Improving Survival of Neonates with Isolated Congenital Diaphragmatic Hernia

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Despite advances in neonatal care including prenatal diagnosis, conventional ventilation, surfactant, high frequency oscillation, nitric oxide and extracorporeal membrane oxygenation (ECMO) the diagnosis of CDH is reported to carry a high mortality rate. Pulmonary hypoplasia and persistent pulmonary hypertension are major factors that contribute to death. In an effort to improve the survival of these infants a protocolized approach was adopted. In summary, this involves antenatal use of steroids if CDH antenatally diagnosed, sedation and muscle relaxation following tracheal intubation, administration of surfactant, gentle ventilation with permissive hypercapnia, trial of nitric oxide, preoperative ECMO for those infants failing therapy and delayed repair of the CDH. With the use of this protocolized approach the survival of infants with isolated CDH was 96 % for inborn and 81% for outborn infants.

Key words: *Diaphragmatic hernia, Neonate.*

Congenital Diaphragmatic Hernia (CDH) has an incidence of between 1 in 3000 and 1 in 5000 live births(1). There is a high incidence of stillbirth and 30% of cases of CDH have associated malformations or chromosomal abnormalities(2-3). Despite recent advances in prenatal therapies and neonatal intensive care, including conventional ventilation (CMV), surfactant, nitric oxide (NO), high frequency oscillation (HFO) and extracorporeal membrane oxygenation (ECMO), the mortality rate for infants with CDH remains high(4).

Two recent large series of cases showed a survival rate of 61% and 69% respectively for neonates with CDH(5). With increasing experience with fetal ultrasound, prenatal identification of CDH is becoming increasingly more common, which allows for counselling of parents and the development of an integrated prenatal and postnatal treatment plan.

Infants with CDH present with a combination of pulmonary hypoplasia and increase in pulmonary vascular resistance which produces pulmonary hypertension and hypoperfusion of the lungs(6). Since 1993, we have used a protocolized approach for the management of these patients with the objective of improved survival and decreased morbidity in infants born with CDH(7).

The objective of this study is to review our experience in the management of infants with isolated CDH since the implementation of such protocol and to compare our experiences with the current literature.

Subjects and Methods

In this retrospective study, hospital records of term and near-term infants with a diagnosis of isolated CDH admitted to the NICU at the Royal Alexandra Hospital in Edmonton from April 1993 to April 1999

were reviewed. Infants with other anomalies were not included.

If a prenatal diagnosis of CDH was made, we offered a careful level 2 antenatal ultrasound to rule out other malformations, a fetal echocardiogram, amniocentesis for chromosomal abnormalities and a weekly prenatal dose of steroids starting at 34 weeks gestational age.

A multidisciplinary team composed of a perinatologist, a neonatologist and a pediatric surgeon met with the parents to discuss treatment options and the risk of short and long term morbidities and mortality associated with CDH.

At delivery of an inborn infant known to have CDH, we provided endotracheal intubation, paralysis, sedation and insertion of a nasogastric tube to avoid distention of the bowel in the thoracic cavity. A dose of bovine surfactant (4-5 mL/kg), if tolerated, was also given in the delivery room to all the in-born infants. Infants were paralyzed with pancuronium and sedated with a continuous infusion of fentanyl.

A strategy of gentle ventilation with low peak inspiratory pressure (<25 cm H_2O) and permissive hypercapnia was adopted. A $PaCO_2$ value of 65 torr or less was considered acceptable. Bicarbonate infusion was used to correct metabolic acidosis. If the infant developed $PaCO_2$ retention with conventional ventilation ($PaCO_2$ >65 torr), the infant was given a trial of HFO. If there were problems with oxygenation, oxygenation index (OI > 25), infants had a trial of NO at 20 ppm.

ECMO was offered when conventional therapy failed. For all infants the criteria for initiating ECMO included three OI of 40 or greater within a 2-hour window while on a mean airway pressure >18 cm H_2O. Surgery was delayed until infants were stable on minimal ventilation and after ECMO decannulation.

None of the published predicting factors of poor outcome (early prenatal diagnosis, ventilatory index, polyhydramnios, presence of intrathoracic stomach, presence of liver in the chest, best postductal PaO_2 or $PaCO_2$) were considered exclusions for maximal support(8-10). Prenatal therapies such as prenatal surgery or temporary occlusion of the fetal trachea were not offered.

