Congenital Diaphragmatic Hernia

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Abstract. Over the last two decades there has been a constant improvement in the understanding of the pathophysiology of Congenital Diaphragmatic Hernia (CDH) and its management. However, the ideal treatment remains elusive. The earlier management strategy of immediate surgery is replaced by the principle of physiological stabilisation and delayed surgery. Conventional mechanical ventilatory techniques, with high pressures and hyperventilation to reverse ductal shunting and cause alkalinization, are being questioned because of the risks of barotrauma and consequent broncho-pulmonary dysplasia. It has also been shown that paralysis with pancuronium bromide for patients on conventional mechanical ventilation results in increased incidence of sensorineural hearing loss in childhood survivors of CDH. With the introduction of the concept of permissive hypercapnia and high frequency oscillation ventilation, the complications of pulmonary barotrauma are circumvented. Although ECMO therapy is invasive, yet has improved survival by about 15% independently, especially in critically ill infants who have the predictive mortality rate of more than 80%. Further insights into the pathophysiology of CDH and the introduction of less invasive therapeutic techniques in the form of high frequency oscillation ventilation, inhalation nitric oxide, surfactant, and perfluorocarbon liquid ventilation may even make the need for ECMO redundant. **[Indian J Pediatr 2000; 67 (9) : 665-670]**

Key words : *Congenital diaphragmatic hernia; High frequency oscillation ventilation*

Despite advances in neonatal resuscitation and intensive care over the last two decades, congenital diaphragmatic hernia (CDH) diagnosed in the first six hours still carries a mortality of over 50%. Besides pulmonary hypoplasia, it is now recognized that persistent pulmonary hypertension of the newborn (PPHN) is the major complication following repair of CDH. Many approaches have been used in the management of pulmonary hypertension including pulmonary vasodilators, pharmacological paralysis, high frequency ventilation and extra corporeal membrane oxygenation (ECMO). These therapies have shown early promise but have not made any significant impact on the high mortality from this condition.

ANTENATAL DIAGNOSIS

The prenatal diagnosis of CDH is made by the ultrasound examination. The diaphragm is imaged as an echo free space between the thorax and the abdomen. Polyhydramnios is an important indicator and is often present. The parameters for defining polyhydramnios vary. Chamberlain defined it as a pocket of amniotic fluid greater than 8 cms. Polyhydramnios is present in upto 75% of pregnancies complicated by CDH. Fetal CDH is identified by presence of stomach (90% of cases) or liver (50% of cases) shadow in the thorax, next to the heart shadow. Mediastinal shift to the opposite side may be discernable. The degree of pulmonary hypoplasia is assessed by the presence or absence of fetal breathing movements. The lung area can be quantified by using the ultrasound. The contralateral lung area is assessed at the level of axial four chamber view. The survival rate is better if the contralateral lung area is equal to or greater than one half the area of hemithorax. The presence of the liver in the chest predicts the requirement of post natal extra corporeal membrane oxygenation (ECMO).

The prenatal diagnosis of congenital diaphragmatic hernia can help in better management of both the child and the mother. The mother should be transported to a tertiary care center where a CDH can be managed.

PREOPERATIVE MANAGEMENT

Clinical Features

The severely affected babies present with respiratory distress in the form of cyanosis, tachypnoea, sternal

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recessions and scaphoid abdomen with increase in anterior-posterior diameter of chest. The heart sounds will be displaced to the opposite side, and bowel sound may be heard in the affected side of the chest. Some babies remain asymptomatic and present in later life with gastrointestinal symptoms or may be discovered accidentally by a chance X-ray for some other ailment.

Diagnosis

X-ray of chest and abdomen is diagnostic with air filled loops of bowel seen in the chest. The abdomen may be airless or very few gas shadows may be present. The heart is displaced to the opposite side. Barium studies are rarely necessary.

Preoperative

Babies with minimal or no respiratory distress require only a naso-gastric tube to be passed into their stomach to avoid further bowel distension. No other special preoperative care is necessary. Babies with respiratory distress are admitted in an intensive care unit. Overhead radiant warmers are provided to keep the babies warm. Visual and electronic monitoring devices are used to monitor the babies heart rate, respiratory rate and SaO_2. Arterial blood gas and pH studies are done. Endotracheal tube is passed and artificial ventilation initiated. The aim is to achieve adequate ventilation with lowest airway pressures. CDH babies with respiratory distress are acidotic with high partial pressure of carbondioxide in their blood. High oxygen concentrations, rapid respiratory rates and low tidal volumes are necessary to bring down the pH and $PaCO_2$. Repeated blood gas analysis titrated with ventilator settings are required to achieve the optimum state.

Pneumothorax should be avoided at this stage but if it occurs, an intercostal tube is passed. Supportive measures such as intravenous fluids, fresh frozen plasma and dopamine are given as required to maintain adequate perfusion. If acidosis is not corrected by resorting to the highest ventilator settings then sodium bicarbonate is given.

