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CONGENITAL DIAPHRAGMATIC HERNIA: GENERAL OVERVIEW AND MEDICAL INTERVENTIONS

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Abstract: The present article is a systematic review of the literature using PubMed and LILACS databases. 10 articles were selected that were in accordance with the proposal. Congenital diaphragmatic hernia (CDH) is characterized by the absence or failure of the diaphragm to close after 10 weeks of gestation, an age at which it must already have its formation process complete and without defects. Its etiology is still poorly understood, but it is presumed to be multifactorial. This communication between cavities allows abdominal organs to move into the chest, putting pressure on the lungs and preventing their proper development. The main consequences of CDH are variable degrees of hypoplasia and pulmonary hypertension, gastroesophageal reflux and intestinal obstruction, leading to high morbidity and mortality. For early diagnosis and effective management of cases, it is essential to identify and study diagnostic methods, such as ultrasound and magnetic resonance imaging; of the main pre (Endoluminal Tracheal Occlusion or "FETO") and postnatal (Extracorporeal Membrane Oxygenation or "ECMO") medical interventions, in addition to current protocols for oxygenation and pH management after birth.
Keywords: "Congenital Diaphragmatic Hernia"; "Pulmonary Hypoplasia"; "Pulmonary hypertension"; "ECMO"; "FETUS".

INTRODUCTION

Congenital Diaphragmatic Hernia (CDH) is a congenital defect of the diaphragm that occurs in about 1:3000 live births, resulting from a failure in the separation of the abdominal cavity and the thoracic cavity during critical stages of embryonic development. Thus, the organs of the abdominal cavity are allowed to herniate into the thoracic cavity, preventing the normal development of the lung ipsilateral to the defect, which also leads to inadequate development of the terminal bronchioles, alveoli and pulmonary vessels, leading to severe respiratory failure, hypoplasia pulmonary hypertension and pulmonary hypertension at birth. It predominantly affects newborn males (1.5:1), but there is no difference in incidence between races. Anatomically, the occurrence of posterolateral (or Bochdalek's) hernia is more frequent, with the majority occurring on the left (80%). It occurs less frequently on the right, bilaterally, anteriorly (or Morgagni's), or centrally. About 30% of patients have associated chromosomal anomalies, such as trisomy 13 or 18 or other associated defects, the most frequent being cardiac.

The pathogenesis of CDH is complex and poorly understood, probably being multifactorial in origin. The development of the diaphragm occurs around the 4th to the 12th week of gestation, derived from embryonic structures such as the septum transversus and the pleuroperitoneal leaflet, which fuse under normal conditions, along with the growth of the esophageal mesentery and muscle tissue that grows into the esophagus. from the body wall. The union of these structures is responsible for forming the muscular part of the diaphragm, which must be fully formed around the 9th week of pregnancy. If these structures do not go through the proper fusion process, congenital diaphragmatic hernias occur, in which the viscera contained in the abdominal cavity herniate into the thoracic cavity, so that the abdominal organs present within the thorax (generally the liver, stomach and intestine) act as masses that prevent the lung from growing, compressing the organ and compromising its proper development. This compression leads to bilateral pulmonary hypoplasia, as there is mediastinal shift and compression of the contralateral lung also occurs. There is also hypertrophy of the middle layer of pulmonary

arterioles and increased pulmonary vascular resistance, a process responsible for leading to pulmonary hypertension which, depending on its severity, can lead to the persistence of the fetal pattern of circulation, metabolic and respiratory acidosis and neonatal death.

There is a hypothesis that postulates that the cause of CDH is primary pulmonary hypoplasia, occurring before the formation of the diaphragm, with environmental and genetic alterations as precedent. In turn, this pulmonary alteration would lead to diaphragmatic malformation. As a consequence, the ipsilateral lung of the diaphragmatic defect would still suffer from the interference caused by the compression of the lung parenchyma by the herniated organs.

METHODOLOGY

The literature review was carried out by consulting the PubMed and LILACS databases, with the keywords: "congenital diaphragmatic hernia", and with the filters: "Books and Documents, Review, Systematic Review, in the last 10 years, English, Portuguese, Humans", obtaining 324 results on the Pubmed platform and 20 on the Lilacs platform. Ten articles were selected for the preparation of a systematic literature review. The criteria for selecting the articles were: to be written in Portuguese or English, to have been written between the years 2012 and 2022, to be a case report or book chapter and to be in accordance with the work proposal.

