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Anesthetic Management and Perioperative Care in Neonates with Esophageal Atresia: A Case Report

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A B S T R A C T

Introduction: Esophageal atresia is a congenital disorder that requires immediate surgical intervention. Careful anesthetic management and perioperative care are crucial for successful therapy in neonates with this condition. **Case presentation:** A 20-day-old male infant with esophageal atresia underwent anastomotic thoracotomy surgery. Premedication, induction, and maintenance of anesthesia were performed with a combination of Sevoflurane, Ketamine, and Fentanyl. Postoperatively, the baby was treated in the NICU with mechanical ventilation and antibiotic therapy. **Conclusion:** Comprehensive anesthetic management and perioperative care in neonates with esophageal atresia include prevention of aspiration, adequate ventilation, pain management, and close postoperative monitoring to ensure optimal outcomes.

1. Introduction

Esophageal atresia is a relatively common congenital abnormality, with an incidence of approximately 1 in 2500 to 4500 live births. This disorder is characterized by the absence of continuity of the esophageal lumen, thereby preventing the normal passage of food and fluids from the mouth to the stomach. Esophageal atresia is often accompanied by tracheoesophageal fistula, which is an abnormal connection between the esophagus and trachea. Esophageal atresia is a congenital malformation that occurs during early embryological development, in which the esophagus does not form or develops imperfectly. This condition can occur in isolation or in association with other syndromes, such as VACTERL syndrome (Vertebral anomalies, Anal atresia, Cardiac defects, Tracheo-Esophageal fistula, Renal anomalies, and Limb defects). The incidence of esophageal atresia varies worldwide, with some studies reporting higher rates in Europe and North America.[1,2]

Esophageal atresia is classified based on the presence or absence of a tracheoesophageal fistula

and the location of the fistula. The most commonly used classification is Gross's classification, which divides esophageal atresia into five main types: Type A: Esophageal atresia without fistula; Type B: Esophageal atresia with proximal tracheoesophageal fistula; Type C: Esophageal atresia with distal tracheoesophageal fistula (most common); Type D: Esophageal atresia with proximal and distal tracheoesophageal fistula; Type E: Tracheoesophageal fistula without esophageal atresia (H-type fistula). Babies with esophageal atresia usually show clinical symptoms soon after birth. The most common symptoms are: The baby cannot swallow saliva or milk, which causes regurgitation and choking. Excessive saliva production due to inability to swallow. Cyanosis occurs due to aspiration of saliva or milk into the lungs through a tracheoesophageal fistula. Abdominal distension, especially in atresia. esophagus with distal tracheoesophageal fistula, where air enters the stomach through the fistula.[3,4]

The diagnosis of esophageal atresia is made based on clinical symptoms and supporting examinations. Radiological examinations, such as chest and abdominal X-rays, can show the presence of a closed upper esophageal pouch and the absence of air in the stomach. Insertion of a nasogastric tube (NGT) that cannot enter the stomach is also a typical sign of esophageal atresia. Esophageal atresia can cause various serious complications, including Aspiration of stomach contents into the lungs can cause serious infections, and the inability to swallow food normally can cause impaired growth and development, This condition can worsen symptoms and increase the risk of aspiration and Narrowing of the esophagus can occur after repair surgery.[2,4]

The primary therapy for esophageal atresia is surgical repair. This procedure involves severing the tracheoesophageal fistula (if any) and joining the two separate ends of the esophagus. In some cases, additional procedures may be needed such as a gastrostomy to provide temporary nutrition or esophageal dilatation to treat stenosis. Anesthetic and perioperative management of neonates with esophageal atresia is a challenge. These infants are at high risk of aspiration, respiratory distress, and hemodynamic instability. In addition, the unique physiology of neonates, such as immature organ function and limited physiological reserve, adds complexity to perioperative management. Therefore, thorough anesthetic preparation, selection of the right anesthetic technique, and intensive postoperative care are very important to ensure the success of the operation and long-term outcomes. Effective pain management is also an important aspect of perioperative care to reduce stress and increase infant comfort. Although there has been significant progress in the management of esophageal atresia, there are still many questions that need to be answered through further research. The study of optimal anesthetic techniques, effective pain management strategies, and comprehensive postoperative care approaches will help improve outcomes and quality of life for infants with esophageal atresia.[4,5]

