Delivery room surgery: an applicable therapeutic strategy for gastroschisis in developing countries

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Background: **The survival rate of infants with gastroschisis has improved significantly. It is over 90% in developed countries, but 50% in developing countries. This study aimed to investigate the factors improving the survival rate of infants with gastroschisis in developing countries.**

Methods: **Neonates meeting the inclusion criteria, who presented to our center since the establishment of delivery room surgery, were enrolled into this retrospective study. Data were evaluated specifically to determine the role of delivery room surgery in reducing the mortality and morbidity of infants with gastroschisis and to identify factors optimizing the conditions of outborn infants.**

Results: **A total of 64 infants were identified. The overall survival rate of the infants was 60.9%. The survival rate of infants in inborns was 76.5%, and the survival rate of infants in outborns was 43.3%. Infants of the outborn group took more time to reach full enteral feeding, and were more likely to require a prolonged stay in hospital when compared with those of the inborn group. Logistic analysis identified that the surgical technique, the presence of sepsis and intestinal necrosis could be expected to influence the outcome of gastroschisis.**

Conclusions: **The strategy of delivery of patients in a center prepared to perform delivery room closure of gastroschisis appears to improve the survival of patients with gastroschisis. Further reduction in mortality rates will depend on improved conditions of outborn infants.**

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Original article

Introduction

Gastroschisis is one of the most common birth defects in pediatric surgery, and the birth prevalence of gastroschisis has increased steadily throughout the world. The condition now occurs in about 5 per 10 000 live births.[1] Advance in neonatal intensive care, parenteral nutrition, and the evolution of surgical strategies have reduced infant mortality rates for gastroschisis from 60% in the 1960s to 3%-10% in the mid 1990s.[2,3] In developing countries, despite the availability of neonatal intensive care and parenteral nutrition, mortality from gastroschisis remains high, and the condition is associated with significant morbidity resulting in high treatment costs because of prolonged need for neonatal intensive care, hospitalization, and parenteral nutrition.[4]

Coughlin et al[5] reported that early management of gastroschisis was associated with a better outcome, measured by time to extubation, time to total enteral feeding, and length of hospital stay. Based on Coughlin's study, our center set up a special team of delivery room surgery in 2000, consisting of pediatric surgeons, neonatologists, and obstetricians. In the present study we evaluated the effect of delivery room surgery on the outcome of gastroschisis and identified factors contributing to the morbidity and mortality. However, in developing countries, due to limited resources available, delivery room surgery is not always possible. The defect may not be diagnosed prenatally, the infant may be delivered ahead of schedule, or a pediatric surgical team may not be available at the place of delivery. Thus, we also investigated factors to optimize the condition of these infants, hoping to improve the survival rate of gastroschisis in developing countries.

Methods

Patients and data collection

This study was carried out at a tertiary center of pediatric surgery, where delivery room surgery had been performed routinely since 2000. The study protocol was approved by the Ethics Committee of our institution.

From January 2000 through June 2012, we retrospectively reviewed the medical records of all newborns with gastroschisis who were born at our center (inborn group) and all newborns with gastroschisis who were born elsewhere and transferred to our center (outborn group). We collected data on maternal age, gestational age, mode of delivery, birth weight, gender, presence of associated anomalies, size of defect, condition of eviscerated bowel, delivery-management interval, and surgical management approach (primary or staged closure). Patients in both inborn and outborn groups were investigated in prespecified subgroups by a novel scoring tool, gastroschisis prognostic score (GPS, the Canadian Pediatric Surgery Network).[6] We looked at outcomes in patients of the inborn group, outborn group, simple gastroschisis subgroup (defined as infants with a GPS less than 4), and complicated gastroschisis subgroup (defined as infants with a GPS of 4 or more). The outcomes included the length of ventilation, duration of total parental nutrition (PN), length of stay (LOS), rates of intestinal failure, and intestinal failure associated liver disease (IFALD), episodes of sepsis, occurrence of short bowel syndrome, occurrence of necrotizing enterocolitis, unplanned reoperation, and survival rate. Furthermore, patients' laboratory data at admission, such as arterial blood gas, liver function, kidney function, blood coagulation function, and complete blood count, were also collected.

