumin levels. The observation group, however, showed lower levels of serum IL-6 compared to the other group ($P < .05$). There were no significant differences between the groups in terms of serum hs-CRP and albumin levels following the interventions ($P >$ .05) (Table 7).

DISCUSSION

Structural malformations present from birth are the most prevalent birth defects in China. They have a complex etiology and significantly impact the survival and development of children, leading to high rates of mortality and disability in children.[9,10] The use of fetal diagnosis can help reduce the risk of complications during delivery, facilitate appropriate postnatal interventions, improve treatment outcomes, and alleviate parental anxiety and depression.[11,12] The effectiveness of surgical management for fetal structural malformations depends on factors such as gestational age, diagnostic accuracy, fetal anomalies, the support of the child's family, and medical and economic conditions.[13] However, prenatal diagnosis can sometimes yield false positive or negative results. Therefore, there is an urgent need to improve the management of fetal congenital disorders.[14]

The procedure conducted in the delivery room involves performing surgery on fetal diseases after birth without posing any risks to the mother's health. It offers effective management of malformations in children.[15] This model eliminates transferring the patient to an operating room. Instead, pediatric surgeons, supported by anesthesiologists, promptly intervene after the cesarean section to correct any deformities in the child.

Extensive research has demonstrated that early diagnosis and treatment of gastrointestinal malformations significantly improve patient prognosis. The salient advantages of early intervention for correcting neonatal malformations without leaving the delivery room after birth[16] include (a) avoiding the need for transferring the patient to an operating theater, which reduces the risk of infection and lowers mortality rates, (b) reducing gas in the gastrointestinal tract, facilitating perioperative preparation and an uneventful surgery, (c) addressing the root cause of the disease, leading to disease control and a higher quality of life, (d) early correction of malformations, alleviating the mental distress experienced by parents and families, and (e) shorter hospital stays and lower medical costs, resulting in maximum efficiency.

Due to variations in administrative structures, certain institutions continue to perform prenatal diagnosis within their obstetrics department while consultations are conducted in the pediatric surgery department. However, this approach necessitates frequent communication between different departments. For instance, the pediatric surgeon must provide feedback to the obstetrician on the diagnosis and corresponding management. This enables the obstetrician to gain a comprehensive understanding of the treatment progress for severe structural malformations and the prognosis of the fetus, ultimately reducing perinatal mortality rates.

The MDT model involves the neonatal surgeon taking the lead, with input from departments such as obstetrics and gynecology, anesthesiology, neonatology, and ultrasound. The goal is to develop the most appropriate management protocol for the child. In this model, neonatal surgeons actively participate in prenatal diagnosis and evaluate fetuses, bridging the gap in understanding fetal surgical diseases within obstetrics. This allows for scientific prenatal diagnosis and evaluation, the development of reasonable treatment plans, and an improvement in the survival rate for children with neonatal structural malformations.[17]

ERAS originated from the clinical advancement of MDT diagnosis and treatment and was discovered to enhance postoperative recovery in pediatric patients.[18] In the present study, MDT intervention was implemented for 15 cases of neonatal congenital malformations. Following ultrasound diagnosis, the researchers' prenatal MDT provided expert medical guidance to the parents, enabling them to comprehend accurately the disease risks, post-birth disease progression, risks associated with corrective surgery for malformations, complications, and long-term prognosis. Abdominal cleft is a severe developmental malformation of the abdominal wall in newborns, with an incidence rate of 2/10 000-3/10 000. Research has indicated that early emergency abdominal cleft repair after birth can enhance the success rate of one-stage operations and decrease the risk of postoperative infections.[19]

The present study summarizes experiences in treating children with diaphragmatic hernias. Furthermore, it successfully performed obstetric surgery on 4 children with diaphragmatic hernia using the MDT model. The study also implemented ERAS during the perioperative period, resulting in satisfactory outcomes.[20]

Neonatal diaphragmatic hernia is a common congenital diaphragm defect with an incidence of 1/5000-1/20000. It is considered one of the surgical emergencies in newborns due to its rapid progression and high morbidity and mortality rates.[21] Children with congenital diaphragmatic hernia often experience concomitant pulmonary dysplasia and pulmonary hypertension. In severe cases, respiratory support may be required after birth. Protective tracheal intubation has been shown to improve the prognosis for these children.[22] In the observation group of this study, there were 6 children with diaphragmatic hernia. One child with severe diaphragmatic hernia underwent ex utero intrapartum treatment and was subsequently transferred to a neonatal intensive care unit once their airway was established. All 6 cases underwent thoracoscopic diaphragmatic hernia surgery within 48 hours and were assigned to the neonatal intensive care unit for continued respiratory support after surgery and were discharged successfully.

