orphanaesthesia

Anaesthesia recommendations for patients suffering from

Congenital diaphragmatic hernia

Disease name: Congenital Diaphragmatic Hernia (CDH)

ICD 10: Q 79.0

Synonyms: CDH (congenital diaphragmatic hernia)

In congenital diaphragmatic hernia (CDH) the diaphragm does not develop properly so that abdominal organs herniate into the thoracic cavity. This malformation is associated with lung hypoplasia of varying degrees and pulmonary hypertension. These are the main reasons for mortality. CDH can also be associated with other congenital anomalies (e.g. cardiac, urologic, gastrointestinal, neurologic) or with different syndromes (Trisomy 13, 18, Fryns-Syndrome, Cornelia-di-Lange-Syndrome, Wiedemann-Beckwith-syndrome and others). This malformation may be detected by prenatal ultrasound or MRI-investigation. There are several parameters which correlate prenatal findings with postnatal survival, need for ECMO-therapy, need for diaphragmatic reconstruction with a patch and the development of chronic lung disease. These findings include; observed-to-expected lung-to-head-ratio on prenatal ultrasound, relative fetal lung volume on MRI and intrathoracic position of liver and / or stomach in left-sided CDH.

Depending on disease-severity, treatment can be challenging for neonatologists, paediatric surgeons and anaesthesiologists as well.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Typical surgery

According to the CDH-EURO-Consortium there is a consensus on surgical repair of diaphragmatic hernia after sufficient stabilization of the neonate (delayed surgery). The definition of stability, determining readiness for surgery, depends on several parameters that have been proposed (see below).

Depending on the size of the diaphragmatic defect either a primary reconstruction of the diaphragm can be achieved or prosthetic patches or muscle-flaps have to be used to achieve closure of the defect. Different patch materials have been used including the use of non-absorbable patch-material which reduces the risk of hernia recurrence. Surgery can either be performed via an open abdominal (and possibly thoracic) approach, or with minimally-invasive methods (laparoscopy, thoracoscopy). Minimally-invasive techniques should only be applied in patients who can tolerate CO_2-insufflation. The timing of surgical repair will be determined by stability of the patient. Factors to consider are: severity of lung hypoplasia, need for ECMO-therapy, iNO requirement and amount of inotropic support. Also it has to be taken into account, that patch-implantation in large defects is technically more challenging and takes longer operating times. Recurrence-rates have been reported to be higher after minimally-invasive reconstruction of the diaphragm.

On the other hand, in open surgery there is a risk for intestinal obstruction due to adhesions, while recurrence is mostly limited to large diaphragmatic defects requiring patch repair, which may require secondary surgery. In neonates with large diaphragmatic defects and a small abdominal cavity, the implantation of an abdominal wall patch may be needed to prevent abdominal compartment syndrome. A median laparotomy approach in severely affected children is often used for this reason. Further associated gastrointestinal malformations can also be taken care of at the same time. The abdominal wall patch is usually removed later in life, while the prosthetic patch in the diaphragm will be left in place. Secondary surgery later in life may also be necessary, for example for severe gastro-esophageal reflux with placement of a percutaneous feeding tube, hiatoplasty or fundoplication. To perform a fundoplication at the time of primary surgery does not seem to be beneficial in the long-term.

Type of anaesthesia

Surgery is always performed under general anaesthesia. In our institution, we prefer leaving the child on the ventilator used in the intensive care unit. We therefore use total intravenous anaesthesia (TIVA), mainly with Midazolam (0.03-0.1mg/kg/h) and Fentanyl (4-10µg/kg/h). Muscle relaxation is provided for the duration of surgery using Rocuronium or Vecuronium. To our knowledge no reports about the use of regional anesthesia in infants with CDH exist. Additional epidural anesthesia generally is possible in these cases, for open abdominal repair caudal anesthesia appears reasonable. Some centres perform intercostal block after thoracoscopic surgery. Considering the need for postoperative mechanical ventilation over a period of several days and the thereof resulting need for sedation, we currently don`t see considerable benefit from regional anesthesia in this group of patients.