Definitions

The GPS is an easy, efficient, reproducible, robust and sensitive method for outcome prediction in neonates with gastroschisis that can be completed at the bedside without the need for monitoring or laboratory data. The score's component variables included the following: (a) bowel matting (none, 0; mild, 1; or severe, 2); (b) bowel necrosis (absent, 0; focal, 1; or diffuse, 2); (c) bowel atresia (absent, 0; suspected, 1; or present, 2), and (d) bowel perforation (absent, 0; or present, 2). A composite score of 4 or more identifies a high risk of adverse outcome (including mortality).[6] Here, we separated patients and stratified outcome results based on the detailed prognostic scale of the Canadian Pediatric Surgery Network.[6] For the purposes of this study, we defined intestinal failure as a requirement for more than 28 days of parenteral nutrition; sepsis as any positive culture that required antibiotic treatment; intestinal failure associated liver disease as liver dysfunction (cholestasis in association with raised serum alkaline phosphatase and total bilirubin concentrations) in infants receiving parenteral nutrition; and short bowel syndrome as small bowel length less than 75 cm for term neonates or less than 50 cm for premature neonates or dependence on parenteral nutrition for longer than 42 days.[7]

Treatment protocol

The patients of the inborn group were diagnosed with gastroschisis before birth by prenatal ultrasonography and delivered via elective caesarian section at our center. The delivery was attended by a delivery room surgery team, which included an obstetrician and fellow, a pediatric surgeon and fellow, a neonatologist, a pediatric anesthesiologist, and nurses. On delivery, the newborn was placed in an overhead warmer. Intravenous access was established and resuscitation initiated. A nasogastric tube was passed and placed to low intermittent suction. A pediatric surgeon and a neonatologist evaluated the baby together and ascertained whether the herniated organs can be reduced immediately. If complete reduction was not possible, a spring loaded silo was placed without general anesthesia. If complete reduction was deemed safe, the herniated organs were covered with moist warm gauze and the baby was transferred to the operating room directly adjacent to the delivery room. Then the baby was intubated and general anesthesia was provided. Temperature, electrocardiograph, blood pressure, and oxygen saturation were monitored. The operation proceeded with reduction and primary fascial closure. After surgical management, the baby was transferred to the neonatal intensive care unit (NICU).

All the patients of the outborn group were delivered at other hospitals and transferred to our center for treatment. If complete reduction was deemed safe, the patients were moved to the operation room for primary reduction. If complete reduction was not possible, the patients were managed in a standard fashion by placing spring loaded silos at the bedside in the NICU. When these patients were stable and most of the viscera could be replaced into the abdominal cavity, delayed fascial repair was performed. During the study period, other aspects of care were similar in both subgroups.

Statistical analysis

From the database, SPSS 10.0 was used for statistical analysis. Comparisons between unpaired groups with respect to continuous variables were performed with Student's *t* test. For the comparison of small numbers of patients, Fisher's exact test was used. Logistic and linear regression analysis was also performed. *P* values less than 0.05 were considered statistically significant.

