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ORIGINAL ARTICLE

Meconium aspiration syndrome requiring ECMO in newborns with gastroschisis: incidence and surgical outcomes

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Abstract

Aim of the study To evaluate the incidence of respiratory failure requiring ECMO in newborns with gastroschisis (GC), compare it to the incidence in the general population, review the surgical outcomes of newborns with GC requiring ECMO and compare them to newborns with GC not requiring ECMO.

Methods This is a retrospective review of all neonatal admissions for GC from December 2010 to September 2015.

Main results 110 newborns with GC were admitted to our NICU between 12/2010 and 9/2015; 36 were term. Four cases, all term, all prenatally diagnosed, all outborn, developed respiratory failure requiring ECMO secondary to meconium aspiration syndrome (MAS). This 11% (4/36 term GC) represents a 300-fold increase in the incidence of MAS-associated respiratory failure requiring ECMO compared to the general population of term newborns (0.037%). Median time on ECMO was 12 (9–20) days. The time to achieve full enteral feedings in the GC/ECMO group was twice the time of the 106 newborns in the GC/non-ECMO group [median: 70 (48–77) vs. 35 (16–270) days, respectively]. Time to hospital discharge was three times longer in the GC/ECMO group compared to the GC/non-ECMO group (median: 42 [20–282] versus 125 [69–223] days, respectively). All patients survived.

Conclusion The incidence of respiratory failure requiring ECMO is remarkably higher in patients with GC than in the general population and much higher in the subgroup of term GC. While infrequent, the possibility of this event supports the concept that fetuses with GC benefit from being delivered at tertiary centers with immediate pediatric surgery and ECMO capabilities.

Keywords Gastroschisis · Respiratory failure · Meconium aspiration syndrome · Extracorporeal membrane oxygenation

Introduction

Patients with gastroschisis (GC) can develop a variety of complications, both in utero and after birth. The most common complications are related to the gastrointestinal tract (e.g., intestinal necrosis), the closure of the abdominal wall (e.g., dehiscence, compartment syndrome), and the presence of central lines for parenteral nutrition [1]. Respiratory failure is a less commonly observed complication but can occur due to a variety of reasons and can range in severity from mild to life threatening [2]. Meconium aspiration syndrome (MAS) is a relatively common condition defined as respiratory insufficiency in newborns born through meconium-stained amniotic fluid whose symptoms cannot be otherwise explained. MAS occurs mainly in term and post-term neonates with an incidence of approximately 4.6% in term newborns in the general population, and even though it can be life threatening, the need for extracorporeal membrane oxygenation (ECMO) is remarkably infrequent [3, 4]. In this article, we present a series of patients with prenatal diagnosis of GC who developed severe respiratory insufficiency at birth secondary to MAS and required ECMO. The aim of this report is twofold: (1) to compare the incidence of MAS-related respiratory failure requiring ECMO in newborns with GC versus the incidence in healthy newborns, and (2) to compare the surgical outcomes of newborns with GC requiring ECMO versus the outcomes of newborns with GC not requiring ECMO.

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Methods

After obtaining Institutional Review Board approval (IRB 17-013720) we conducted a retrospective review of all admissions to our neonatal intensive care unit (NICU) with a diagnosis of GC between December of 2010 and September of 2015. We divided the cohort of patients according to their gestational age at birth into preterm (< 37 weeks) and term (≥ 37 weeks). We identified all patients who developed respiratory insufficiency, identified the cause, and identified those who required ECMO. We compared the incidence of respiratory insufficiency requiring ECMO in our cohort of patients with GC to the incidence among newborns without GC but with the same respiratory pathology. We evaluated the surgical outcomes of all patients in the cohort and compared them between those of patients who required ECMO and patients who did not require ECMO. The following surgical outcomes were evaluated: time to initiation of enteral feedings, time to discontinuation of parenteral nutrition, time to achieve full enteral feedings, and time to hospital discharge.

Statistical significance was determined by *t* test and Chi-square test for means and proportions, respectively. Continuous data were reported as medians and ranges. A *p* value less than 0.05 was considered statistically significant.