The stabilization period can last from six to sixteen hours. The calculation of ventilatory index (VI) at this stage can given an indication of prognosis.

VI = Ventilatory Rate × Mean Airway Pressure.

Neonates achieving normocarbia with VI less than 1000 have a 100% survival.

Neonates who persist with hypercarbia with VI more than 1000 have very low survival rates.

Neonates who achieve normocarbia with VI of over 1000 (i.e. mean airway pressure more than 20 cms of water and respiratory rates of over 60) have an unpredictable outcome.

Hyperventilation is very useful in managing neonates with CDH because ductal shunting can be readily reversed by raising pH to above 7.5 and reducing $PaCO_2$ to below 30 mmHg. The neonate's pulmonary vascular bed is very sensitive to changes in PaO_2 and $PaCO_2$. Hyperventilation is thus one of the mainstays in the management of a newborn with congenital diaphragmatic hernia.

The rationale for delayed surgical repair : It was earlier assumed that hypoxia and hypercarbia seen with this anomaly were the direct result of lung compression by the intenstinal contents which had herniated into the chest. Thus the reduction of the hernia and repair of the defect became an urgent priority and it was believed that gas exchange would improve after the repair.

Many groups have since observed that rather than improving oxygenation and carbon dioxide elimination, the carbon dioxide may actually accumulate following surgery necessitating an increase in ventilator settings.

Bon *et al* studied respiratory system compliance before and after surgery. To their surprise, they found that thoracic compliance, rather than improving, actually fell in eight of the nine infants studied. They also noticed that when the decrease in compliance was more than 50% compared to the pre operative values, the mortality fingure reached 100%. The reasons for the same could be :

- Downward displacement and stretching of the hemi-diaphragm may lead to a distortion of the chest wall.
- Tight abdominal wall closure in the underdeveloped abdomen leads to upward pressure on the diaphragm and hence decrease in the chest wall complicance.
- Mediastinal shift to ipsilateral side following reduction of hernia leads to increased pulmonary vascular resistance which accentuates the problem.

Thus, to avoid deterioration, initial approach should be to stabilize the patient on conventional ventilation. Thus if $PaCO_2$ is less than 40 on a ventilatory index of less than 1000, elective repair is taken up in 12 to 24 hours. If $PaCO_2$ is less than 40 on VI of more than 1000, the surgical repair is deferred for 24 hours hoping to achieve proper levels by that time. If $PaCO_2$ remains beyond 40 even with VI index above

1000 the prognosis remains very poor with authors reporting 100% mortality if these patients are taken up for surgery.

Such patients are then switched over to high frequency oscillatory ventilation (HFOV) or ECMO. Repair is only done if the patient can be put back on conventional mechanical ventilation and maintain a normal $PaCO_2$. With these measures there is overall decrease in mortality rates but the number of patients who die without surgery increase.

SURGICAL TECHNIQUE

The abdominal approach is preferred. It gives an adequate exposure and it is easier to pull down the abdominal contents than push them down from the thorax. The accompanying malrotation is looked into and corrected. If the abdominal cavity is inadequate additional procedures may be necessary to accommodate the herniated contents. The thoracic approach is used by some surgeons as it gives a good exposure of the defect.

With the patient in supine position, the subcostal approach is used. A blunt instrument or a foley catheter is introduced into the chest cavity to equalize the pressures and thus aid in reducing the contents. The stomach is reduced first, followed by small intestine, caecum, the ascending colon, the transverse colon and spleen in this order. If sac is present an incision is made to permit air into the abdominal cavity, which is then delivered into the abdominal cavity and edges are trimmed to close the defect. For the defect the edges are usually folded onto itself, an incision over the same denudes the edge and the defect can be closed. If the defect cannot be closed mesh may be required. Vicryl mesh[1] and reverse lattisimus dorsi flaps[2] have been used but the most preferred one today is the poly tetrafluoroethylene (PTFE) patch[3]. Primary closure of the abdomen, without compromising the respiratory effort is the aim, but if it cannot be achieved, additional procedures may be needed. These include manual stretching of the abdominal wall, resection of lower two or three ribs or creation of a silastic chimney.

A chest tube is inserted on the ipsilateral side. This is kept clamped and released every three hours for a few minutes. This is done to equalize pressures on either side of the diaphragm. There are authors who prefer to put the chest tube on the contralateral side as well, this again to equalize pressures on both sides. Gastrostomy is also preferred by others who claim that this procedure avoids abdominal distension and hence does not compromise respiration.