DISCUSSION

PATHOPHYSIOLOGY OF COMPLICATIONS

There are three main complications due to failure of the diaphragm to close in the eighth week of embryonic life: herniation of the intestine into the thoracic cavity, hypoplasia associated with pulmonary hypertension, and cardiac deformity. The intestine, which was in the process of growing into the umbilical cord, returns to the abdomen in the tenth week and herniates into the thoracic cavity due to intra-abdominal pressure. Being in the thorax, the intestine will not undergo its natural process of intra-abdominal rotation and fixation and will begin to compress the lungs. This compression ends up causing developmental arrest at various stages, resulting in pulmonary hypoplasia.

Pulmonary hypoplasia is characterized by a reduced number of bronchioles and alveoli (less pneumocytes II and consequently less surfactant). In addition to the number of arteries being lower than normal, they have a smaller diameter and thick muscular walls, making it difficult to exchange respiratory gases. These modifications of the air space originate alterations in the pulmonary vessels, a decrease in the number of these vessels, hyperplasia of the tunica media, peripheral extension of the muscle towards the intra-acinar arterioles and thickening of the tunica adventitia.

The hypertrophy of the wall of the small pulmonary arteries causes an increase in pulmonary vascular resistance and conditions arteriolar hyperreactivity, leading to the appearance of pulmonary hypertension and persistence of fetal circulation, with maintenance of the right-to-left shunt via the foramen ovale and ductus arteriosus after birth. Pulmonary hypoplasia and vascular changes are more intense in the ipsilateral lung but are also seen, to a lesser extent, in the contralateral lung, depending on the degree of mediastinal shift.

DIAGNOSTIC METHODS OF DIFFERENT TYPES OF HDC

CHD is classified into Bochdalek's Hernia, Morgagni's Hernia and Esophageal Hiatus Hernia. The clinic and the physical examination are essential for the diagnosis, which must be fast and accurate.

Overall, the diagnosis is usually an unexpected finding on routine morphologic ultrasound performed in the second trimester. Thus, the prenatal diagnosis can be made in 40-90% of cases by Ultrasonography, from the 18th week of gestation, although there are references that mention the possibility of detecting CDH by ultrasound at 15 weeks of gestation. Maternal polyhydramnios is present in up to 80% of cases, due to the kinking of the abdominal esophagus or stomach, which prevents swallowing and absorption of amniotic fluid by the fetus. Plain chest and abdominal X-ray postnatally will show bowel loops in the chest, mediastinal shift, and little gas in the abdomen. Simple radiological examination, in some cases, can be confused with imaging of congenital lung cysts. Pulmonary hypertension is confirmed by echocardiography.

Regarding the clinic and physical examination, in the postnatal period, there is respiratory failure in the first 24 hours of life, excavated abdomen associated with thoracic asymmetry, arterial hypotension due to movement of the trachea and great vessels next to the hernia, with return obstruction venous to the heart, generating head and neck hypertension. On auscultation, there is absence of unilateral breath sounds, translocated heart sounds and presence of bowel sounds in the chest. In cases that are not diagnosed during the prenatal period, the infant will present, in the postnatal period, a clinical condition compatible with the aforementioned physical examination, in clear acute respiratory distress.

To diagnose the different types of HDC, we seek to identify the uniqueness of each type. In the case of Bochdalek's hernia, the echographic findings that suggest its diagnosis are: in cross-sections of the thorax in the four-chamber view of the heart, the existence of deviation of the heart and mediastinum is visualized, in addition to the presence of stomach, intestinal loops or liver. In the longitudinal sections, the absence of integrity of the left and/or right hemidiaphragm is seen. In addition to the echographic findings, indirect signs of Bochdalek's hernia are the presence of paradoxical movements of the abdominal viscera towards the ipsilateral hemithorax during respiratory movements, the absence of visualization of the stomach or gallbladder in the abdomen, the anomalous position of the stomach or gallbladder biliary tract, liver or umbilical vein in the abdomen and the presence of polyhydramnios.

