REVIEW

Congenital diaphragmatic hernia: a literature review

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ABSTRACT

Congenital diaphragmatic hernia is a structural defect in the diaphragm that allows abdominal organs to protrude into the thoracic cavity during fetal development, the main consequence of which is pulmonary hypoplasia. The incidence of congenital diaphragmatic hernia is estimated at 1 to 4 cases per 10,000 live births. Specialist centers report survival rates of up to 85%, although this is associated with increased long-term morbidity. The etiology of congenital diaphragmatic hernia is related to genetic and environmental factors that influence the development of the diaphragm and other somatic structures. The presentation of the hernia may be left-sided (85 %), right-sided (13 %), or bilateral (2 %). About 30-70 % of cases are isolated, while 30-50 % are complex and associated with other congenital anomalies. Prenatal diagnosis

of congenital diaphragmatic hernia is usually made by anatomical ultrasound between 18 and 22 weeks of gestation. Early detection is essential for effective management and prognosis of diaphragmatic hernia. It also allows the severity of pulmonary hypoplasia to be assessed and the presence of congenital anomalies or associated genetic syndromes to be ruled out. Birth can then be planned in a medical center specializing in stabilizing neonatal pulmonary and cardiovascular function and, if necessary, corrective surgery. Our study is a non-systematic review of the literature on congenital diaphragmatic hernia.

Keywords: Infant, Newborn; Pediatrics; Hernias, Diaphragmatic, Congenital (Source: MeSH)

Hernia diafragmática congénita: una revisión de literatura

RESUMEN

La hernia diafragmática congénita es un defecto estructural en el diafragma que permite la protrusión de órganos abdominales en la cavidad torácica durante el desarrollo fetal y cuya consecuencia más relevante es la hipoplasia pulmonar. La incidencia de hernia diafragmática congénita se estima en 1 a 4 casos por cada 10 000 recién nacidos. Los centros especializados reportan tasas de supervivencia que pueden alcanzar hasta un 85%, aunque esto va acompañado de un incremento en la morbilidad a largo plazo. La etiología de la hernia diafragmática congénita se asocia con factores tanto genéticos como ambientales que influyen en el desarrollo del diafragma y otras estructuras somáticas. La presentación de la hernia puede ser en el lado izquierdo (85%), derecho (13%) o ser bilateral (2%). Entre el 30-70% de los casos son aislados, mientras que el 30-50% son complejos y se presentan junto con otras anomalías congénitas. El diagnóstico prenatal de la hernia diafragmática congénita generalmente se realiza mediante ecografías anatómicas entre las semanas 18 y 22 de gestación. La detección temprana es vital para el manejo efectivo y el pronóstico de la hernia diafragmática. Asimismo, esta permite evaluar la severidad de la hipoplasia pulmonar y descartar la presencia de anomalías congénitas o síndromes genéticos asociados. Así, se puede planificar el nacimiento en un centro médico especializado en la estabilización de la función pulmonar y cardiovascular neonatal y en la realización de la cirugía correctiva cuando sea necesario. La presente es una revisión de la literatura no sistemática sobre hernia diafragmática congénita..

Palabras clave: Recién Nacido; Pediatría; Hernias Diafragmáticas Congénitas (Fuente: DeCS)

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INTRODUCTION

Congenital diaphragmatic hernia (CDH) is a diaphragmatic defect resulting in herniation of abdominal contents into the thoracic cavity during gestation, with an estimated incidence of 1 to 4 cases per 10,000 live births. The main consequence of CDH is pulmonary hypoplasia, affecting the left lung, right lung, or both, depending on the location of the defect. The morbidity and mortality of CDH are influenced by the presence of pulmonary hypoplasia, pulmonary hypertension, and association with other malformations (1,2). Although there has been an improvement in the survival rate to approximately 85% in the last three decades due to advances in neonatal care (3), this improvement is accompanied by an increase in long-term morbidity (1). In developing countries, the survival rate is even lower.

Therefore, a review and synthesis of the available evidence from the literature were deemed necessary to enable health professionals in training to understand critical aspects of the etiopathogenesis, diagnostic features, treatment, and follow-up of CDH.

METHODS

A non-systematic review of the literature was conducted. The search strategy included querying the PubMed database, using "congenital diaphragmatic hernia" as a keyword. In addition, this search was complemented with the review of current consensus and reference texts in neonatology.

ETHIOPATHOGENY

Pulmonary development during the critical period from the third week post-conception to 16 weeks gestation can be significantly affected by congenital diaphragmatic hernia (CDH). This condition originates when the pleuroperitoneal folds fail to close correctly between the fourth- and tenth-week post-conception, allowing herniation of abdominal viscera into the thoracic cavity. This herniation disrupts normal pulmonary development and can result in adverse consequences such as reduced bronchiolar branching and truncation of the pulmonary arterial tree. These changes result in structural vascular remodeling and vasoconstriction. As a result of these processes, lung mass loss leads to postnatal pulmonary hypoplasia, characterized by dysfunction of the surfactant system and hypoplasia of ipsilateral cardiac structures. The severity and range of these adverse effects in an affected fetus depend on the gestational age at which visceral herniation occurs.

