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CDH: Lung to Head Ratio

Congenital diaphragmatic hernia (CDH) is a birth defect associated with a high mortality due to lung hypoplasia and pulmonary hypertension. A defect in the diaphragm allows the abdominal organs to herniate toward the thoracic cavity leading to compression of the lungs, abnormal lung development, with pulmonary hypoplasia and persistent pulmonary hypertension after birth. The diagnosis can be made with prenatal ultrasound early in pregnancy. Pulmonary hypertension is a common cause of mortality and morbidity among survivors of CDH. The presence of pulmonary hypertension in infants with CDH is due to decreased pulmonary arterial density and abnormal arborization leading to a significant reduced distal cross-sectional vascular area. The lung-to-head ratio (LHR) is a prenatal prognostic indicator for CDH. The LHR as measured by prenatal ultrasound is the ratio of the area of the lung contralateral to the hernia defect to the fetal biparietal head circumference. The area of the lung is measured at the level of the four-chamber view of the fetal heart and is defined as the product of the longest two perpendicular transverse diameters in milliliters. The LHR is then calculated as a simple ratio of lung area (in square millimeters) to head circumference (in milliliter) ideally between 24 and 28 weeks of gestation. LHR enables an indirect assessment of the contralateral fetal lung volume. LHR has been suggested as a way to estimate the degree of pulmonary hypoplasia and predict outcomes in children born with CDH. Lower LHR is associated with increased mortality and needs of use of ECMO. A threshold LHR of 0.85 predicts mortality with 95% sensitivity and 64% specificity. There are few long-term survivors in infants with an LHR < 1.0. Prenatal markers identified to help predict perinatal outcomes in children with left-sided CDH include low LHR, liver position, intrathoracic position of the stomach, mediastinal shifts, polyhydramnios, and early diagnosis before 25 weeks' gestation. Prenatal prediction of survival in CDH relies mostly on indirect measurement of fetal lung volumes providing physicians with insight into the potential severity of postnatal pulmonary deficits and helping select appropriate therapeutic interventions including prenatal surgical intervention. Serial ultrasound evaluation of fetuses with CDH have demonstrated increasing LHR values in survivors as gestational age advances, while in non-survivors there is no apparent increase in the LHR throughout gestation. During normal fetal development the LHR increases over the course of gestation in babies not affected by CDH because the pulmonary area increases four times more than the cephalic circumferences. This means that the LHR takes gestational age into account. The observed to expected US lung-to-head ratio express the measured lung-to-head ratio as a centile of the normal median to gestational age. Similarly, the fetal lung volume measured by MRI and expressed as a percentage of the expected fetal lung volume for gestational age has a prognostic predictive value. The

LHR and fetal lung volume predict survival, need for ECMO and development of chronic lung disease in fetuses with left-sided CDH. The correlation does not reach statistical significance at any time of gestation for cases with right-sided CDH. Long term outcomes regarding neurological development, musculoskeletal development, and nutritional status in moderate to severe CDH are not predicted by measurement in LHR. Quantification of the extent of liver tissue herniation in right sided CDH by US or MRI or position of the stomach in the thorax are more predictive for survival, even independent of the LTH ratio. In isolated left sided CDH patients the LTH predicts survival and development of chronic lung disease in survivors in an era of standardized neonatal treatment protocol.

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Distal Intestinal Obstruction Syndrome

Distal intestinal obstruction syndrome (DIOS) is a common and characteristic complication of children with cystic fibrosis (CF). CF is an autosomal recessive disease characterized by exocrine pancreatic insufficiency and progressive pulmonary disease. CF is caused by a mutation in the cystic fibrosis transmembrane conductance regulator gene which encodes a protein whose main function is to regulate chloride ion transport. DIOS is characterized by the accumulation of viscid fecal material within the lumen of the bowel combined with sticky mucoid material intestinal content adherent to the intestinal wall affecting the terminal ileum and cecum. This fecal material connects strongly with the crypts and villi being very difficult to remove. Intermittently the child with DIOS due to cystic fibrosis develops bowel obstruction. The clinical presentation can be acute, or chronic with intermittent abdominal pain associated with abdominal distension and vomiting. Occurrence of DIOS is related to the severity of the CF genotype. DIOS affects between 10-22% of individuals with CF. Adults are more commonly affected than children by DIOS. DIOS affected children have a right lower quadrant mass which is usually palpable and can be seen as fecal material in plain abdominal films. DIOS is defined a complete or incomplete bowel obstruction with fecal mass in the ileocecum. In CF defective cystic fibrosis transmembrane conductance regulator function leads to reduced chloride and fluid secretion in the intestinal epithelium