In Morgagni's hernia, there is usually liver herniation. The stomach may remain below the diaphragm and ascites, pleural effusion, or pericardial effusion may occur. There is a certain degree of difficulty in identifying herniation from the liver into the thoracic cavity, due to the similarity in echogenicity between the liver and the lung. Thus, the use of color Doppler and spectral Doppler to verify the presence of the portal vein at or above the diaphragm is an interesting tool for diagnosing this type of hernia. In addition, visualization of the portal vein at or above the diaphragm and the presence of an intrathoracic stomach in a posterior position are considered, by some authors, to be the best predictive factors for the presence of an intrathoracic liver. Nuclear Magnetic Resonance (NMR) to confirm the presence of intra-thoracic liver can be used after using the aforementioned Doppler techniques; and Doppler flowmetry visualization of the mesenteric vessels extending into the thoracic

cavity also confirms the diagnosis of CDH.

Hiatal hernias are rare in children. Symptoms are similar to those in adults with retrosternal pain and vomiting. In paraesophageal hernia, when there is a large portion of the intrathoracic stomach, a gastric volvulus and its consequences may occur. Gastroesophageal reflux does not always occur when there is a hiatal hernia. The diagnosis is made by contrast radiography of the esophagus and stomach, which will show gastric herniation.

ENDOLUMINAL TRACHEAL OCCLUSION (FETO)

FETO (Fetoscopic endoluminal tracheal occlusion) or Fetal Tracheal Occlusion is a surgery that must be indicated for only a few cases of HDC. First, the baby's chances of surviving without intrauterine intervention must be analyzed, that is, when the severity markers are present. They are: when part of the liver also rises to the thorax and/or the ratio of lung area to head perimeter is unfavorable. These markers are the echographic findings identified in hernias in which a large amount of abdominal viscera has risen to the thorax, causing severe obstruction to proper lung development, making the case potentially fatal after birth. In these situations, where the baby will have virtually no chance of survival, Fetal Tracheal Occlusion is attempted to expand the lung

To perform the FETO procedure, the pregnant woman undergoes epidural anesthesia and sedation, while the fetus undergoes general anesthesia. Through puncture of the skin of the maternal abdomen, the fetoscope and a micro introducer catheter coupled to the empty balloon are introduced. By direct visualization, the amniotic sac is navigated and, through the fetal mouth, the larynx is reached and the fetoscope-microcatheter-balloon set is introduced into the tracheobronchial tree. It progresses to the bifurcation of the bronchi, confirming the tracheal position. Then, the set is withdrawn to a position immediately inferior to the larynx, where the balloon is inflated and detached from the microcatheter, which remains at this level and occludes the trachea. The liquid, then retained in the lungs, induces lung enlargement. This surgery does not require incisions and is classified as minimally invasive.

Fetal Tracheal Occlusion was only performed in humans after a series of tests with positive conclusions in animals. In these tests, it was proven that the surgery ensured the development and recovery of type II pneumocytes and the production of pulmonary surfactant even during the intrauterine period.

The length of gestation also impacts the decision to perform the surgery, which is usually performed between the 26th and 29th week. Removal of the Endotracheal Balloon occurs between the 32nd and 34th week of pregnancy, because prolonged treatment can lead to a decrease in type II pneumocytes and production of pulmonary surfactant. It is also known that the balloon causes mild alterations in the trachea, with local inflammatory changes, and limited epithelial defects, such as a decrease in the contact surface with air.

EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

HDC is one of the most common indications for starting ECMO (Extracorporeal Membrane Oxygenation), given that this extracorporeal therapeutic modality allows the temporary stabilization of the patient in pulmonary and/or cardiac failure.

Postnatal factors associated with severe pulmonary hypertension (low PaO2), pulmonary hypoplasia (high PaCO2), large defect requiring *patch* repair, ventricular

dysfunction, and the need for vasoactive agents and/or ECMO are associated with increased mortality. Overall mortality, however, is significantly higher compared to that reported in large centers where extracorporeal membrane oxygenation is available.