Failure of normal diaphragmatic closure is unknown. Genetic or environmental triggers may disrupt the differentiation of mesenchymal cells during the formation of the diaphragm and other somatic structures (4,5). Classification can be made according to the location of the defect, with left (85%) being the most frequent, followed by right (13%) and bilateral (2%), the latter considered lethal. Other less frequent forms of presentation are anterior, Morgagni type, or parasternal. The most frequent form of presentation is left posterolateral (Bochdalek's) (2-6).

It is estimated that 30-70 % of CDH cases are isolated, with pulmonary hypoplasia, intestinal malrotation, and cardiac dextroposition as hemodynamic or mechanical consequences of the hernia. On the other hand, approximately 30-50 % of cases are complex, non-isolated, or syndromic, associated with additional anomalies, including major structural malformations, chromosomal abnormalities, and single gene disorders (7). These malformations can affect all major organ systems with no specific pattern.

From 10-15% of CDH cases with associated anomalies are syndromic. Fryns syndrome is the most common of these autosomal recessive syndromes, characterized by CDH, pulmonary hypoplasia, craniofacial anomalies, distal limb hypoplasia and characteristic internal malformations (8). Other syndromes include Donnai-Barrow (LRP2 mutation) and Pallister-Killian mosaicism syndrome (12p isochromosome). They occasionally can be a component of syndromes such as Apert, CHARGE, Coffin-Siris, Goltz, Perlman, Swyer, Brachmann-Cornelia De Lange, Goldenhar sequence, Beckwith-Wiedemann, Simpson-Golabi-Behmel, Matthew-Wood, Jarcho-Levin, Fraser, Stickler, Pierre Robin, Wolf-Hirschhorn, Emanuel, among others (9,10,11).

DIAGNOSIS

Diagnosis of diaphragmatic hernia is usually prenatal nowadays, which allows a comprehensive and multidisciplinary evaluation of the prognosis and facilitates decision-making in collaboration with the family. These decisions may range from prenatal treatment and expectant prenatal management to postnatal intervention, postnatal palliative care, or termination of pregnancy, according to the laws of each country (12).

More than 60% of CDH can be detected by routine anatomical fetal ultrasound performed between 18 and 22 weeks (9). Identification at later gestational stages is often due to a lack of early herniation of abdominal contents into the fetal thorax, a minor defect, or errors in the interpretation of a previous examination. Milder cases may not be identified until postnatal life when the patient presents with mild gastrointestinal or respiratory symptoms or by chest radiography (13).

On ultrasound, mediastinal deviation is a critical diagnostic parameter. Differentiating meconium-free loops from the lung can be complicated since, at 22 weeks, both have the same echogenicity, so the main indication is mediastinal deviation. In the diagnosis of left CDH in the second trimester, without gastric chamber herniation, the only sonographic suspicion is cardiac dextroposition. The diagnosis of right CDH is more complicated and is characterized by a homogeneous mass (liver) in the right thorax, often resulting in a shift of the mediastinum to the left.

Abdominal ultrasound evaluation helps report the location of the liver. In some cases, the gallbladder can be seen in the thorax, a crucial clue for diagnosing right CDH. In addition, polyhydramnios is another characteristic finding detectable in most cases after 26 weeks.

Differential diagnosis

During prenatal ultrasound diagnosis, it is essential to distinguish CDH from other pathologies that may present similar characteristics. The most relevant differential diagnoses are congenital pulmonary malformations, manifesting as pulmonary cysts or masses, bronchogenic cysts, bronchial atresia, enteric cysts, and mediastinal teratomas (14,15). Likewise, it is crucial to consider and rule out diaphragmatic eventration. Eventration refers to the elevation of a portion of the diaphragm which, although intact, is thinned due to incomplete musculature (16). This thin, redundant diaphragm resulting from the eventration of abdominal contents may move into the thoracic cavity and be mistaken for CDH.

SEVERITY ASSESSMENT AND PROGNOSTIC FACTORS

The assessment of the severity and prognosis of CDH must be individualized. However, crucial elements guide the medical team and help prepare parents. CDH is a significant cause of pulmonary hypoplasia, which is one of the most severe complications and a cause of mortality from respiratory distress. Detecting its presence in utero is crucial to establishing accurate prognoses, being present in 50 to 70 % of newborns with CDH. Ultrasound measures the area of the lung contralateral to the CDH and the head circumference to determine the degree of severity. These measurements are related to the LHR (lung-to-head ratio), which is subsequently compared to the LHR in normal fetuses (LHR O/E). The LHR indirectly assesses the degree of pulmonary hypoplasia and mediastinal deviation. The predictive value of LHR decreases after 30 weeks of gestation, with the optimal time for LHR being between 20 and 30 weeks. According to the LHR, the classification is divided into severe (ratio ≤ 25 %), moderate (26-45 %) or mild (> 45 %). A ratio < 1.2 is associated with less than 38 % survival, whereas a value of 1.4 raises the survival rate by nearly 100 % (17).

