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Congenital diaphragmatic hernia

Glutaric acidaemia type 1

orphan**anesthesia**

a project of the German Society
of Anaesthesiology and Intensive Care Medicine

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OrphanAnesthesia –

ein krankheitsübergreifendes Projekt des Wissenschaftlichen Arbeitskreises Kinderanästhesie der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V.

Ziel des Projektes ist die Veröffentlichung von Handlungsempfehlungen zur anästhesiologischen Betreuung von Patienten mit seltenen Erkrankungen. Damit will Orphan Anesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patienten mit seltenen Erkrankungen benötigen für verschiedene diagnostische oder therapeutische Prozeduren eine anästhesiologische Betreuung, die mit einem erhöhten Risiko für anästhesieassoziierte Komplikationen einhergehen. Weil diese Erkrankungen selten auftreten, können Anästhesisten damit keine Erfahrungen gesammelt haben, so dass für die Planung der Narkose die Einholung weiterer Information unerlässlich ist. Durch vorhandene spezifische Informationen kann die Inzidenz von mit der Narkose assoziierten Komplikationen gesenkt werden. Zur Verfügung stehendes Wissen schafft Sicherheit im Prozess der Patientenversorgung.

Die Handlungsempfehlungen von OrphanAnesthesia sind standardisiert und durchlaufen nach ihrer Erstellung einen Peer-Review-Prozess, an dem ein Anästhesist sowie ein weiterer Krankheitsexperte (z.B. Pädiater oder Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, so dass die Handlungsempfehlungen grundsätzlich in englischer Sprache veröffentlicht werden.

Ab Heft 5/2014 werden im monatlichen Rhythmus je zwei Handlungsempfehlungen als Supplement der A&I unter www.ai-online.info veröffentlicht. Als Bestandteil der A&I sind die Handlungsempfehlungen damit auch zitierfähig. Sonderdrucke können gegen Entgelt bestellt werden.

OrphanAnesthesia –

a project of the Scientific Working Group of Paediatric Anaesthesia of the German Society of Anaesthesiology and Intensive Care Medicine

The target of OrphanAnesthesia is the publication of anaesthesia recommendations for patients suffering from rare diseases in order to improve patients' safety. When it comes to the management of patients with rare diseases, there are only sparse evidence-based facts and even far less knowledge in the anaesthetic outcome. OrphanAnesthesia would like to merge this knowledge based on scientific publications and proven experience of specialists making it available for physicians worldwide free of charge.

All OrphanAnesthesia recommendations are standardized and need to pass a peer review process. They are being reviewed by at least one anaesthesiologist and another disease expert (e.g. paediatrician or neurologist) involved in the treatment of this group of patients.

The project OrphanAnesthesia is internationally oriented. Thus all recommendations will be published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommendations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). Thus they can be accessed and downloaded via www.ai-online.info. As being part of the journal, the recommendations will be quotable. Reprints can be ordered for payment.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

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orphananesthesia

Anaesthesia recommendations for Congenital diaphragmatic hernia

Disease name: Congenital diaphragmatic hernia (CDH)

ICD 10: Q79.0

Synonyms: -

Disease summary: 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 various syndromes (trisomy 13, trisomy 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 foetal lung volume on MRI and intrathoracic position of liver and/or stomach in left-sided CDH.

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

Medicine is in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong



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

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Typical surgery

According to the CDH EURO Consortium, there is a consensus on the surgical repair of diaphragmatic hernia after sufficient stabilisation of the neonate (delayed surgery). The definition of stability and 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 the closure of the defect. Various patch materials have been used, including non-absorbable patch-material which reduces the risk of hernia recurrence. Surgery can either be performed by an open abdominal (and possibly thoracic) approach or minimally invasive methods (laparoscopy, thoracoscopy). Minimally invasive techniques should only be applied in patients who can tolerate CO₂ insufflation. The timing of surgical repair will depend on the 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, there is a risk of intestinal obstruction due to adhesions in open surgery, 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 an 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, whereas the prosthetic patch in the diaphragm will be left in place. Secondary surgery later in life may also be necessary, for example, in cases of severe gastro-oesophageal reflux with placement of a percutaneous feeding tube, hiataloplasty 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 (0.03–0.1 mg/kg/h) and fentanyl (4–10 µg/kg/h). Muscle relaxation is provided for the duration of surgery using rocuronium or vecuronium. To our knowledge, no reports of regional anaesthesia in infants with CDH exist. In general, additional epidural anaesthesia is possible in these cases for open abdominal repair, caudal anaesthesia appears reasonable. Some centres perform an intercostal block after thoracoscopic surgery. Considering the need for postoperative mechanical ventilation over a period of several days and the resulting need for sedation, we currently do not see any considerable benefit from regional anaesthesia in this group of patients.

Pre-operative management in the intensive care unit:

Pre-operative 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 to prevent bowel insufflation. An

orogastric 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 H₂O, application of PEEP (3–5 cm H₂O), a ventilation frequency of 40–60/min and tidal volumes of 5–6 ml/kg body weight [2]. The ventilation strategy is aiming for a preductal saturation of 85–95% and arterial CO₂ levels between 50 and 70 mmHg (pH > 7.2). High-frequency oscillatory ventilation is an alternative in case conventional mechanical ventilation fails. 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 10–20 ml/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 > 1 ml/kg/h and lactate concentration < 3 mmol/l. Increasing systemic vascular resistance can be used as a treatment option in case of substantial right-to-left-shunting. The treatment of pulmonary hypertension should be initiated if the preductal saturation falls below 85%, pre- and postductal saturation difference is > 10% and/or there are signs of poor end-organ-perfusion. The 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 centres 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 stabilisation defined as the following [1]:

- Mean arterial blood pressure normal for gestation
- Preductal saturation levels of 85–95% on F_iO₂ below 50%
- Lactate below 3 mmol/l
- Urine output more than 1 ml/kg/h.