Common indications for ECMO in infants with CHD include refractory hypotension secondary to left ventricular systolic dysfunction, preductal saturation <80% refractory to ventilator manipulation and medical therapy, oxygenation index > 40, peak inspiratory pressure > 25cm, resistance to blood pressure hypotensives, severe air leak and mixed acidosis (pH < 7.2). The use of ECMO is generally restricted to babies weighing more than 2 kg and gestational age > 34 weeks, in the absence of significant intracranial hemorrhage, chromosomal abnormalities, or other congenital anomalies.

Prenatal diagnosis of CDH, the best imaging modalities, and the use of fetal echocardiography can provide information that helps determine survival success and the need for ECMO. Magnetic resonance imaging has demonstrated a superior predictive value than ultrasound in assessing lung volume, with the percentage of predicted lung volume (PPLV) < 15% and total lung volume (TLV) < 20 mL seem to be strong predictors of poor outcome and increased use from ECMO. Furthermore, early assessment of cardiac function by echocardiography in newborns with CHD shows that decreased cardiac function is a better predictor of ECMO need than the severity of pulmonary hypertension. Furthermore, gestational age at delivery may be inversely correlated with the need for ECMO and liver herniation indicates a possible greater defect in the diaphragm, with a greater impact on lung development and a greater likelihood of needing extracorporeal life support.

In contrast, patients with a pre-ECMO PCO2 < 70 mmHg do not have a good survival rate, even with the use of extracorporeal life support. Therefore, the decision to offer ECMO to a patient with lung failure is challenging, as it still does not show positive results in many cases and adds many costs to the treatment.

With regard to possible complications, studies identify CHD survivors who underwent ECMO as the highest risk group for developing gastroesophageal reflux, in addition to the fact that ventilation time and ECMO use are significant predictors of future neurological deficits. Even so, the improvement in survival of these patients shows a promising trend. Studies show that the use of ECMO allowed the reversal of hypoxia, hypercapnia and acidosis, allowing the lung to remain at rest for several days, which may reduce local hypertension and restore gas exchange capacity. Cardiopulmonary collapse that accompanies severe left ventricular failure in CHD has thus been best treated with ECMO.

Finally, maternal transfer to a center capable of using ECMO before delivery is recommended, as it may improve survival for the most severely affected newborns.

OXYGENATION MANAGEMENT

Due to pulmonary hypoplasia and hypertension, patients with CDH are difficult to manage ventilation, in addition to presenting right-to-left shunt, hypoxia, hypercapnia and mixed acidosis as a consequence of pulmonary hypertension. Postnatal management has evolved in recent years and now includes low parameter ventilation, permissive hypercapnia, surgical repair delayed until after clinical stabilization, and use of inhaled nitric oxide (iNO), high frequency oscillatory ventilation (HFOV) and ECMO as therapies rescue.

It is recommended that delivery take place in a fully equipped center capable of performing newborn resuscitation. While still in the delivery room, infants with severe CHD must be intubated. Mask ventilation must be avoided as it leads to gastric distention of the intrathoracic viscera. Also, in order to avoid complications caused by gastric distention, gastric decompression can be performed via a suction tube or by inserting an orogastric tube.

Pulmonary hypertension is recognized as the major cause of morbidity and mortality in newborns with CHD, and today it is understood that CHD is a physiological emergency, not a surgical one, so that the adequate initial management of CHD is primarily aimed at the control of pulmonary hypertension. The overarching goal of initial care is to provide oxygenation and ventilation without causing further damage to poorly developed lungs or triggering vasospasm. This means accepting lower oxygen saturation rates and hypercapnia while trying to keep the pH above 7.2. Also includes meticulous control of mechanical ventilation.

Mechanical ventilation in CHD follows the principle of low parameter ventilation, which incorporates peak insufflation pressure control, limiting ventilation pressure while tolerating an oxygen saturation of 85% and an increase in blood pCO2 (permissive hypercapnia). This strategy promotes adequate oxygenation while avoiding lung injury from positive pressure. In children with resistant pulmonary hypertension, allowing a PCO2 of 40-60 mmHg (permissive hypercapnia) improved the survival rate, allowing management with lower volume and pressure on mechanical ventilation. Several studies have shown better results with these strategies despite using different ventilation modes.