Results

A total of 110 newborns with GC were admitted to our NICU between December of 2010 and September of 2015. All patients were diagnosed prenatally. The vast majority of the patients ($n = 98$; 89%) were born at our institution whereas only 12 patients (11%) were outborn. There were 74 patients born preterm and 36 patients born at term. Four patients in the cohort, all delivered at term and all outborn, developed respiratory failure requiring ECMO which was secondary to meconium aspiration syndrome (MAS) in all cases. These four patients represent 3.6% (4/110) of all patients with GC, and 11% (4/36) of all *term* patients with GC. The four patients who required ECMO were delivered vaginally and developed respiratory failure immediately after birth requiring endotracheal intubation in the delivery room. All patients underwent silo placement at birth, the silo was kept in place during the ECMO run, and after the ECMO run until the time of closure. ECMO was required within the first 12 h of life in three cases and on the 5th day of life in one case (Table 1). Two patients underwent veno-venous and two patients underwent veno-arterial ECMO cannulation. Median time on ECMO was 12 (9–20) days. The abdominal wall defect was closed 4, 6, 8 and 14 days after ECMO decannulation. One patient had colonic atresia. In the group of *term* patients with GC not requiring ECMO ($n = 32$, all inborn), five patient had mild transient respiratory distress requiring nasal cannula for 3–10 days, and four patients had moderate transient respiratory distress requiring mechanical ventilation for 1, 3, 3, and 10 days, respectively. Among these nine patients, only one patient was born through meconium-stained amniotic fluid (MSAF) and fulfilled the criteria for MAS. Additionally, in the group of *term* patients with GC not requiring ECMO, 18 patients were delivered vaginally versus 14 by cesarean section, and there were 21 silo placements and 11 primary reductions. One patient in this group had jejunal atresia and two patients developed one episode of medical necrotizing enterocolitis.

The median time to initiation of enteral feedings was 21 (6–180) days in the group of *all* GC/no-ECMO patients ($n = 106$), 17 (7–71) days in the group of *term* GC/non-ECMO patients ($n = 32$), and 45 (37–51) days in the group of GC/ECMO patients ($n = 4$); *p* value between the last two groups = 0.003 (Table 2). The median time to the discontinuation of parenteral nutrition was 35 (15–235) days in the group of *all* GC/non-ECMO patients, 29 (16–101)

Table 1 Demographic and outcome data of patients with gastroschisis (GC) who developed meconium aspiration syndrome and required ECMO

	Patient 1	Patient 2	Patient 3	Patient 4
Gestational age at birth	$37^{0/7}$ weeks	$38^{1/7}$ weeks	$38^{6/7}$ weeks	$37^{1/7}$ weeks
Prenatal diagnosis	Yes	Yes	Yes	Yes
Birth weight (g)	2500	3000	2500	2700
Delivery mode	Vaginal	Vaginal	Vaginal	Vaginal
Comorbidities	None	Colonic atresia	None	None
Time to ECMO cannulation*	< 12 h	< 12 h	5 days	< 12 h
Type of ECMO cannulation	V–A	V–V	V–V	V–A
Duration of ECMO	14 days	10 days	9 days	20 days
GC closure (days post-ECMO)	14	14	8	6
Age at discharge (days)	93	223	69	157
Survival	Yes	Yes	Yes	Yes

*The time to ECMO cannulation is counted from the time of birth

Table 2 Surgical outcomes of patients with gastroschisis (GC) according to gestational age at birth and need for ECMO

	GC patients without ECMO ($n=106$)	Term GC patients without ECMO ($n=32$)	GC patients with ECMO ($n=4$)	p*
Median age at initiation of enteral feedings (days)	21 (6–180)	17 (7–71)	45 (37–51)	0.003
Median age at discontinuation of PN (days)	35 (15–235)	29 (16–101)	51 (45–61)	0.04
Median time to achieve full enteral feeding (days)	35 (16–270)	29 (17–88)	70 (48–77)	0.004
Hospital stay (days)	42 (20–282)	33 (21–105)	125 (69–223)	0.0001
Neonatal survival rate	100%	100%	100%	–

PN parenteral nutrition

*p values compare groups 2 and 3

days in the group of *term* GC/no-ECMO patients, and 51 (45–61) days in the group of GC/ECMO patients (p value between the last two groups = 0.04). The median time to achieve full enteral feedings was 35 (16–270) days in the group of *all* GC/non-ECMO patients, 29 (17–88) days in the group of *term* GC/no-ECMO patients, and 70 (48–77) days in the group of GC/ECMO patients (p value between the last two groups = 0.004). The median time to hospital discharge was 42 (20–282) days in the group of *all* GC/non-ECMO patients, 33 (21–105) days in the group of *term* GC/non-ECMO patients, and 125 (69–223) days the group of GC/ECMO patients (p value between the last two groups = 0.0001).

All patients in the study survived to hospital discharge.