Recently, the position of the stomach has been identified as a relevant prognostic factor, correlating with postnatal morbidity and mortality independently of the LHR O/E (13). A grade 4 position, where most of the stomach is located in the right hemithorax next to the atrium, has a 12% survival rate (18-19). In addition, the position of the liver is also a critical severity factor; its intrathoracic location is associated with a poor prognosis, with a survival of 43%, compared to a survival of 93% if it is intra-abdominal.

Among the postnatal mortality indices is the McGoon Index, based on the measurement of the diameter of the right pulmonary artery plus the diameter of the left pulmonary artery, divided by the diameter of the descending aorta at the level of the diaphragm [(RPA+LPA)/DA]. An index of 1.3 is associated with a mortality close to 80% (18). Likewise, factors such as prematurity, the presence of polyhydramnios, association with other malformations, and pulmonary hypertension are also indicators of poor prognosis.

On the other hand, prenatal cardiac evaluation is essential after the diagnosis of CDH since cardiovascular defects are common, occurring in one-third of cases, with 15% having no associated syndromes (20,21). In addition, the possibility of association with chromosomal defects makes it advisable to consult a geneticist and perform amniocentesis for karyotyping and array-CGH. Therefore, one must be thorough in the evaluation of severity, the establishment of possible prognoses, and the choice of the place of birth. This evaluation also allows the selection of patients who could benefit from intrauterine fetal treatment.

PRENATAL TREATMENT

In cases of severe CDH with poor prognosis, treatment by fetoscopic endoluminal tracheal occlusion (FETO) may be considered. Inclusion and exclusion criteria for treatment vary among medical centers. The FETO procedure involves the endoscopic balloon insertion into the fetal trachea to retain pulmonary fluid. This increases airway pressure and promotes lung growth. The optimal time for balloon insertion varies according to the protocols of each center, but it is generally performed between 26 and 30 weeks of gestation and is removed between 34 and 36 weeks (15,16,17).

FETO treatment has improved survival: from 24% to 49% in left CDH and from 0% to 35% in right CDH (22). Treatment is followed up with ultrasound scans every four weeks to monitor lung growth and amniotic fluid volume. In cases of polyhydramnios and cervical shortening, additional interventions may be necessary. However, it should be noted that there is a risk of fetal death of approximately 5% (19). This treatment is offered in a limited number of hospitals in the world. Currently, the Hospital Sant Joan de Déu in Barcelona is one of the most experienced centers in evaluating and treating CDH, having performed more than 300 fetal surgeries for this condition.

Birth and birth planning in cases of CDH

The birth of a baby with CDH should be planned in a specialized medical center with expertise in stabilizing neonatal pulmonary and cardiovascular function, as well as performing corrective surgery when necessary. Since up to 50% of these patients may require extracorporeal membrane oxygenation (ECMO), delivery should occur in a tertiary center with ECMO (23,24), as even patients with favorable pulmonary parameters may experience severe pulmonary hypertension.

Determining the optimal time for delivery is a matter of debate. Hutcheon et al. conducted a retrospective study of 928 patients, in which a significant difference in neonatal mortality was observed between gestations terminated at 40 weeks (16.7%) compared to births at 37 weeks (25%) (25). However, other studies examining the relationship between

gestational age, mortality, and mode of delivery (natural delivery or cesarean section) found no significant differences (26,27). Due to the lack of consensus and in light of current knowledge, it seems advisable to plan the birth from 39 weeks of gestation, as long as maternal and fetal conditions permit, and coordinate with the surgical service. The choice of a cesarean section will be based on standard obstetric indications since there is no evidence to suggest that a routine cesarean section is more beneficial for these cases (26,27).

Clinical manifestations and physical examination

The clinical manifestations of congenital diaphragmatic hernia can vary widely. The spectrum ranges from acute respiratory distress at birth, the most common presentation, to minimal or no symptoms seen in a small group of patients diagnosed later in life. In neonates, the degree of respiratory distress is directly related to the severity of pulmonary hypoplasia and the development of pulmonary hypertension (PH). After birth, hypoxemia and acidosis may increase the risk of PH by inducing a reactive vasoconstrictive element, added to the pre-existing component of fixed arterial muscular hyperplasia. In some cases, pulmonary hypoplasia is so severe that it may be incompatible with life.

Physical findings in patients with CDH include a barrel-shaped thorax and a keeled abdomen due to loss of abdominal contents into the thorax. In addition, the absence of breath sounds on the ipsilateral side may be observed. In patients with left-sided CDH, a displacement of the heartbeat to the right is expected due to the displacement of the mediastinum (2,20,24).

Medical management of CDH

Although there are no randomized clinical trials, case series suggest that initial medical management followed by surgical correction improves survival in neonates with CDH (28). This supportive medical management includes reducing pulmonary compression, providing cardiovascular support with fluids and inotropic agents, and providing ventilatory support with conventional or high-frequency ventilation (HFV). ECMO is reserved for severe cases of patients who do not respond to other medical interventions.