Preoperative management in the intensive care unit:

Preoperative management is one of the key factors, probably the most important one, in caring for infants with CDH. The "CDH Euro Consortium Consensus Statement" (1) provides a good overview of the accepted standard of care. Intubation immediately after birth and avoidance of bag-mask-ventilation are recommended for prevention of bowel insufflation. An oro- or nasogastric tube with continuous or intermittent suction should be placed to reduce bowel distension which may increase lung compression. The key principles are avoidance of

high airway pressures and establishment of adequate perfusion and oxygenation, measured by preductal oxygen saturation. Conventional mechanical ventilation is recommended as the initial strategy with ventilator settings of a peak inspiratory pressure < 25 cm H_20, application of PEEP (3-5 cm H_2O), a ventilation frequency of 40-60/min and tidal volumes of 5-6 ml/kilogram body weight (2). The ventilation strategy is aiming for a preductal saturation of 85-95% and arterial CO_2 levels between 50 and 70 mmHg (pH > 7.2). High frequency oscillatory ventilation is an alternative in case of failure of conventional mechanical ventilation. A preductal arterial line and central venous access should be inserted as soon as possible. Blood pressure should primarily be kept at normal values for gestational age. In case of hypotension a crystalloid fluid bolus of 10-20ml/kg can be given twice within the first two hours. If necessary, this should be followed by inotropic and/or vasopressor support. Signs for appropriate end-organ perfusion are a heart rate within the normal range, urine output > 1ml/kg/h and lactate concentration < 3mmol/l. Increasing systemic vascular resistance can be used as a treatment option in case of substantial right-to-left-shunting. Treatment of pulmonary hypertension should be initiated if preductal saturation falls below 85%, pre- and postductal saturation difference is > 10% and/or there are signs of poor end-organ-perfusion. Method of choice should be the initiation of inhaled nitric oxide (iNO). If no or an insufficient response is seen, iNO should be stopped after 1h. Intravenous prostacyclin or phosphodiesterase type 5 inhibitors can be used as further treatment. Criteria for initiation of ECMO can be found in detail in the mentioned Consensus Statement (1) .

Surgery should be performed electively. Controversies still exist regarding patients on ECMO. While some centers prefer to wean the children from ECMO before performing surgery others report favourable outcomes when operating while on ECMO (3) (4) (5). If a patient needs to be operated upon on ECMO, early during the ECMO course may be the ideal time as the ECMO circuit is less pro-coagulant. The CDH EURO Consortium recommends performing surgery after clinical stabilization defined as the following (1):

- Mean arterial blood pressure normal for gestation
- Preductal saturation levels of 85–95% on F_iO_2 below 50%
- Lactate below 3 mmol/l
- Urine output more than 1 ml/kg/h.

Necessary additional diagnostic procedures (preoperative)

Echocardiography should be performed within the first 24h after birth. Goals of the investigation are ruling out cardiac anomalies, assessing right ventricular function and determining the amount of pulmonary hypertension. Echocardiography may be repeated during the course of the disease to follow-up pulmonary hypertension. A chest X-ray should be obtained for evaluation of mediastinal shift. Besides a complete physical examination, ultrasound assessment of the brain and kidneys to rule out anomalies should be performed. Preoperative assessment is completed by laboratory studies including blood count, kidney function, coagulation studies and infection parameters. Levels of B-type natriuretic peptide (BNP) can be used as a prognostic marker for development of pulmonary hypertension and the need for ECMO (1) (6) (7).

Antenatally used markers of severity for CDH are left- vs. right-sided hernia, observed to expected lung-to-head-ratio and percent liver herniation (8). For postnatal prognostication, a prediction model based on data from the CDH Study Group can be used. This model evaluates a CDH patient's risk for mortality based on: birth weight, 5-minute Apgar score, the

presence of severe pulmonary hypertension, and the finding of a cardiac or chromosomal anomaly and stratifies neonates into low, intermediate or high risk mortality groups (9).SNAP II Score (Simpilified neonatal acute Physiology Score) is a validated measure of illness severity in newborns and can be used as a prognostic index in infants with CDH. It consists of six physiological parameters, namely lowest mean arterial pressure (MAP), worst ratio of partial pressure of oxygen (P_aO_2) to fraction of inspired oxygen (F_iO_2), lowest temperature (in ^oF), lowest serum pH, occurrence of multiple seizures, and urine output (<1mL/kg/hr). Another simplified postnatal outcome predictor in infants with CDH is the Wilford Hall/Santa Rosa formula ((highest P_aO_2 - highest P_aCO_2) generated from arterial blood gas values obtained during the initial 24 hours of life before surgical correction). A positive value is associated with better clinical outcome.