2. Case Presentation

The patient is a 20-day-old baby girl weighing 2.2 kg with esophageal atresia. The patient complained of frequently spitting up and choking when given breast milk. The patient was born spontaneously at term, and complaints of fever, cough, runny nose, and shortness of breath were denied. The patient vomits greenish in color. The patient was diagnosed with type C esophageal atresia with tracheoesophageal fistula, severe respiratory distress, late-onset neonatal sepsis, normochromic normocytic anemia, hyperbilirubinemia with ASA III physical status. Anesthesia plan with general anesthesia. Blood laboratory examination showed an increase in total bilirubin (Table 1). A babygram examination showed a suspected picture of esophageal atresia type C (Figure 1).

Table 1. Preoperative blood laboratory.

Inspection	Results	Unit	Reference
Routine hematology (September 26th, 2022)			
Hemoglobin	11.3	g/dl	14.9-23.7
Hematocrit	32	%	47-75
Leukocytes	11.1	Thousand/ul	9.4-34
Platelets	437	Thousand/ul	150-450
Erythrocytes	4,05	Million/ul	3.70-6.50
Blood type	-	-	-
Hemostasis (September 22nd, 2022)			
PT	14.9	Second	10.0-15.0
APTT	35.7	Second	20.0-40.0
INR	1.140	-	-
Clinical chemistry (September 26th, 2022)			
Albumin	3.6	g/dl	2.8-4.4
Urea	8	mg/dl	-
Creatinine	0.4	mg/dl	-
Bilirubin total	10.92	and/or	-
Electrolyte			
Sodium	131	mmol/L	129-147
Potassium	3.6	mmol/L	3.6-6.1
Calcium ion	1.00	mmol/L	1.17-1.29
Antigen COVID-19			
Swab antigen	Negative	-	Negative
HbsAg	Non reactive	-	Non reactive

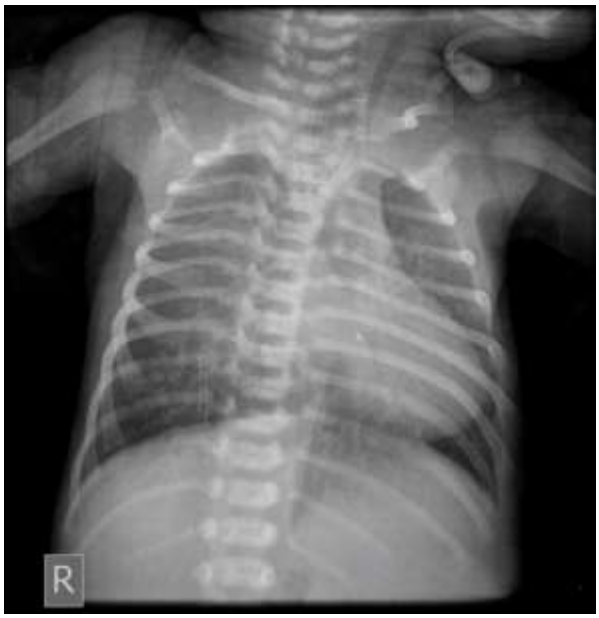

Figure 1. Babygram examination.