Monitoring is crucial after birth, maintaining adequate heart rate, pre- and post-ductal saturation, and blood pressure. The goal is to maintain saturation between 80-95%, ensuring adequate perfusion. In the first two hours after birth, saturation levels up to 70 % can be tolerated if the patient improves without changes in ventilatory parameters, maintaining pH > 7.2 and pCO_2 < 65 mmHg.

The European Consensus recommends immediate post-birth orotracheal intubation for all newborns with a prenatal diagnosis of CDH and should be performed with prior premedication (1). Management should be gentle, maintaining low airway pressures (less than 25 mmH_2O) to protect the contralateral healthy lung. Medication administration before intubation is advisable to avoid increases in systemic and intracranial blood pressure and a fall in heart rate and saturation. Using neuromuscular blockers in the initial treatment in the delivery room has not shown benefits and should be avoided, as they impair pulmonary compliance. Other agents are recommended to maintain sedation and analgesia of the newborn. In addition, the placement of a nasogastric or orogastric tube is another indication at birth to avoid overdistension and compression of the ipsilateral lung by the stomach.

Transfer of patients with CDH

Planning the place of birth after an appropriate prenatal diagnosis allows for the coordination of the best environment for delivery and neonatal treatment. An experienced tertiary center should be chosen, i.e., one that handles more than five patients annually.

It is necessary to consider that more than one-third of patients go into spontaneous labor before 35 weeks. Therefore, the idea is to coordinate the intrauterine transfer, preferably at 34 weeks of gestation (29), if the hospital where the birth is scheduled is far from the mother's residence.

If the transfer is performed post-birth, European guidelines recommend that it be done with the patient on mechanical ventilatory support, avoiding the self-inflating bag to minimize high pressures. In the absence of a ventilator, a neonatal pneumatic resuscitator can be used. After the first hour of life, saturation should be maintained between 85% and 95%.

During transfer, the patient should be placed in an incubator and positioned at 45º to avoid aspiration of gastric contents and improve ventilatory dynamics. Electrocardiographic monitoring, pulse saturation monitoring, and placement of an orogastric tube in the aspiration position should be implemented. It is essential to have at least one vascular access.

PREOPERATIVE MANAGEMENT

Vascular accesses

In the preoperative management of patients with CDH, the placement of adequate vascular access is crucial. First of all, it is recommended to establish an arterial line, preferably in the right radial artery. This location is ideal for monitoring preductal arterial oxygenation, which is essential to determine the level of oxygen reaching the patient's brain. In addition, this arterial access facilitates blood pressure monitoring and allows for efficient blood sampling.

Although umbilical arterial catheterization is a safe alternative for long-term arterial access, it is considered less desirable in this specific context because it reflects the patient's post-ductal situation. Having at least two central venous vascular accesses is essential for venous access. Recommended options include a percutaneous central venous catheter and an umbilical venous catheter. It should be noted that the correct placement of the umbilical venous catheter can be complicated in situations of hepatic herniation. Therefore, it is recommended that at least one central venous catheter be dual lumen to optimize its functionality and versatility in patient management.

Chest radiographic evaluation

As part of the initial patient evaluation, perform early chest radiography. Figure 1 shows radiographs of the different types of CDH.

Patient monitoring

During the different phases of treatment, health professionals should ensure that patients are at average values for preductal saturation, post-ductal saturation, heart rate, invasive blood pressure, pulmonary pressure by echocardiogram, naso- or orogastric tube, and diuresis. Table 1 shows the recommended values.

Preoperative Ventilatory Management in Newborns

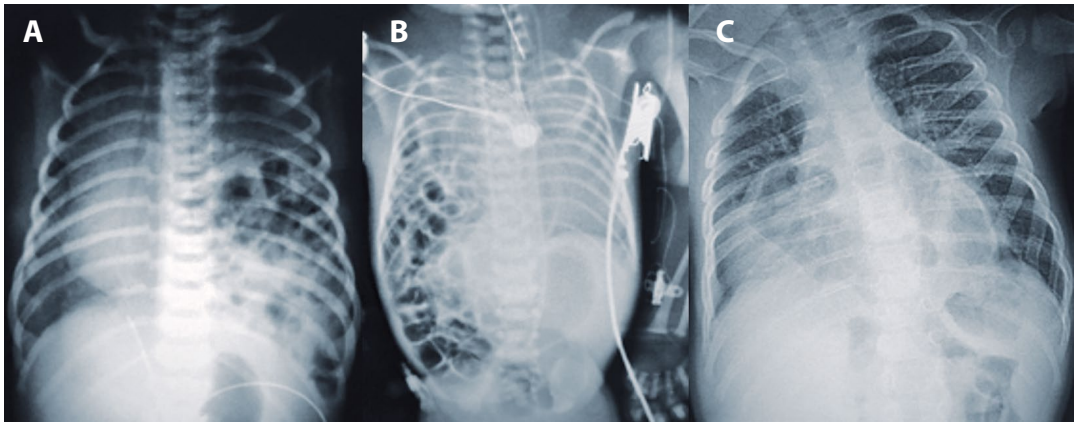
In the management of newborns with a prenatal diagnosis of CDH, immediate ventilation is crucial. Consideration may be given to maintaining spontaneous breathing to minimize the risk of lung injury associated with mechanical ventilation, especially if fetal studies indicate good lung development, as in cases of left-sided defect with an O/E LHR greater than 50% and the liver in an inferior position (1).