PROGNOSTIC FACTORS

1. *Polyhydramnios :* Harrison[4] considered that presence of polyhydramnios was a poor prognostic indicator. Fifty five per cent survival was associated with absence of polyhydramnios, whereas the presence of polyhydramnios had a survival of only 11%. Since then a number of studies have refuted this fact and have shown that presence of polyhydramnios has no impact on the eventual outcome of an infant with CDH[5].
2. *Antenatal quantification of lung area :* A survival rate of 86% has been reported when contralateral lung area is equal to or greater than one half of the hemithorax.
3. *Antenatal ultrasound :* Evidence of liver in the chest cavity predicted the need for ECMO
4. *Arterial blood gas analysis :* (i) pH at admission >7.2-100% survival; < 7.2-50% survival; < 7.0-90% mortality; (ii) Ventilatory index (VI) = product of resp. rate, mean airway pressure and $PaCO_2$. If $PaCO_2$ could be reduced to less than 40 with ventilatory index less than 1000, all patients survived[6]; (iii) First six hours $PaCO_2$ < 40 survival 97%; > 40 Survival 10%.
5. *Preoperative FRC :* The function residual capacity as measured by Helium dilution method if less than 9 ml/kg denotes a 100% mortality[7]. Some authors consider the compliance of the respiratory system measured on day one to be a better indicator of prognosis than FRC[8].
6. *Position of stomach :* If stomach was located properly below the diaphragm it denoted a 100% survival rate, but if the stomach was herniating into the chest a survival of only 30% was reported[9]. Other studies have failed to show any predictive value of such positioning[10].
7. *Side of the defect :* Right sided defects have been associated with worse prognosis[11].
8. In an inborn population based review of neonatal CDH between 1983 and 1995, the best prediction of survival was the presence or absence of other anomalies and the preoperative $PaCO_2$ and pH. The survival rate was >80% when $PaCO_2$ was less than 50 mmHg and pH more than 7.25.
9. Antenatal diagnosis of congenital diaphragmatic hernia is a bad prognostic sign giving a mortality of up 80%[12].
10. Left ventricular hypoplasia may be a better predictor of outcome and pulmonary hyperten-

sion, but more studies are needed to verify this assessment[12].

11. Antenatal lung to head ratio of more than 1.4 predicts a good outcome, while a ratio of less than 1 predicts a poor outcome. With ratio in between 1 and 1.4, a 38% survival has been reported[13].
12. Multivariate analysis by Keshen identified four variables as statistically significant. These being VI, best pre-op $PaCO_2$, birth weight and Apgar score at 5 minutes[14].

ROLE OF HIGH FREQUENCY VENTILATION

High frequency ventilation (HFV) is a relatively new form of mechanical ventilation. This method uses small tidal volumes often less than anatomic dead space, and extremely rapid ventilatory rates. This method is used in situations where the Conventional Mechanical Ventilation (CMV) has failed. The advantage of HFV over CMV is its ability to deliver adequate minute volumes with lower proximal airway pressures. The volume of gas that is delivered nears the dead space values. Traditional wisdom says that this should produce little, if any, alveolar ventilation. The fact that gas exchanges does occur and often more efficiently than during CMV, is preplexing and intriguing. This method is a useful rescue technique or a bridge to ECMO. It has clear but limited usefulness as a rescuer or temporizing measure in pulmonary hypoplasia and persistent pulmonary hypertension.

ROLE OF EXTRACORPOREAL MEMBRANE OXYGENATION

Extracorporeal membrane oxygenation (ECMO) is an aggressive life support system that employs partial heart lung bypass for long periods of time. In congenital diaphragmatic hernia it is difficult to ascertain the extent of pulmonary hypoplasia and pulmonary hypertension in a given patient before the infant is born. ECMO is of no help in overwhelming pulmonary hypoplasia in which no meaningful gas exchange occurs once the infant is born. A preductal $PaCO_2$ gives a fair indication of the extent of pulmonary hypoplasia.

It is helpful in patients with adequate lung parenchyma but intractable in recurrent pulmonary hypertension.

Certain infants after repair show variable gas exchange. This is called the honeymoon period. Subsequently, the patient's pulmonary vascular bed develops high vascular resistance as in the prenatal state.

The honeymoon period indicates that there may be adequate lung parenchyma for gas exchange but the deterioration is due to a dynamic state in the pulmonary vascular bed, i.e. an increase in pulmonary vascular resistance. Such an infant may survive a period of heart lung bypass during which time the pathologically increased pulmonary vascular tone can revert to a more physiological condition. The selection of patients with adequate lung volume but intractable pulmonary hypertension is based on the following facts.

At sometime in the honeymoon period, the highest preductal $PaCO_2$ should be greater than 80 torr on FiO_2 of 1.0 and the lowest preductal $PaCO_2$ should be less than 50 torr. The duration of honeymoon period is the interval during which preductal $PaCO_2$ is more than 55 torr.