Results

From January 2000 through June 2012, 69 newborns

with gastroschisis were admitted to our center. In the 69 patients, 5 were excluded because they were not treated for economic reasons. Of the remaining 64 patients, 34 were included in an inborn group and 30 in an outborn group. Of the 34 patients included in the inborn group, 13 had a GPS of 4 or more (complicated gastroschisis subgroup), 21 had a GPS less than 4 (simple gastroschisis subgroup). Of the 30 patients included in the outborn subgroup, 18 had a GPS of 4 or more, and 12 had a GPS less than 4. Demographic and clinical characteristics are listed in Table 1. There was no difference in the mean maternal age, male to female ratio, size of defect, associated anomalies between newborns in the inborn group or the outborn group. There were significant differences between the two groups in the mode of delivery, gestational age, birth weight, condition of eviscerated bowel, delivery-management interval and initial surgical approach. The outcomes of infants between the two groups are shown in Table 2, and those of infants with simple and complicated gastroschisis in Table 3. Infants in the outborn group (both simple and complicated subgroups) took more time to reach full enteral feeding, and were more likely to require a prolonged hospital stay when compared with those in the inborn group. Moreover, the patients in the outborn group had a higher risk to develop intestinal failure, IFALD, sepsis, short bowel syndrome, necrotizing enterocolitis, and were more likely to require unplanned operation.

Logistic analysis revealed that the surgical technique (OR=18.31, 95% CI=9.46-128.73), the presence of intestinal necrosis (OR=12.46, 95% CI=5.32-89.84) and sepsis (OR=10.33, 95% CI=2.32-76.68) could influence the outcome of gastroschisis as measured by mortality, LOS, and duration of PN.

Ninety percent of the patients (27/30) in the outborn group showed lower serum protein concentrations. The mean serum total protein level was 44.1 g/L, and the mean serum albumin level 26.3 g/L. In contrast, the level of serum protein concentrations in the patients of the inborn group was nearly normal. The mean serum total protein level was 58.5 g/L, and the mean serum albumin level 33.4 g/L.

The overall survival rate of the patients was 60.9%. The survival rate in the inborn group was 76.5% (85.7% for simple subgroup and 61.5% for complicated subgroup), and that in the outborn group was 43.3% (58.3% for simple subgroup and 33.3% for complicated subgroup). The survival rate was significantly higher in the inborn group (both simple and complicated subgroups) than in outborn group (P<0.05). Causes of death are summarized in Table 4.

Table 1. Demographic and clinical data for both groups and for all of the newborns included in the study

Variables	Inborns group (n=34)	Outborns group (n=30)	P value
Maternal age (y)*	25.8±5.2	25.4±3.7	0.83
Mode of delivery (n)			<0.01
Cesarean	34	16	
Vaginal	0	14	
Gestational age (wk)*	38.2±0.9	36.4±1.0	0.04
Birth weight (g)*	2765.1±224.7	2333.3±198.1	0.03
M/F ratio	15/19	14/16	0.12
Size of defect (cm)*	3.3±1.0	3.5±1.1	0.55
Initial surgical management (n)			<0.01
Primary closure	23	4	
Staged repair	11	26	
Delivery-management interval (h)*	0	17.8±9.1	<0.01

*: Data presented as mean±standard deviation. F: female; M: male.

Table 2. Outcomes for both groups and for all of the newborns included in the study

Variables	Inborns group (n=34)	Outborns group (n=30)	P value
Mean time on TPN (d)*	13.1±6.6	29.4±8.2	0.01
Mean length of hospital stay (d)*	21.4±10.8	46.3±15.6	0.02
Mean time to extubation (d)*	3.9±3.3	5.6±4.9	0.55
Survival (%)	76.5%	43.3%	0.02
Postoperative complications (n, %)			<0.01
Intestinal failure	2 (5.9%)	10 (33.3%)	
IFALD	5 (14.7%)	16 (53.3%)	
Sepsis	15 (44.1%)	22 (73.3%)	
Short bowel syndrome	2 (5.9%)	7 (23.3%)	
Necrotizing enterocolitis	2 (5.9%)	7 (23.3%)	
Abdominal compartment syndrome	0 (0%)	2 (6.7%)	
Jejunocutaneous fistula	0 (0%)	3 (10.0%)	
Required unplanned operation (n)	0	9	<0.01

*: Data presented as mean±standard deviation. IFALD: intestinal failure associated liver disease; TPN: total parenteral nutrition.