Conventional ventilation is the preferred method of initiating mechanical ventilation. This modality has been found to reduce the duration of ventilation, decrease the need for inhaled nitric oxide (iNO) or Sildenafil, limit the use of inotropes, and reduce the likelihood of requiring ECMO (1).

Ventilatory parameters should be adjusted to maintain a PaO2 between 50 and 70 mmHg. Peak inspiratory pressures (MIP) should be as low as possible. Ideally, less than 25 cmH2O and PEEP (positive end-expiratory pressure) should be maintained between 3-5 cmH2O (see Table 2). This approach of permissive hypercapnia and "gentle ventilation" has been shown to improve survival of newborns with CDH. If MIPs greater than 28 cmH2O are required to maintain pCO2 and saturation within target ranges, switching to high-frequency oscillatory ventilation or using ECMO should be considered. Weaning from ventilation should be initiated by reducing peak pressure, followed by decreasing rate or PEEP, as long as pCO2 remains below 50 mmHg.

Hemodynamic management in newborns with CDH

Newborns with CDH often present with hemodynamic instability, so timely detection, identification of the underlying cause, and effective treatment to optimize perfusion and mitigate the effects of severe pulmonary hypertension are crucial.



A. Left CDH, Bochdalek hernia **B**. Right CDH **C**. Morgagni's CDH

Figure 1. Radiological characteristics of the different types of CDH.

The cardiovascular system in patients with CDH can be affected in several ways. One of the main factors is pulmonary hypoplasia, which can decrease pulmonary return blood flow to the left atrium during fetal life, halving the flow through the pulmonary vessels. This negatively impacts the development of the pulmonary vasculature and airway (30). In addition, the abnormal position of the cardiac axis within the fetal thorax may obstruct venous return to the right heart chambers and affect minute volume distribution in the left chambers, worsening the function of an underdeveloped left ventricle (30).

It is expected to find adrenal insufficiency in these patients. A retrospective study of 58 patients showed adrenal insufficiency, defined as a cortisol level ≤15 mcg/dL [415 nmol/L] (31). These patients, who had hepatic herniation, had more severe disease, with increased requirements for vasopressors, high-frequency ventilation (HFV), and prolonged inhaled nitric oxide (iNO) therapy. Therefore, the administration of hydrocortisone is recommended in critically ill patients with hypotension (31).

It is advisable to limit fluid management to 40 cc/kg/day during the first 24 hours of life, adjusting according to the water balance. If positive water balances persist, diuretics should be administered, provided that hypovolemia has been ruled out. An adequate supply of nutrients is essential, so parenteral feeding should start from birth until a proper enteral supply is achieved.

Table 1. Characteristics of monitored patients with CDH

	Observations
Preductal saturation	85% to 95% after the first hour of life. First two hours of life acceptable up to 70% if: improving trend without changes in ventilator, good perfusion, pH > 7.2 and adequate ventilation pCO2 less than 65 mmHg. Avoid hyperoxia.
Postductal saturation	> 70%
Heart rate	120-160
Invasive blood pressure	According to GA, in general MAP > 50 mmHg
Pulmonary pressure by echocardiogram	Normal range 18-25 mmHg
Naso- or orogastric tube	Continuous or intermittent suctioning, prevent distension and additional ipsilateral lung compression
Diuresis	> 1 mL/kg/hour

Table 2. Recommended ventilatory parameters

Parámetro	Objetivo
PIM	< 25 cmH2O
PEEP	3-5 cmH2O
Preductal saturation	80-95% first hour of life 85-95% *
Postductal	
pCO2	50-70 mmHg if pH between 7,25 to 7,40

***Note**: * En las horas posteriores de vida*

In blood pressure management, it is crucial to maintain mean arterial pressure levels ≥40 mmHg to minimize right-to-left shunt. Support includes isotonic fluids and inotropic agents such as dopamine, dobutamine, and hydrocortisone. On the other hand, if the neonate has pulmonary hypoplasia and pulmonary hypertension that is difficult to manage, along with systemic hypotension and good cardiac function, low dose norepinephrine (0.01 - 0.5 µg/kg/min) may be effective. In cases with cardiac dysfunction, Milrinone (0.35 - 0.75 µg/kg/min up to a maximum of 1 µg/kg/min) can be added after evaluation and correction of blood volume.