The patient arrived at the IBS transit room on September 28th, 2022 at 11.00 WIB. The handover was carried out with the nurse in the transit room on ETT because the patient was not yet familiar with the environment. The patient was taken to the operating room and remained in the incubator without sedation. Prepare in the operating room by turning off the AC and placing a heating blanket on the operating table. Preparation of anesthesia tools and machines. The patient entered the operating room and had an O_2 saturation monitor, blood pressure, and electrocardiography installed, BP data was 65/40 mmHg, heart rate 128 x/minute, RR 40 x/minute, ECG showed sinus tachycardia rhythm. The patient was given oxygenation of 6-8 L/minute FiO_2 100% and obtained SpO_2 99-100%. Premedication uses SA 0.1 mg, Induction is carried out with Ketamine 2 mg, and Fentanyl 45 mcg. Maintenance with Oxygen: airbar = 2 : 2 L/minute. Sevoflurane 2-3.2 vol%. Meanwhile, the drug that was administered during the operation was Metamizole 40 mg. The operation lasted 2.5 hours. During the operation, the patient was in the supine position, in stable condition, heart rate between 135-155x/minute, and oxygen saturation of 98-100%. After the thoracotomy anastomose operation, the patient was admitted to the NICU with an ETT number 3.5 cm on venti PC mode, PEEP 6, PC above 12, RR 40, Fio_2 50%, I:E ratio 1:1.5. The patient received the drugs Cefoperazone (50mg/kg/12 hours), Amikacin (12mg/kg/24 hours) 22 mg/24/hour Ketamine (0.1 mg/kg/hour). The patient was treated for 3 weeks after surgery.

3. Discussion

Perioperative management of neonates with esophageal atresia is a crucial aspect in determining the success of therapy and long-term prognosis. Understanding the pathophysiology of esophageal atresia and implementing appropriate perioperative management strategies is critical to minimizing complications and optimizing outcomes in these vulnerable neonatal patients. Esophageal atresia is a congenital disorder that occurs due to failure of esophageal development during embryogenesis. Although the exact cause of esophageal atresia is not completely understood, several genetic and environmental factors are thought to play a role in its pathogenesis.[5,6]

During embryonic development, the esophagus originates from the foregut, the anterior portion of the primitive intestinal tube. In the 4th week of pregnancy, the foregut undergoes longitudinal separation into two parallel tubes: the ventral tube which will develop into the trachea, and the dorsal tube which will become the esophagus. This separation process is regulated by various growth factors and molecular signals. In esophageal atresia, the process of foregut separation is disrupted, resulting in abnormalities in the development of the esophagus. This disorder can occur at various stages of development, resulting in various types of esophageal atresia with or without tracheoesophageal fistula. Esophageal atresia, despite being one of the common congenital anomalies of the digestive tract, still leaves big questions regarding the exact mechanism of its cause. Several hypotheses have been proposed to explain how these abnormalities can occur during embryonic development. The three main mechanisms that are the focus of research are impaired vascularization, failure of apoptosis, and genetic factors.[7,8]

The impaired vascularization hypothesis postulates that esophageal atresia occurs due to ischemia or impaired blood flow to the foregut during critical stages of embryonic development. The foregut is the anterior part of the primitive intestinal tube that will later develop into the esophagus, stomach, proximal duodenum, liver, pancreas, and biliary system. During normal development, the foregut receives its blood supply from arteries originating from the dorsal aorta. Disturbances in the formation or development of these arteries can cause ischemia in the foregut, thereby disrupting the growth and differentiation of esophageal tissue. This can result in failure to form an esophageal lumen or incomplete lumen formation, which ultimately causes esophageal atresia. Several lines of evidence support this hypothesis. Studies in animal models show that ligation of the arteries supplying the foregut can induce esophageal atresia. In addition, clinical studies in humans have also found an association between

esophageal atresia and other vascular abnormalities, such as pulmonary artery and aorta anomalies. However, the hypothesis of impaired vascularization cannot explain all cases of esophageal atresia. In some cases, no significant vascular abnormalities were found. Therefore, further research is needed to reveal the exact role of vascularization disorders in the pathogenesis of esophageal atresia.[9,10]