Table 3. Outcomes for infants with simple and complicated gastroschisis

Variables	Inborns group	Outborns group	P value
GPS<4	n=21	n=12	
Mean time on TPN (d)*	7.9±1.8	16.4±2.6	0.02
Mean length of hospital stay (d)*	14.7±3.4	21.6±5.3	0.04
Survival (%)	85.7%	58.3%	0.02
GPS≥4	n=13	n=18	
Mean time on TPN (d)*	21.4±4.6	32.3±7.2	0.03
Mean length of hospital stay (d)*	29.6±6.2	57.7±10.4	<0.01
Survival (%)	58.3%	33.3%	<0.01

*: Data presented as mean±standard deviation. GPS: gastroschisis prognostic score.

Table 4. Causes of death of newborns with gastroschisis

Variables	Inborns group (n=34)	Outborns group (n=30)	Total (n=64)
Mortality	23.5%	56.7%	39.1%
Causes of death			
Sepsis	6 (17.6.%)	6 (20.0%)	12 (18.8%)
Intestinal necrosis	2 (5.9%)	6 (20.0%)	8 (12.5%)
ACS	0 (0.0%)	2 (6.7%)	2 (3.1%)
Hypothermic	0 (0.0%)	1 (3.3%)	1 (1.6%)
Intraventricular hemorrhage	0 (0.0%)	1 (3.3%)	1 (1.6%)
Asphyxia	0 (0.0%)	1 (3.3%)	1 (1.6%)

ACS: abdominal compartment syndrome.

Discussion

Despite the survival rate of above 90% for neonates with gastroschisis in developed countries, the mortality in China is still very high. With the communication and cooperation of obstetricians, neonatologists, pediatric surgeons, pediatric anesthesiologists, and nurses, the survival rate of patients in the inborn group was much better that that reported in other developing countries.[4] Moreover, when data of simple gastroschisis subgroups and complicated gastroschisis subgroups were analyzed and compared respectively, both simple and complicated subgroups in the outborn group demonstrated a high risk of adverse outcome (including mortality). The findings may reflect the role of delivery room surgery in reducing the mortality and morbidity of patients with gastroschisis.

Compared with developed countries, the survival of patients with gastroschisis has improved, but their mortality rate remains high. In our series, when the database was analyzed for factors associated with poor outcome, surgical technique, sepsis and intestinal necrosis were significant. In developed countries, sepsis is not a major determinant of infant mortality from gastroschisis.[8,9] In our study, however, the presence of sepsis was the most important factor for prognosis after surgical technique. The incidence of sepsis was 44.1% (15/34) in the inborn group and 73.3% (22/30) in the outborn group, which could explain the reason why the mortality even in the inborn group was high. Among the causes of sepsis in the inborn group, ventilator associated pneumonia and catheter associated blood stream infections were the most prominent contributing factors. Furthermore, cross infection was also an important contributing factor. In developing countries, hospital-acquired infection is relatively common because of old medical technology, numerous patients and limited space. Thus, it is very important to provide adequate space in ICU wards and ensure reasonable shunt for severe patients.

It has been suggested that time to surgical management maybe the most significant factor to determine the mortality and morbidity.[10] In our study, the average duration of all patients in the outborn group was about 17.8 hours (range: 2-48 hours). For the 17 patients who died in the outborn group, the mean duration was 29.6 hours. Although the numbers involved are small, the disappointed results on the outborn group could stimulate better antenatal care and referral patterns. In developed countries, antenatal diagnosis is the norm and more than 90% of mothers are referred antenatally for delivery at the tertiary center with available pediatric surgeons. In developing countries, however, mothers infrequently attend antenatal care and usually give birth at regional maternity hospitals which are lack of pediatric surgeons; furthernore, the number of pediatric surgeons is small all over the countries, and they work only in a small proportion of hospitals in the urban area. Therefore, if suitable conditions are available, neonates with antenatally diagnosed gastroschisis should be born in a pediatric surgical center, addressing the fashion of delivery room surgery. If condition does not permit, education of physicians in outlying areas how to stabilize and package these infants for secure transport to other facilities is vitally important. Unfortunately, in developing countries, neonatal transportation is rarely considered a healthcare priority and is generally under-funded and inefficient;[11] therefore, we strongly appeal that government should consider establishing critical neonatal emergency transport system as soon as possible, and training more pediatric surgeons for the shortage. On the other hand, with regarding to the causes of sepsis in outborn infants, infections during transfer could not be overlooked. Thus, training physicians in outlying areas to start antibiotics before transfer is a good way to reduce the incidence of sepsis in outborn infants.