The information collected included prenatal diagnosis, gestational age, birth weight, place of birth, use of HFO, use of NO, ECMO requirement and survival.

Results

A total of 59 infants with isolated CDH with birthweight of 3100 (2100 to 4390) grams and gestational age of 38 (36 to 42) weeks were treated at our institution with an overall survival of 88%. A prenatal diagnosis of isolated CDH was made in 27 (100%) of inborn infants and in 14 (44%) of outborn infants. Forty-seven (80%) of the infants received a dose of surfactant.

Twenty-seven (87%) of the 31 infants that required ECMO had a trial of NO and or HFO compared to 14 (50%) of the 28 infants that did not require ECMO. There were 4 infants that required ECMO as soon they arrived to NICU (all these infants were outborn). ECMO requirement and survival of inborn and outborn infants are shown in *Tables I* and *II*. The overall survival for patients requiring ECMO was 81% and for those who did not require ECMO, 96%. Eleven (40%) of the inborn infants required ECMO compared to 20 (62%) of the outborn infants.

Discussion

The optimal management of CDH remains

unsolved. Different patients have different degrees of pulmonary hypoplasia and pulmonary hypertension secondary to right-to-left pulmonary shunting. Geggel, *et al.* showed hypoplastic lung not only in the ipsilateral but also in the contralateral lung of infants born with CDH(11).

Several studies in animals and humans with CDH showed pulmonary biochemical immaturity with decreased phosphatidyl-choline and surfactant protein A in amniotic fluid(12). In an attempt to improve lung maturation, several investigators have used prenatal steroids and postnatal surfactant with good results(13-15). In our protocol, we therefore, treated mothers with a prenatal diagnosis of CDH with weekly systemic steroids starting at 34 weeks and the infants received prophylactic surfactant instillation in the delivery room. In order to minimize the barotrauma associated with hypoplastic and immature lungs, we adopted the approach of gentle ventilation with permissive hyper-capnia described by Wung, *et al.*(16).

HFO was used to improve ventilation with success in some patients. We switched from CMV to HFO when $PaCO_2$ was above 65.

TABLE I–*Inborn Infants*

	Total	Alive	Survival (%)
ECMO	11	10	91
Non-Ecmo	16	16	100
Total	27	26	96

TABLE II–*Outborn Infants*

	Total	Alive	Survival (%)
ECMO	20	15	75
Non-ECMO	12	11	92
Total	32	26	81

Reyes, *et al*. reported a survival rate of 81% when HFO was used as an additional tool to support infants with CDH(17).

Inhaled NO reduced the need for ECMO in infants with pulmonary hypertension; however, this effect in infants with CDH is less predictable and less well documented than the effects of NO in infants with PPHN associated with meconium aspiration syndrome(18,19). A policy of delayed surgery to allow preoperative stabilization was adopted based on several reports that showed improvement in survival(21-23). In our patients, surgery was undertaken when infants required low ventilatory support and after ECMO. A recent report from the CDH study group showed a significant improvement in the survival rate in those infants requiring ECMO(24). Boloker, *et al.* recently showed an improvement in survival with permissive hypercapnia, delayed surgery and ECMO if needed(25).

We did not offer surgery in utero because its role still remains controversial. A trial of hernia repair in utero did not show any advantage over postnatal repair(26,27).

Preliminary work in animals and now in humans suggested that obstruction of the fetal trachea could correct the pulmonary hypoplasia associated with CDH(28-29).

With this protocolized approach, we found a dramatic increase in survival in newborn infants who had a prenatal diagnosis of isolated CDH.

Infants with CDH had a varying degree of compromise that is difficult to evaluate before birth therefore, these infants should be delivered at a tertiary perinatal center with multimodality support available.

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Key Messages

- None of the published predicting factors of poor outcome (early prenatal diagnosis, ventilatory index, polyhydramnios, presence of intrathoracic stomach, presence of liver in the chest, best postductal PaO_2 or $PaCO_2$) should be considered exclusion for maximal support.
- Infants with antenatally-diagnosed CDH should be delivered in centers that could offer maximal support.

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