and airway. Absence of this gene leads to thickened, dehydrated mucus. Besides, gut transit is prolonged in CF affecting gastric emptying and ileal-colonic transit. Poorly controlled fat absorption contributes to DIOS by altering the viscosity of luminal content. Most children with DIOS are pancreatic insufficient. Previous history of meconium ileus is also a strong risk factor for developing DIOS later in life. Poorly controlled fat malabsorption is frequently reported in DIOS patients. Risk of DIOS increases after lung transplantation. Clinically DIOS is associated with right lower quadrant colicky abdominal pain, nausea, bilious vomiting, and fluid levels. Abdominal CT with contrast can established the diagnosis in the proper setting of a child suffering from CF. CT-scan shows significant proximal small bowel dilatation with inspissated fecal material in the distal ileum. Appendicitis, chronic constipation, and intussusception can mimic DIOS. The clinical presentation of fibrosing colonopathy may be quite similar to DIOS with abdominal pain, distension, vomiting and constipation. Management of DIOS is empirical. Patient with incomplete DIOS respond to oral rehydration combined with stool softeners which contain an osmotic laxative containing polyethylene glycol (golyte). It can be given at a dose of 20-40 ml/kg/hr. up to a maximum of 1L/hr. over 8 hours. The aim of management is to achieve fecal effluent consistent of clear fluid and resolution of pain, abdominal distension, and vomiting. Alternative Gastrograffin can be administered orally or by nasogastric tube at a dose of 50-100 ml in 200 ml of water or juice depending on the age of the child. The use of N-acetyl cysteine administered orally can also be used effectively. N-acetylcysteine exhibits a mucolytic action through its free sulfhydryl group which opens the disulfide bonds in mucoproteins to lower mucous viscosity. It can be given enterally by mouth or feeding tube and also rectally. It may be more effective in relieving incomplete obstruction than complete obstructions. Gastrograffin can be used as a hydrostatic enema retrograde lavage so as to reach the small distal bowel fecal material. Lactulose an oral osmotic laxative is widely used but may cause flatulence or abdominal pain in high doses. Surgery is seldom required and is reserved for the most refractory cases nor responding to medical management. As prophylaxis maintenance laxative therapy should be continued avoiding dehydration and providing adequate pancreatic enzyme dosage.

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Propofol Infusion Syndrome

Propofol is a very common sedative used in anesthesia and surgery. Propofol has many pharmacological advantages over other anesthesia agents such as rapid effect, short action, and fewer side effects like postoperative nausea. Pediatric use of propofol includes induction and maintenance of general anesthesia as well as sedation during non-surgical intervention and ICU care. Propofol exerts its hypnotic actions by activation of the central inhibitory neurotransmitter gamma-aminobutyric acid (GABA). Propofol infusion syndrome (PIS) is defined as the occurrence of acute bradycardia resistant to treatment and progressing to asystole associated with propofol infusion. The bradycardia is combined with one of the following: 1) lipemic plasma, fatty liver enlargement; 2) metabolic acidosis with negative base excess less than 10 mM, and 3) rhabdomyolysis or myoglobinuria. The primary feature of PIS is metabolic acidosis (most common feature), ECG changes and rhabdomyolysis. PIS can lead to cardiac and renal failure. The child can develop symptoms and signs of lactic acidosis, hypotension, renal, cardiac, and circulatory failure, oliguria, rhabdomyolysis, elevated CK, serum urea and serum potassium, with lipemic plasma, liver enlargement, ketonuria, increased liver tests and red colored urine. Risk factors identified include airway infection, poor oxygen delivery, sepsis, serious head injury and high-dose (> 5 mg/kg/hr) long-term propofol sedation for more than 48 hours, associated with increased catecholamines and glucocorticoid serum levels. Lipemia due to failure of hepatic lipid regulation leads to sequestration of propofol into the lipid phase leading to lowered free propofol levels and insensitivity to propofol. Mortality is more common in children below 19 years of age, males and those receiving vasopressors in the ICU. The syndrome can be associated with a right bundle branch block in the EKG. PIS occurs with the use of high doses of propofol for prolonged periods of time. Pathological findings in PIS include cytolysis of skeletal and cardiac muscle. Free fatty acids are a pro-arrhythmic risk factor in PIS. Is theorized that an hereditary fatty acid metabolism impairment resembling medium-chain acyl-CoA dehydrogenase deficiency is responsible for the susceptibility of developing PIS. Propofol impedes the electron flow through the respiratory chain and coenzyme Q is the main site of interaction with propofol interfering with mitochondrial energy production. Low carbohydrate supply is a risk factor for PIS due to energy demand which is satisfied by lipolysis when carbohydrates are low. PIS has no definitive diagnostic test; early detection is highly crucial for initiating early treatment. Management of PIS include stopping immediately the infusion of propofol. Hemodynamic stabilization should be achieved along with carbohydrate substitution. Hemodialysis or hemofiltration is recommended for elimination of propofol and toxic metabolites. Extracorporeal membrane oxygenation has also been reported as beneficial in some cases. Propofol is not approved for sedation in some pediatric intensive care unit’s patients. A dose limit of 4 mg/kg/hr. is recommended for sedation of adult patients and a period of seven days should not be exceeded, preferably not more than 48 hours. Acid base metabolism and CK should be monitored during propofol infusion use. Total intravenous anesthesia with propofol is regarded as a safe procedure with few side effects in pediatric patients and is considered a standard procedure. Alternatives for propofol use include dexmedetomidine or midazolam.

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