Fetal interventions:

As known from animal studies and fetuses with congenital high airway obstruction, in utero occlusion of the trachea promotes lung growth. In a highly selected subset of infants with CDH, fetoscopic tracheal occlusion can result in reduced lung hypoplasia. Some fetal therapy centers therefore perform temporary minimally invasive, endoscopic tracheal balloon occlusion during pregnancy. Balloon removal has to be performed before birth or in an ex utero intrapartum treatment (EXIT-procedure). Fetal tracheal occlusion (FETO) for CDH remains an investigational therapy for which the long-term benefits have yet to be proven in well-controlled studies.

Currently a randomized-controlled-trial is being carried out to detect the benefit of tracheal balloon occlusion in severely and moderately affected neonates with left-sided CDH and to determine the risk and impact of prematurity on survival (The TOTAL Trial). Therefore, at the moment, there is the recommendation to perform FETO only in the setting of the TOTAL trial.

Particular preparation for airway management

The recommended standard of care is intubation immediately after birth. For children undergoing thoracoscopic repair a cuffed endotracheal tube is recommended to minimize air leak. Laryngoscopy and intubation are usually not more challenging than in infants without CDH. However, CDH can be associated with various syndromes predisposing for a difficult airway such as Cornelia-de-Lange-syndrome, Fryn-syndrome or Pallister-Killian-syndrome (10).

Particular preparation for transfusion or administration of blood products

Even though massive bleeding is a rather rare complication of CDH surgery, blood products must be ordered and issued preoperatively, especially in patients requiring surgery on ECMO. The children often present for surgery with hemoglobin levels in the lower normal range. Transfusion threshold in these cardiopulmonary severely ill patients should not be set too low. Hemoglobin levels should be kept above 12 g/dl.

Particular preparation for anticoagulation

No particular preparation for anticoagulation is necessary. In patients on ECMO anticoagulation is necessary and is most commonly performed with unfractionated heparin. The range of activated clotting time and mode of monitoring in general remains a matter of debate (11).

Particular precautions for positioning, transport or mobilisation

Transport of these critically ill patients carries a considerable risk of complications and should be undertaken with the utmost caution. The team should be prepared for major respiratory and cardiovascular problems and should therefore be equipped with immediately available medication such as sedatives, muscle relaxants and catecholamines. In addition to the risks related to complications of transport, severe CDH patients with severe pulmonary hypertension have an extremely labile balance and any apparently little factor (for example body temperature reduction) may break the achieved stability. Due to the high risk of transport and positioning we prefer to perform surgery on the sickest and most vulnerable patients in the intensive care unit.

Probable interaction between anaesthetic agents and patient's long-term medication

Sildenafil is a non-selective PDE-5-inhibitor use to treat acute and chronic pulmonary hypertension in neonates and infants with CDH. Due to its property of being non-selective, systemic hypotension is a common side effect and has to be taken into account when caring for children on sildenafil.

Milrinone is PDE-3-inhibitor with inotropic and lusitropic effects. It furthermore inhibits the breakdown of cAMP in smooth muscle cells and therefore functions as a vasodilator. Systemic hypotension appears to be a rather rare complication of milrinone in infants.

Bosentan is an ET_A-Receptor-Antagonist promoting pulmonary vasodilation. It can be used as acute or chronic therapy but is currently not approved for the treatment of pulmonary hypertension in children or PPHN. A possible side effect is elevation of transaminases or liver failure. It can also cause anemia, leukopenia and thrombocytopenia (12) .

In treatment of chronic heart failure in infants and children with CDH, furosemide, ACE-inhibitors and spironolactone are commonly used for reduction of after- and preload. These therapies usually should not be discontinued perioperatively.

Anaesthesiologic procedure

Open abdominal repair:

Surgery is performed in the supine position. The central venous line usually is placed in the femoral vessels, as this saves the cervical vessels for possible ECMO-cannulation later. Lines for inotropes and sedatives are connected in close proximity to the catheter. An additional peripheral line for blood transfusion and fluid boluses is recommended. The

children are usually placed with the arms up, so the arterial and peripheral line are easily accessible. Ventilation follows the same principles as in the intensive care unit setting. Ventilation often improves after repositioning of the herniated viscera. However, these children suffer from a true developmental lung hypoplasia and do not have a lot of recruitable lung tissue. Intraoperative volume shift can be considerable and a careful evaluation of the child's fluid state is essential to avoid volume overload. Due to the often decreased baseline hemoglobin levels and the need for intravenous hydration, erythrocyte transfusion can become necessary even without substantial blood loss. In tachycardic children with high volume needs and need for moderately-dosed inotropic support, blood transfusion may be necessary.