The patients are only placed on ECMO if the honeymoon period ends and they develop sustained hypoxemia, having a preductal $PaCO_2$ of less than 40 torr and pH less than 7.2 and an alveolar-arterial oxygen gradient of more than 600 torr for ten hours or more despite maximal conventional therapy.

The current multicenter extracorporeal life support organization (ELSO) registry data show that infants with CDH treated with ECMO have a survival rate of 58%[15].

The timing of surgery on ECMO is controversial. Some authors have recommended surgery on ECMO[16] and report high survival rates of 80%. The ELSO registry data points to high rates of hemorrhagic complications (57%). As of today, it is recommended to do the surgery after decannulation from the ECMO.

Thibeault determined that a minimum lung volume of 45% of the value predicted from age matched control is required for survival in ECMO treated infants[17]. Intracerebral hemorrhage or cardiac anomalies rule out ECMO. The analysis of the developmental profile of the pulmonary vasculature in CDH has revealed that there is failure of the normal arterial remodelling processes occurring in the perinatal period, and the pulmonary vascular morphology does not differ between the groups with pulmonary hypoplasia or persistent pulmonary hypertention as the primary cause of death. The adventitial thickening of the pulmonary arteries resulting in pulmonary hypertension appears to partially reverse by the institution of ECMO. This constitutes one of the mechanisms of alteration of pulmonary hypertension associated with CDH. ECMO also spares the infant's lungs from the detrimental effects of high airway pressures and high inspired oxygen content, thus allowing physiological reversal of pulmonary hyper-

tension during the period of lung rest. ECMO significantly improves survival rates in those infants who have an otherwise predictive mortality rate of more than 80%.

OUTCOME

Harrison *et al* have reported an overall survival of 40% in CDH[18]. This includes all prenatally diagnosed cases of CDH. In most other studies only the patients who reach the treating center alive are included in the study. This method preselects the survivors of antenatally detected cases of other studies. The CDH group study, including centers across Amercia, Europe and Australia, give a mean survival rate of 63%[1]. Individual authors report survival ranging from 72% to 92%[19-22]. These authors have used all available means for management including CMV, HFOV and ECMO where indicated.

FUTURE DIRECTIONS

1. Nitric oxide (NO) is a potent mediator of vasodilatation. It is a highly diffusible gas that is inactivated by binding to hemoglobin. It is delivered to the pulmonary vasculature by mechanical ventilation. It has been shown to increase the oxygen saturation when given to neonates having respiratory failure due to PPHN[23]. In animal models of PPHN, nitric oxide decreased pulmonary artery pressures and improved the oxygen saturation without any detectable side-effects. Trials of NO in CDH have had mixed results[24]. The exact relationship of NO to the pathology of CDH remains to be determined.

2 It has been shown that increased phosphodiesterase type V activity impedes the increase in vascular smooth muscle cyclic guanosine monophosphate (CGMP) in response to inhalation nitric oxide.

Dypiridamole, a specific PDE-V inhibitor augments the response to inhalation of nitric oxide in pulmonary hypertension associated with CDH. Combined therapy of inhalation nitric oxide and dypiridamole improves pulmonary vasodilatation and reduces the need for ECMO.

3. Fetal surgical intervention is a concept that holds exciting options. This evolved after experimental studies in lambs that removal of compressive forces on the fetal lung resulted in its proper growth and function[25]. The clinical studies have so far been disappointing. As a direct extension of this principle, fetal tracheal ligation has been attempted. Tracheal occlusion or PLUG therapy (plug the lung until it grows) has resulted in improved oxygenation and ventilation after birth when compared to untreated control animals[26]. Clinical trials for this form of therapy are being carried out. The basic question whether fetal intervention has a role in the treatment of this condition is yet to be answered. An advantage with PLUG therapy as shown by experimental studies is that it reduces pulmonary hypertension[27].

The dark side of this story is that plugging decreases the type II pneumocytes. As an upshot of this is the decrease in the surfactant[28,29]. A period of unplugging is necessary for normalization of these pneumocytes.

4. Liquid ventilation techniques with perflurocarbons have reached a stage of clinical applicability. Significant increases in $PaCO_2$ levels, a fall in $PaCO_2$ levels, with static total pulmonary compliance measurements have been reported[30]. Postnatal lung growth has also been accelerated by continuous intrapulmonary distension with perflurocarbons. The established after limits for its usage in neonates is seven days but this is not sufficient to promote lung growth[31,32].

5. The use of prenatal intra-amniotic dexamethasone administration has been experimentally shown to be capable of preventing pulmonary hypoplasia in fetus with CDH[33]. Maternal administration of dexamethasone in experimental studies has been shown to prevent pulmonary vasculature thickening[34].

6. *In utero* repair of the CDH is feasible and can reverse the pulmonary hypoplasia but only in fetus without liver herniation. At present, fetal surgery does not improve survival and babies without liver herniation should be treated postnatally.

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