Apoptosis, or programmed cell death, is an important physiological process in embryonic development. Apoptosis plays a role in eliminating unnecessary or damaged cells, thereby ensuring normal organ formation. During esophageal development, apoptosis plays a role in the formation of the esophageal lumen. The cells in the middle of the esophagus undergo apoptosis, resulting in an empty space which will become the lumen of the esophagus. Failure of apoptosis at this stage can cause esophageal atresia, where the esophageal lumen does not form or forms incompletely. Several studies have identified genes involved in the regulation of apoptosis during esophageal development. Mutations in these genes can disrupt the apoptosis process and cause esophageal atresia. For example, mutations in the BAX and BCL-2 genes, which are genes that regulate apoptosis, have been associated with esophageal atresia in some cases. However, the exact role of apoptotic failure in the pathogenesis of esophageal atresia is still not completely clear. Further research is needed to identify other genes involved in the regulation of apoptosis in the esophagus and understand how mutations in these genes can cause esophageal atresia.[11,12]

Genetic factors are thought to play an important role in the occurrence of esophageal atresia. Several studies have identified specific genes associated with esophageal atresia, although no single gene has been consistently identified as the primary cause. SOX2 is a gene that plays an important role in the development of the esophagus and trachea. Mutations in the SOX2 gene can disrupt the differentiation of esophageal and tracheal cells, causing esophageal atresia and tracheoesophageal fistula. Nkx2.1 is a gene that plays a role in the development of the lungs and esophagus. Mutations in the Nkx2.1 gene can disrupt the formation of esophageal tissue and cause esophageal atresia. Apart from SOX2 and Nkx2.1, several other genes such as FOXF1, GLI3, and MYCN have also been associated with esophageal atresia.[10,12]

Esophageal atresia causes various pathophysiological consequences that impact the infant's respiratory, digestive, and nutritional functions. Babies with esophageal atresia are at high risk of aspiration of stomach contents into the lungs, especially if there is a tracheoesophageal fistula. Aspiration can cause aspiration pneumonia, which is a serious and life-threatening complication. A tracheoesophageal fistula can cause air to enter the stomach during ventilation, resulting in gastric distension and respiratory distress. Apart from that, aspiration can also cause airway obstruction and impaired gas exchange. The inability to swallow food normally causes nutritional disorders in babies with esophageal atresia. These babies require parenteral nutrition to meet their nutritional needs during the healing period. Esophageal atresia is often accompanied by gastroesophageal reflux, namely the backflow of stomach contents into the esophagus. Reflux can worsen aspiration symptoms and cause esophageal irritation.[12,13]

Comprehensive and careful preoperative preparation in neonates with esophageal atresia is crucial to ensure optimal conditions before undergoing surgical intervention. The primary goals of preoperative preparation are to identify and treat underlying medical problems, minimize the risk of perioperative complications, and optimize surgical outcomes. Neonates with esophageal atresia often experience significant physiological disorders due to the inability to swallow and the presence of a tracheoesophageal fistula. This condition can cause dehydration, electrolyte imbalance, metabolic acidosis, and respiratory problems. The inability to swallow fluids normally can cause dehydration in babies. Dehydration can be assessed based on clinical signs such as decreased skin turgor, dry mucous membranes, sunken eyes, and sunken fontanelles. Intravenous (IV) fluid administration with electrolyte solutions such as Ringer's Lactate or 0.9% NaCl is essential to correct dehydration and maintain body