We also found that 90% of outborn infants had lower serum protein concentrations. Lower levels of serum protein could lead to reduced colloid osmotic pressure in the plasma, and consequent leak of liquid to the interstitium and anasarca. This phenomenon may involve the lungs and ventilator mechanics, resulting in prolonged days on mechanical ventilation. Given that endotracheal tube is one of the main sources of infection, we could explain the significant difference in incidence of sepsis between outborn infants and inborn infants. Fortunately, a preformed silo is very easy to place and would prevent a lot of the water loss and protein loss in these infants during prolonged transports.

There is controversy over how herniated bowel should be managed. Although the mode of closure was not correlated with mortality,[12] primary closure is considered the ideal closure technique for its association with less parenteral nutritional use and a shorter length of hospital stay.[13-15] However, the goal of surgery for neonates with gastroschisis is to safely reduce the evisceration and close the defect. The management approach should be based on the appearance of the intestine, size of the abdominal wall defect, and hemodynamic status. In our center, silo bag would be advocated when any risk of viscero-abdominal disproportion or intestinal compromise is suspected. As a result, secondary closure was performed in complicated cases or in neonates with inadequate abdominal space.

Another controversy over the management of patients with gastroschisis is the ideal gestational age of delivery. Previous studies[16,17] showed that gastrointestinal dysfunction in patients with gastroschisis was caused by the prolonged exposure of eviscerated bowel to amniotic fluid. As a result, elective preterm delivery was advocated. However, recent studies[18,19] revealed that preterm delivery in

gastroschisis had high morbidities, such as prolonged hospital stay and delayed full feeding, and the term delivery was likely to minimize the morbidity. In their opinion, the intestinal dysfunction and the need for long periods of PN result from delayed maturation of the enteric nervus plexus other than the prolonged exposure of eviscerated bowel to amniotic fluid. Thus it is not benefitial to perform preterm cesarean section in the treatment of patients with gastroschisis while reducing the incidence of gastrointestinal dysfunction. According to these studies, the obstetric policy in our center has been elective cesarean delivery after 37 weeks of gestation. Except for 6 neonates who underwent emergency cesarean delivery before 37 weeks of gestation because of fetal distress, all neonates in the inborn group followed this obstetric policy.

In conclusion, we want to emphasize that the strategy of delivery room surgery should not be limited to the delivery room operation alone, but rather a collection of prenatal care, avoidance of the stress and risk of transfer, the controlled delivery and early, definitive care by a dedicated team of specialists. As we recognized that improvements were needed for the outborn group, we would like to refine a brief protocol for training local physicians and general surgeons how to stabilize and package infants with gastroschisis: 1) The eviscerated bowel should be covered with plastic (silo bag), and should be supported over the abdomen to minimize vascular occlusion; 2) Intravenous access should be established and fluid resuscitation should be initiated; 3) A nasogastric tube should be inserted and placed to lower intermittent suction; 4) Antibiotics should be administered; 5) It is necessary to contact a pediatric surgeon in the referral center, and make sure that all the required neonatal and pediatric surgery preparation have been done; 6) The infant should be transferred with monitoring of temperature, electrocardiogram, blood pressure, and oxygen saturation.

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