Management of pulmonary hypertension (PHT)

PHT occurs after birth when abnormally high pulmonary vascular resistances are maintained, resulting in decreased pulmonary flow and a right-to-left shunt through the ductus or patent foramen ovale. It is a condition of variable severity, which determines different degrees of hypoxemia. The cardiopulmonary development of most patients with PAH is normal. Still, it can also occur concomitantly with pulmonary diseases with arrested alveolar or vascular development (congenital pulmonary malformations and pulmonary hypoplasia).

The deviation of the mediastinum, with the anomalous position of the heart in patients with CDH, could explain the frequent development of PHT in these patients since it impacts the development of the fetal circulation and the heart in the intrauterine stage (30).

One of the strategies that should be considered for managing these patients is reopening the ductus arteriosus with prostaglandin E1 to protect the right ventricle from excessive overload due to increased afterload. This is associated with the concomitant use of Milrinone since this improves proper ventricular function and oxygenation index.

Vasopressin is a drug whose use is increasing in the neonatal setting, being a tool that can be included in the management of severe persistent pulmonary hypertension (see Figure 2). Vasopressin acts on different receptors; through V1 receptors found in the vascular smooth muscle cell system, it causes vasoconstriction in the skin, liver, and pancreas. Stimulation of V2 receptors causes vasodilatation in pulmonary, coronary, and CNS vessels. It is helpful in cases of refractory shock (dopamine-adrenaline-corticoids) or severe PHT with no response to standard treatment. The recommended dose is 0.0001 - 0.02 units/kg/min, up to a maximum dose of 0.04 units/kg/hour. Strict monitoring of renal function and internal milieu is recommended (32).

Regarding sedation and analgesia, using the analgesic scale and sedoanalgesia protocol of each unit where the patient is being attended is recommended, avoiding muscle blockers since they have not demonstrated beneficial effects (1). The routine use of surfactants is not recommended in term patients for whom there is no reason to think there is a surfactant deficit. It is reserved for cases of deficiency related to prematurity. A regular Doppler echocardiogram is recommended as part of the hemodynamic management of these patients. At birth and in the first hours of life, its importance lies in defining cardiac anatomy and function, estimation of the McGoon Index, and severity of pulmonary hypertension. In the postoperative period, the heart's position must be evaluated, and its return to a normal position after surgical repair of the defect is associated with unfavorable evolution (30).

In addition to determining the position of the heart, which we have already mentioned may be altered due to the herniation of the abdominal contents at the thoracic level, the development of the ventricular mass may also be changed, so it is essential to measure it using Doppler echocardiography. The decrease in left ventricular mass has been recognized as a factor of worse prognosis. Another echocardiographic finding that could correspond to decreased left ventricular mass is the ratio between pulmonary and aortic valve flow compared to healthy fetuses (30,33). Finally, at a later stage, the Doppler echocardiogram performed at two to three weeks of life has predictive value for adverse outcomes if there is persistent pulmonary hypertension beyond 14 days of life.

USE OF EXTRACORPOREAL MEMBRANE OXYGENATION

ECMO is used as rescue therapy in newborns with CDH who remain unstable despite optimal medical management. Although the evidence on its usefulness is contradictory, case

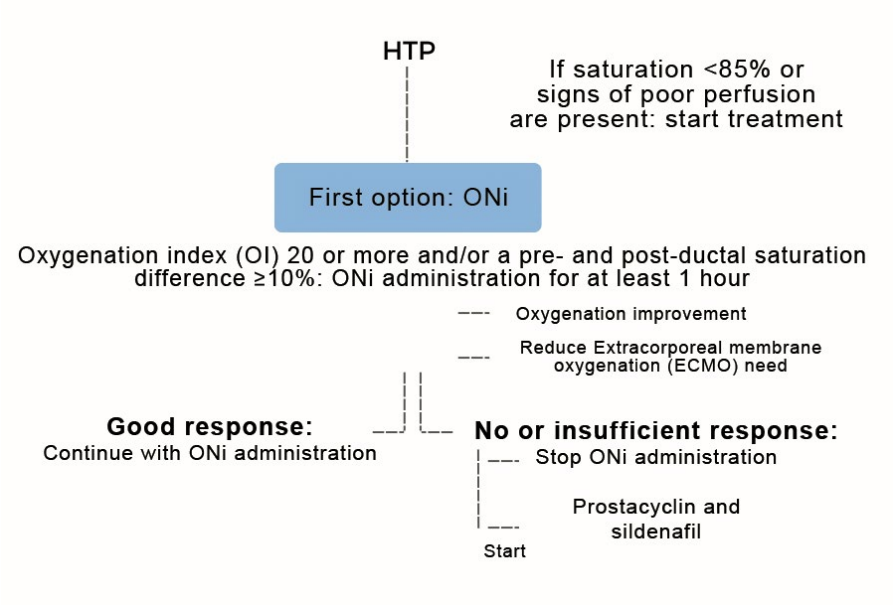


Figure 2. Management of pulmonary hypertension

series suggest its benefit in patients with high severity (34). Approximately 30 % of newborns with CDH receive ECMO, this being the most common cause of ECMO for respiratory failure in neonates (35).