Small intestine atresia is a common developmental abnormality of the gastrointestinal tract in neonatal surgery, occurring in approximately 1 in 5000 cases.[23] The diagnosis of small intestine atresia is typically suspected through ultrasonography during the later stages of pregnancy and confirmed through clinical examination after birth. It has been reported that children with prenatal diagnoses experience improved therapeutic outcomes and prognosis.[24] In this study, the observation group consisted of 12 children with small bowel atresia who underwent surgery using an MDT approach. The surgical procedure resulted in a short operative time, reduced postoperative hospital stay, and a low rate of postoperative complications. Only one child in the group developed a postoperative pulmonary infection, but it was successfully treated with anti-infection therapy.

Congenital esophageal atresia is a common abnormality in the gastrointestinal tract in newborns, with an incidence rate of 1 in every 3500 cases and an unknown cause.[25] It has long posed challenges in neonatal surgery. Transoral feeding of children with esophageal atresia is highly prone to mis-aspiration, leading to aspiration pneumonia and affecting the prognosis of the infants. In the present study, 6 cases of esophageal atresia were highly suspected based on prenatal ultrasound and diagnosed by esophagogram after birth.[26] The proximal esophagus was decompressed through continuous suction, followed by thoracoscopic end-to-end esophageal anastomosis and ligation of the esophagotracheal fistula. All 6 cases exhibited promising recovery with short-term postoperative ventilator treatment. One child with esophageal atresia developed postoperative gastroesophageal reflux, which was relieved with feeding correction and medication.

Sacrococcygeal teratoma is a common fetal tumor, with 80% of cases being benign.[27] Children diagnosed early have a long-term survival rate of up to 92-95% after birth.[28] This highlights the importance of early detection in improving patient prognosis. The MDT model, which involves prenatal diagnosis and postnatal treatment of fetal tumors, helps to decrease the anxiety of pregnant women and their families. It has proven a practical approach to providing successful treatment.[29] In this study, 2 children with teratoma in the observation group received MDT intervention following the ERAS program and experienced satisfactory recovery. One child did develop a superficial incisional infection after surgery, but it healed completely with proper medication and rest. Overall, the family expressed high levels of satisfaction.

Surgical operations are the leading cause of stress and inflammation, for which ERAS aims to reduce the perioperative stress response significantly. Cortisol and C-peptide are markers for stress hormones, with cortisol primarily secreted by the adrenal cortex. When the body experiences a stress response, cortisol levels in the blood rise, impacting the glycemic effect and leading to increased C-peptide secretion.

CRP is a protein the liver produces in response to various injuries or inflammation and tissue damage. IL-6, on the other hand, is an early indicator of systemic inflammation and tissue damage. The levels of these 2 markers in the blood are positively associated with surgical trauma and the resulting damage.[30] In the observation group, the serum concentrations of cortisol and C-peptide were significantly lower compared to the control group. This suggests that following the ERAS protocols, multimodal analgesic anesthetic management can effectively reduce the surgical stress response in neonates. Although not statistically significant, the observation group showed slightly elevated levels of hs-CRP and IL-6. This could be attributed to postoperative infections, such as incisional infection after sacrococcygeal teratoma surgery or pulmonary infections following intestinal atresia.

When these infections are appropriately managed and cured, they may cause a temporary increase in levels of inflammatory markers. It is important to note that these changes in inflammatory markers are likely a response to the stress of surgery and the recovery process rather than indicators of other pathological conditions. The observation group showed lower FLASS pain scores at 2, 12, and 24 hours after surgery than the control group, indicating that pain management guided by the ERAS program provided more pain alleviation. Additionally, the observation group had shorter hospital stays and lower costs compared to the control group, highlighting the superior treatment outcomes and cost-effectiveness associated with the ERAS approach. It is worth noting that ERAS is an advanced care concept that does not require additional treatment measures but aims to reduce unnecessary medical and pharmacological interventions.[31]

The advancement of medicine should transition from relying on personal experiences to adopting evidence-based practices guided by empirical evidence and offering patients the best possible care. The detection and treatment of birth defects in newborns began relatively recently in China. This highlights the significance of conducting clinical studies and treatment at multiple centers to develop early detection methods, establish standardized treatment guidelines, and explore new surgical techniques and improved supportive therapies. These endeavors will yield valuable insights for shaping health and economic policies concerning such diseases in China. However, it is crucial to acknowledge that the current study had limitations due to its small sample size and short-term follow-up. Therefore, future investigations are necessary to validate these findings.

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