Thoracoscopic repair:

Anaesthesia for thoracoscopic repair is essentially different from open abdominal procedures. Children are placed in the right lateral decubitus position (for left-sided CDH) close to the edge of the operating room table and must therefore be well fixed and secured. A close communication with the surgeon is essential for placement of ecg-electrodes, lines and tubes. Even though all children have an arterial line, we usually have a non-invasive blood pressure measurement in place in case the arterial line gets lost. As the light gets dimmed for thoracoscopy one must have a flashlight ready for illumination under the drapes. Insufflation of gas into the child`s hemithorax can cause considerable deterioration of ventilation and oxygenation. As these children are at increased risk for pulmonary hypertensive crisis, one must carefully evaluate the benefits of minimally invasive surgical repair against the risks of progressive cardiorespiratory failure. Some authors fear worsening respiratory acidosis and reduced cerebral tissue oxygenation in thoracoscopic repair (13). Other studies report no difference regarding ventilation and oxygenation between thoracoscopic and open abdominal repair (14). From our point of view, after a careful selection of patients, thoracoscopic procedures offer more advantages then disadvantages. Markers for sufficient organ perfusion are a lactate level < 3 mmol/l, urine output > 1ml/kg/h and a heart rate close the normal range. A minimum P_aO_2 of 60 mmHG must be maintained and the lowest acceptable blood pH is 7,25. Peak inspiratory pressure should not exceed 25 cm H_20. In case of doubt, thoracoscopic repair has to be stopped and repair has to be performed via the abdominal approach.

Particular or additional monitoring

All children should be equipped with an arterial and multi-lumen central venous line. For measurement of arterial blood gases, pre-ductal placement of the arterial line is desirable. Placement of the central venous line seems most reasonable in the femoral vessels, as this saves the cervical vessels for possible ECMO-cannulation later. Capnography is especially important in thoracoscopic surgery, as it enables the anaesthesiologist to quickly conceive ventilatory problems. Near infrared spectroscopy can be used to monitor regional brain oxygen saturation. It is not yet widely spread and further investigation needs to be awaited for giving definitive recommendations.

Possible complications

The most serious complication in infants with CDH is pulmonary hypertensive crisis with right-to-left-shunting. The most common triggers are hypoxia, hypercarbia and acidosis. Hypothermia and hypoglycemia can also trigger pulmonary hypertension. Due to a patent foramen ovale and/or ductus arteriosus, a rise in pulmonary artery pressure usually causes

significant right-to-left-shunting, further worsening hypoxia and hypercarbia. The mainstay of care for these severely ill children therefore is avoidance of hypoxia, hypercarbia and acidosis. In case of persistent pulmonary hypertension under optimized ventilator settings inhaled NO is the treatment of choice. Sildenafil, Milrinone, Bosentan or Prostanoids can also be used (15). High frequency oscillatory ventilation or ECMO are second line therapies for cases of treatment failure. In thoracoscopic repair, ventilation and oxygenation are often hindered. If maintaining proper oxygenation or ventilation is not possible, surgery has to be converted into open abdominal repair. Even if blood loss is mostly minimal, fluid shift can be significant and transfusion of red blood cells can be necessary.

Postoperative care

Surgical repair of a CDH is a stressful procedure and transient impairment of general and cardio-respiratory conditions may be expected after surgery. Postoperative care in the intensive care unit follows the same principles as described above for preoperative management. As soon as the cardiopulmonary situation is stabilized, patients should be started to be weaned from the ventilator.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the diseases, e.g.:

Systemic hypotension in response to deepened sedation, especially in combination with neuro-muscular blocking agents and lateral positioning in thoracoscopic repair, is possible and always has to de differentiated from circulatory failure due to pulmonary hypertensive crisis.

Ambulatory anaesthesia

The range of physical conditions in children having undergone CDH-repair as infants is extremely wide. Performing anesthesia on a day-case basis is generally possible in toddlers and older children but always has to be based on the individual patient`s comorbidities and physical condition. Combined anesthetic techniques for reducing opioid consumption are preferred.

Obstetrical anaesthesia

Physiology during pregnancy can affect and worsen pre-existing conditions of parturients having undergone CDH-repair as infants. In general, cardiopulmonary function and exercise capacity represent the most important factors. Echocardiographic evaluation, and in case of anomalies cardiology follow-up, appear reasonable. General, regional and combined anesthetic techniques are possible. Interactions between the parturients permanent medication and anesthetic medications should be considered.

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Last date of modification: November 2017

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