The current trend is toward early implementation of ECMO to stabilize the patient prior to surgery (34-36), usually in combination with gentle ventilation and permissive hypercapnia, which helps minimize ventilator-associated lung injury (36). Mortality in this population is high, with a reported Extracorporeal Life Support Organization (ELSO) survival of 51%.

The indications recommended by ELSO for initiating ECMO therapy include hypoxia, preductal saturation sustained below 80-85%, metabolic or respiratory acidosis, hypercapnia with pCO2 greater than 70, hypotension not responsive to intravenous fluids and inotropic support, among others (34-36) (see Figure 3). Relative contraindications include additional major congenital disabilities, lethal chromosomal abnormalities, severe intraventricular hemorrhage, prolonged mechanical ventilation with high pressures, low birth weight, and gestational age less than 34 weeks (34-36).

Regarding the type of ECMO, there are no significant differences in survival between veno-arterial (VA) and veno-venous (VV) ECMO. VA ECMO could offer some advantages since it could be used in children of lower weight, and due to its characteristics, it would offer advantages in patients with associated cardiac dysfunction (34).

Complications associated with ECMO include intracranial bleeding and seizures (more common in VA ECMO) and decreased renal perfusion (more frequent in VV ECMO) (34, 36). The current trend is to use ECMO in patients with increasingly severe clinical profiles, which could explain the observed high mortality rates. However, randomized clinical trials and standardized clinical guidelines are needed to improve the quality of evidence and the management of these patients.

SURGERY IN NEWBORNS

Surgery aims to reposition the viscera in the abdominal cavity and close the diaphragmatic defect. Surgical intervention should be considered when the patient is hemodynamically stable and maintains a preductal oxygen saturation between 85-95% (1). In those patients requiring ECMO, a study by Dao et al. suggests that early surgical repair improves survival compared to late repair (37).

Closure of the defect can be performed in different ways, including first intention closure with sutures, closure by placement of a patch of prosthetic material such as Gore-Tex, or closure with the use of autologous latissimus dorsi tissue or abdominal wall muscles. The latter is reserved for patients with significant defects with increased tension that primary repair may compromise thoracic distensibility (38,39). However, patch placement has certain complications, including the risk of infection, chest wall deformity (pectus excavatum, pectus carinatum, and thoracic scoliosis), and increased risk of recurrent hernia. In a meta-analysis performed by Heiwegen et al. (40) to evaluate the incidence of surgical complications in both types of CDH closure (first intention versus patch), they conclude that patients who underwent patch surgery have a 2.8 times higher risk of developing recurrent hernia, compared to patients who underwent first intention closure 2.5 times higher risk of developing a chylothorax and two times higher risk of small bowel obstruction.

There still needs to be a consensus on the approach; the options are endoscopic surgery (by laparoscopy and thoracoscopy) versus conventional surgery (41). Laparotomy is the approach of choice in recent years due to the lower risk of recurrence; however, minimally invasive techniques are associated with a lower risk of postoperative adhesions and a shorter length of hospital stay. The choice of technique should be individualized (37). A meta-analysis of the effectiveness of endoscopic surgery concludes that there is a higher recurrence rate than open surgery. For this reason, thoracoscopy should not be the technique of choice for newborns (40).

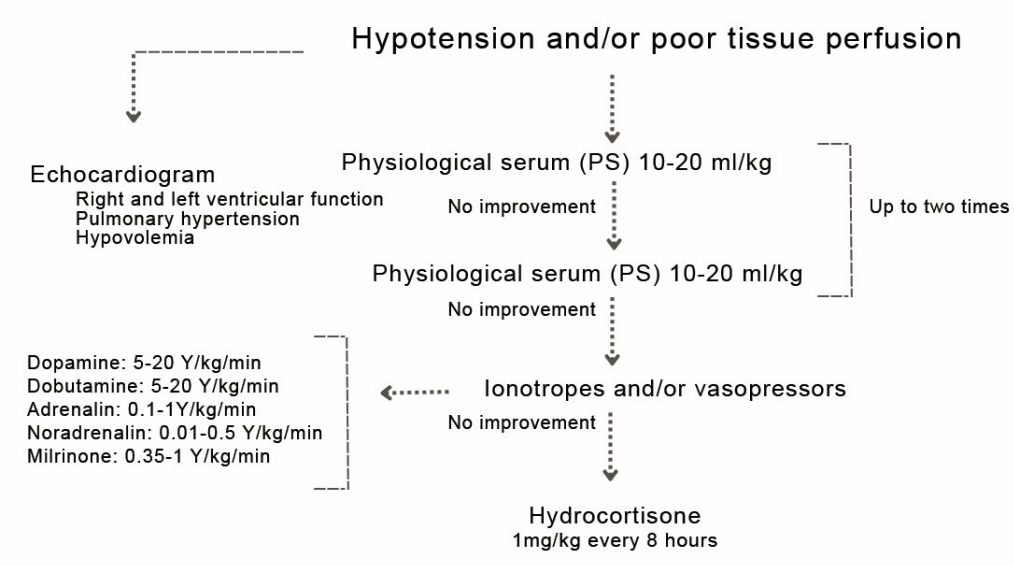


Figure 3. Manejo de la hipotensión y dosis de inotrópicos

POSTOPERATIVE

Post-surgical mechanical ventilation

The parameters and goals of postoperative mechanical ventilation are usually consistent with those established before surgery. Weaning from mechanical ventilation is commonly achieved within the first 48 to 72 hours after surgery (42). However, the surgical procedure may reduce the compliance of the respiratory system, which in turn may extend the need for mechanical ventilatory support (42), thereby increasing the risk of ventilator-associated complications such as barotrauma and oxygen toxicity injury.