High-frequency ventilation (HFOV) has also been widely used, as it allows adequate oxygenation and elimination of CO2 at low pressures, reducing the risk of iatrogenic barotrauma, having shown favorable results in infants with CHD, in addition to representing a pattern closer to normal breathing. physiology of the infant. (HFOV) has been used in perinatal management as "rescue therapy" before ECMO use and as a primary ventilatory strategy to improve survival in patients with CDH.

Adequate blood pressure is important for adequate perfusion of the lung parenchyma and the rest of the body. Severe pulmonary hypertension can lead to right-sided heart failure in young children, resulting in a vicious cycle in which there is increased pulmonary vascular resistance, reduced lung perfusion, and worsened acidosis and oxygenation. Management of right heart failure consists of the use of inotropes (dopamine being the most common agent) and post-ventricular load reduction through vasodilators, the main ones being inhaled nitric oxide (iNO) and sildenafil.

iNO therapy has shown no reduction in ECMO requirements or mortality in CDH in published studies, whereas sildenafil has shown promise as a pulmonary vasodilator, with positive results in small numbers of CDH case series; however, drug availability and therapeutic efficacy may be affected by irregular absorption from the gastrointestinal tract. No prospective randomized trials have shown improvement in patients with severe CHD using these measures.

Currently, preoperative stabilization is prioritized, opting to perform the surgery only after optimization of the respiratory and cardiac status.

SURGICAL MANAGEMENT

The planning of surgical repair in CHD depends on the clinical stability of the infant, especially respiratory and cardiac stability, with regard to adequate pre-ductal saturation, normotension, blood pH stability and pulmonary artery pressure lower than systemic pressure.

The objective of the procedure is to repair the diaphragmatic failure, and the technique used depends on the extent of the failure and the amount of herniated content. Primary closure of the diaphragm is feasible in 60 to 70% of cases, where a subcostal incision is made to correctly reposition the herniated viscera and close the tension-free gap. In cases where the defect is more extensive, it is necessary to use a synthesis material, such as polytetrafluoroethylene screens. Other types of material have been studied to correct the defect, but there are still no studies that demonstrate the superiority of a specific type.

The postoperative period of CDH correction requires caution, given the risk of surgery failure and hernia recurrence. Important risk factors include large defects, use of a minimally invasive technique and the need for a protein patch, with early rupture of the patch occurring in 50% of cases. Postoperative complications related to the procedure, such as chylothorax, pneumothorax and abdominal compartment syndrome, also require careful diagnosis and can be potentially fatal depending on the severity of the case.

CONCLUSION

Congenital diaphragmatic hernia (CDH) is a challenging condition that affects proper lung development and can have serious consequences for affected newborns. Despite recent advances in treatment and the apparent improvement in the survival of these patients in recent decades, mortality and morbidity rates remain high, highlighting the need to deepen knowledge about the ideal approach for affected children.

Early clinical suspicion and knowledge of the pathology are fundamental for an accurate and timely diagnosis, both in the prenatal and postnatal periods. Currently, exams such as morphological ultrasound and ultrasonography allow a quick and accurate intrauterine diagnosis, expanding the possibilities of intervention. The FETO technique has been used in selected cases to expand the lungs of the fetus before birth. In the postnatal period, advanced management aims to control pulmonary hypertension and optimize oxygenation, using strategies such as low parameter ventilation, permissive hypercapnia, and high frequency oscillatory ventilation (HFOV).

In addition, a better understanding of left ventricular hypoplasia and myocardial dysfunction associated with CDH allowed improvements in hemodynamic and pH management. Minimally invasive surgical techniques and extracorporeal life support (ECMO) have also been explored to reduce morbidity in fragile newborns. It is essential that these procedures be performed in highly specialized centers with experienced medical staff and adequate infrastructure.

The continuous joint work between professionals from different specialties and scientific research are crucial to advance the understanding and treatment of this complex condition, providing better care and prognosis for children with CDH. Carrying out this systematic review allowed the synthesis and critical analysis of available scientific evidence on CDH. This rigorous and unbiased approach provides a comprehensive view of the current state of knowledge, serving as a basis to guide informed decision-making by health professionals, educators and others, contributing to strengthen knowledge and improve the therapeutic approach to CHD.

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