Necessary additional pre-operative testing (beside standard care)

Echocardiography should be performed within the first 24 h after birth. The 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 the evaluation of a mediastinal shift. Besides a complete physical examination, ultrasound assessment of the brain and kidneys to rule out anomalies should be performed. The pre-operative 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 the development of pulmonary hypertension and the need for ECMO [1,6,7].

Antenatally used markers of severity for CDH are left-sided 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 (Simplified 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 the lowest mean arterial pressure (MAP), the worst ratio of partial pressure of oxygen (P_{aO_2}) to fraction of inspired oxygen (F_{iO_2}), the lowest temperature (in °F), the lowest serum pH, occurrence of multiple seizures, and urine output (<1ml/kg/h). 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.

Foetal 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 foetal therapy centres 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). Foetal 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 randomised 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 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 minimise 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

Although massive bleeding is a rather rare complication of CDH surgery, blood products must be ordered and issued pre-operatively, especially in patients requiring surgery on ECMO. The children often present for surgery with haemoglobin levels in the lower normal range. The transfusion threshold in these cardiopulmonary severely ill patients should not be set too low. Haemoglobin 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, transportation and mobilisation

A 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 a transport, severe CDH patients with severe pulmonary hypertension have an extremely labile balance and any apparently little factor (e.g. body temperature reduction) may break the achieved stability. Due to the high risk of transporting and positioning, we prefer to perform surgery on the sickest and most vulnerable patients in the intensive care unit.

Interactions of chronic disease and anaesthesia medications

Sildenafil is a non-selective PDE5 inhibitor used 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 a PDE3 inhibitor with inotropic and lusitropic effects. It also 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 ETA 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 consists in the elevation of transaminases or liver failure. It can also cause anaemia, leukopenia and thrombocytopenia [12].

In the 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 should usually not be discontinued peri-operatively.

Anaesthetic 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 lines are easily accessible. Ventilation follows the same principles as in the intensive care unit setting. Ventilation often improves after repositioning the herniated viscera. However, these children suffer from a true developmental lung hypoplasia and do not have a lot of recruitable lung tissue. The intraoperative volume shift can be considerable and a careful evaluation of the child's fluid state is essential to avoid a volume overload. Due to the often decreased baseline haemoglobin 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, a blood transfusion may be necessary.

Thoracoscopic repair:

Anaesthesia for thoracoscopic repair differs significantly from that of 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 the placement of ECG electrodes, lines and tubes. Although 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. The insufflation of gas into the child's hemithorax might cause considerable deterioration of ventilation and oxygenation. As these children are at an increased risk to suffer from a 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 that there is no difference in ventilation and oxygenation between thoracoscopic and open abdominal repair [14]. From our point of view, after a careful selection of patients, thoracoscopic procedures have more advantages than 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. The peak inspiratory pressure should not exceed 25 cm H₂O. In case of doubt, thoracoscopic repair has to be stopped and repair has to be performed by the abdominal approach.

Particular or additional monitoring

All children should be equipped with an arterial and multi-lumen central venous line. When measuring arterial blood gases, a pre-ductal placement of the arterial line is desirable. The placement of the central venous line in the femoral vessels seems to be most reasonable, 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 before definitive recommendations can be given.

Possible complications

The most serious complication in infants with CDH is a pulmonary hypertensive crisis with right-to-left shunting. The most common triggers are hypoxia, hypercarbia and acidosis. Hypothermia and hypoglycaemia 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 is therefore the avoidance of hypoxia, hypercarbia and acidosis. In case of persistent pulmonary hypertension under optimised ventilator settings, inhaled NO is the treatment of choice. Sildenafil, milrinone, bosentan or prostanooids can also be used [15]. High-frequency oscillatory ventilation or ECMO are second line therapies in cases of treatment failure. In thoracoscopic repair, ventilation and oxygenation are often hindered. If maintaining proper oxygenation or ventilation is not possible, surgery will have to

be converted into open abdominal repair. Even if the blood loss is mostly minimal, the fluid shift might be significant and a transfusion of red blood cells might become necessary.

Post-operative care

Surgical repair of a CDH is a stressful procedure and a transient impairment of general and cardiorespiratory conditions may be expected after surgery. Post-operative care in the intensive care unit follows the same principles as described above for pre-operative management. As soon as the cardiopulmonary situation is stabilised one should start to wean patients from the ventilator.

Disease-related acute problems and effect on anaesthesia and recovery

Systemic hypotension in response to deepened sedation, especially in combination with neuromuscular blocking agents and lateral positioning in thoracoscopic repair, is possible and always has to be 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 anaesthesia 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 anaesthetic 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 cardiology follow-up in case of anomalies appear reasonable. General, regional and combined anaesthetic techniques are possible. Interactions between the parturient's permanent medication and anaesthetic medications should be considered.

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