Complications related to barotrauma

A frequent complication associated with barotrauma is pneumothorax, which can occur both preoperatively and postoperatively. Management of this complication may require placement or revision of a pleural drain. In hypertensive pneumothorax, emergency drainage is required and performed by the neonatology or surgical team.

Nutrition and enteral feeding

Reintroduction of enteral feeding is postponed until the patient demonstrates clear gastric residuals of less than 20 cc per day, in addition to stool or hydroaerial noises. Initiation of feeding is gradual, keeping the orogastric tube in place during surgery and placing the patient in an elevated position of 45º (43). It is also recommended to start antireflux therapy when initiating enteral feeding.

Postoperative supportive care

It is common for infants with CDH to require postoperative support, including increased volume support and infusion of inotropes and vasopressors. These interventions respond to hemodynamic changes resulting from normalization of venous return and minute volume after surgical correction of the defect and return of visceral contents to the abdominal cavity (30). These changes may result in a fall in postductal saturation due to the right-to-left shunt generated by pulmonary hypertension (30). If hypoxemia does not improve with mechanical ventilation, inhaled nitric oxide (iNO) initiation is indicated. In addition, in cases of severe pulmonary hypoplasia, patients may experience postoperative rebound pulmonary hypertensive crises, which may benefit from the use of Sildenafil if they do not respond to iNO (30).

Other Postoperative Complications

Additional complications that may arise after surgery include bleeding, chylothorax, bowel obstruction, gastroesophageal reflux, and hiatal hernia.

PROGNOSIS

Postnatal survival rate

Postnatal survival rates for newborns with diaphragmatic hernia treated at tertiary centers have shown a significant increase, with reported figures ranging from 70 to 92 % (44, 45). It is important to note that these data refer mainly to term newborns treated in specialized centers with access to therapies such as extracorporeal membrane oxygenation.

Factors influencing prognosis

Several factors impact the prognosis of these patients, including:

- Gestational age: Survival tends to be lower in preterm infants (46).
- Presence of other congenital disabilities: Concomitant cardiac defects may complicate prognosis.
- Persistent pulmonary hypertension: Especially that which is refractory to the usual treatments.
- Care Center: The facilities and experience of the center can significantly influence outcomes.
- Need for transfer: Newborns who require transfer to another center for specialized care may face additional risks.
- Preductal oxygen saturation: A preductal oxygen saturation below 85% during the first 24 hours of life is associated with reduced survival (47).
- Defect size and location: Right-sided defects are usually larger and often require more complex repairs, such as patching or use of muscle tissue.

FOLLOW-UP

Comprehensive long-term follow-up of patients discharged after congenital diaphragmatic hernia is crucial (48, 49). Due to the diversity of comorbidities associated with this condition, an interdisciplinary team should carry out this follow-up, including neonatologists, pediatricians, pulmonologists, surgeons, gastroenterologists, otolaryngologists, and nutritionists. These comorbidities may include an increased risk of neurological and developmental disorders, hearing loss, chronic obstructive pulmonary disease, pulmonary hypertension, recurrent pneumonia, bronchial hyperresponsiveness, growth problems, gastroesophageal reflux (which may affect up to 80% of these patients), intestinal occlusion, volvulus, hernia recurrence, and various thoracic complications.

Genetic counseling

Genetic counseling should be individualized, especially in cases with associated chromosomal disorders, since the risk of recurrence is high. In the case of isolated diaphragmatic hernia, the risk in the subsequent pregnancy is about 2 % (50).

Conclusion

Congenital diaphragmatic hernia is a complex and challenging condition characterized by protrusion of abdominal organs into the thoracic cavity, leading to pulmonary hypoplasia and often associated with other anomalies. Its management requires a multidisciplinary approach ranging from prenatal diagnosis and intrauterine treatment in severe cases to specialized postnatal management, including ventilatory and surgical support.

Progress in prenatal detection and interventional techniques has significantly improved survival rates. However, these advances also bring challenges in long-term management, given the variety of complications and comorbidities associated with the condition. Postoperative management and long-term follow-up are crucial to address the multiple sequelae and to ensure optimal quality of life.

In summary, although successfully treated in many cases, congenital diaphragmatic hernia remains a considerable challenge in neonatal and pediatric medicine, requiring an integrated and personalized approach for each patient.

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