Discussion

Respiratory distress is not a commonly observed problem in newborns with GC, but it can certainly occur and be life threatening. The overall incidence is about 9% for *all* GC, 6% for *term* GC, 10% for *late preterm* GC (> 34/< 37 weeks of gestation), and 23% for *preterm* GC [5, 6]. Most fetuses with GC are born beyond 34 weeks of gestation, so lung immaturity is not a major cause of respiratory failure at birth. Congenital cardiac anomalies, pulmonary hypoplasia and pulmonary hypertension are not common causes of respiratory failure either, since they are rarely seen in patients with GC. Most patients with GC who develop respiratory distress at birth simply have a slow transition to the extrauterine life and recover spontaneously within a few days without sequelae. A relatively common cause of respiratory distress at birth in the general population, but until now not recognized in patients with GC, is meconium aspiration syndrome (MAS). MAS is a condition diagnosed by a simple clinical feature: respiratory insufficiency in neonates born through meconium-stained amniotic fluid whose symptoms cannot be otherwise explained. MAS is a condition that affects almost exclusively term newborns, and its incidence is directly associated with the quality of prenatal/perinatal care. The current incidence of MAS in the general population is about 1.8% in all live births, and about 4.6% in the subgroups of *term* live births [3]. The incidence, however, is gradually declining worldwide as improved prenatal/perinatal care becomes available to an increasing proportion of pregnant women [4]. In our series of 110 newborns with GC treated at our center over a 5-year period we encountered five cases of MAS (all term newborns), which represents 4.5% of all GC patients and 13.8% of *term* GC patients. This represents an incidence of MAS in patients with GC three times higher than the incidence in the general population. We do not have a definitive explanation for this observation. MSAF, the *sine qua non* condition for the development of MAS, is observed with exponentially increased frequency in term births as the gestation advances, from 6% at 37 weeks to 37% at 44 weeks, with an average rate for all *term* births of about 12% [7–9]. If we take into account this 12% rate of MSAF and the 4.6% rate of MAS in *term* newborns in the general population, roughly 1/3 (38%) of patients with MSAF develop MAS. Since we observed a relatively similar incidence of MSAF in our population of term patients with GC compared to the general population (13.8% versus 12%) but a much higher incidence of MAS (100% versus 38%), it appears that GC may be an independent risk factor for the development of MAS.

We not only found a higher incidence of MAS in patients with GC, but we also found a remarkably high need for ECMO in patients with GC who develop MAS: four out of five patients (80%). This means that in our 110 case cohort 3.6% of all GC patients required ECMO due to severe MAS, a percentage that escalates to 11% if we analyze the subgroup of *term* patients with GC. In a large population-based study of over 415,000 live births, ECMO due to severe MAS was needed in 0.037% of newborns born at term (61 cases out of 162,075 patients) and in 0.014% of all live births [3]. In another even larger population-based study of nearly 2.5 million live births, ECMO due to severe MAS was needed in 0.00047% of all newborns [4]. The 3.6% incidence of MAS requiring ECMO in patients with GC in our cohort represents a 300-fold increase compared to the

general population reported in the first study, and a much higher rate compared to the second study. While the numbers vary widely from study to study and recognizing that our own numbers could change significantly even if just one case was added or removed, it seems appropriate to conclude that patients with GC have a much higher risk of needing ECMO if they develop MAS than newborns without gastroschisis. This information should be communicated to the parents of fetuses with GC at the time of prenatal consultation and serve as yet another argument to support the notion that fetuses with GC should ideally be cared for and delivered at tertiary centers with pediatric surgery and ECMO capabilities [10, 11].

Since MAS affects almost exclusively term and post-term fetuses, it could be argued that the high incidence of MAS should be yet another reason to deliver fetuses with GC before term. We believe that there is no advantage in delivering fetuses with GC before term [12]. However, we realize that for this particular issue (MAS), delivering fetuses with GC before term would be theoretically beneficial. What remains unanswered is whether an incidence of 13.8% (MAS in *term* GC) is high enough to justify preterm delivery in all GC.

To the best of our knowledge, ECMO in patients with GC has been reported only in a handful of publications [13–15]. Interestingly, in the largest group of GC patients requiring ECMO reported from a national ECMO registry, the vast majority of the cases required ECMO due to sepsis and/or congenital heart defects (31/41). Only ten cases required ECMO due to pulmonary hypertension not otherwise specified, and no patient was reported as having MAS (although pulmonary hypertension may be a surrogate for MAS in some cases, unless another cause is identified).

Our report aims to highlight a previously unknown high incidence of MAS in patients with GC, and a much higher severity of MAS cases in GC patients compared to the general population, with most of those patients requiring ECMO. Our set of objective data from a 110 case cohort of patients with GC treated at a single large referral center is useful for maternal–fetal medicine practitioners, neonatologists and pediatric surgeons who counsel parents of fetuses with GC and treat those fetuses after birth.

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Compliance with ethical standards

Conflict of interest All authors declare that there are no conflicts of interest.

Ethical approval 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 This article was a retrospective chart review and does not contain any studies with human participants or animals performed by any of the authors.

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