fluid balance. Electrolyte balance disorders such as hyponatremia, hyperkalemia, or hypokalemia can occur due to vomiting, regurgitation, and impaired kidney function. Regular monitoring of serum electrolyte levels and correction of electrolyte imbalances with appropriate supplementation is essential to maintain vital organ function. Metabolic acidosis can occur due to the accumulation of lactic acid and ketones in the body due to metabolic disorders. Administration of intravenous fluids and correction of electrolyte imbalances can help correct metabolic acidosis. Aspiration of saliva or milk through a tracheoesophageal fistula can cause airway obstruction, atelectasis, and aspiration pneumonia. Babies with significant respiratory distress may require respiratory support such as supplemental oxygen, continuous positive airway pressure (CPAP), or mechanical ventilation. Gastric decompression is an important step in the preoperative preparation of neonates with esophageal atresia. Insertion of a nasogastric tube (NGT) allows air and fluid to be removed from the stomach, reducing the risk of aspiration during induction of anesthesia and surgery. NGT can also be used to provide enteral nutrition slowly after surgery, if possible. A comprehensive preoperative evaluation aims to assess the baby's overall health condition and identify possible comorbidities that may affect perioperative management. Preoperative evaluation includes: History and physical examination: A complete medical history is collected and a thorough physical examination is performed to identify clinical symptoms, vital signs, and other congenital abnormalities; Laboratory examination: Complete blood count, serum electrolytes, kidney function, liver function, and coagulation tests are performed to assess organ function and identify possible metabolic disorders or infections; Supporting examinations: Chest X-ray: Performed to evaluate the position of the NGT, the presence of aspiration pneumonia, and congenital heart defects; Echocardiography: Performed to detect congenital heart defects that often occur in babies with esophageal atresia, such as ventricular septal defects or tetralogy of Fallot; Abdominal ultrasound: Performed to evaluate other gastrointestinal abnormalities, such as duodenal atresia or intestinal malrotation; Prophylactic antibiotic administration: To prevent postoperative infections; Multidisciplinary consultation: Discussion with a multidisciplinary team consisting of a pediatric surgeon, anesthesiologist, neonatologist, and nutritionist is essential to plan optimal perioperative management strategies.[14,15]

Anesthetic management of neonates with esophageal atresia is challenging due to the high risk of aspiration and unique physiology. These infants have immature airway protective reflexes, low functional residual lung capacity, and hemodynamic instability. Therefore, the selection of anesthetic agents, induction techniques, maintenance of anesthesia, ventilation, and positioning of the baby must be done carefully and carefully. Induction of anesthesia is the process of making the patient unconscious and pain-free before the operation begins. In neonates with esophageal atresia, induction of anesthesia is usually performed with intravenous agents such as Ketamine or Propofol. Ketamine is a dissociative anesthetic agent that has some benefits in infants with esophageal atresia. Ketamine has bronchodilation effects that can help keep the airway open and reduce the risk of bronchospasm. In addition, ketamine also has a good analgesic effect, thereby reducing the need for additional analgesic agents. However, ketamine can cause an increase in blood pressure and heart rate, so its use should be careful in babies with unstable cardiovascular conditions. Propofol is a hypnotic anesthetic agent that has a rapid onset and relatively rapid recovery. Propofol has minimal effects on cardiovascular function, so it may be a good choice in infants with hemodynamic instability. However, propofol does not have the bronchodilation and analgesic effects of ketamine, so additional agents may be needed to treat this problem. The choice between ketamine and propofol as anesthesia induction agents must take into account the clinical condition of the baby, the risk of aspiration, and the anesthesiologist's preference. In some cases, a combination of ketamine and propofol may be used to obtain the benefits of both agents. After induction of anesthesia, anesthesia is maintained with

a combination of inhaled agents such as Sevoflurane or Desflurane and intravenous agents such as Fentanyl or Remifentanil. Sevoflurane and Desflurane are inhaled anesthetic agents that have a rapid onset and offset, allowing rapid adjustment of the depth of anesthesia. Both agents have minimal effects on cardiovascular function but can cause respiratory depression, so ventilation should be monitored carefully. Fentanyl and Remifentanil are opioid analgesic agents used to reduce pain during surgery. Fentanyl has a longer duration of action than Remifentanil, making it more suitable for longer operations. Remifentanil has a very rapid onset and offset, allowing precise dose titration according to the baby's needs. The combination of inhalation and intravenous agents allows achieving adequate anesthesia with minimal side effects. Close monitoring of vital signs, oxygen saturation, and blood pressure is essential during the maintenance of anesthesia to ensure hemodynamic stability and oxygenation of the baby. Mechanical ventilation is an important aspect of anesthetic management in neonates with esophageal atresia. The goal of ventilation is to maintain adequate oxygenation and ventilation while minimizing the risk of gastric distension and aspiration.

Positive pressure ventilation can be provided via a face mask or endotracheal tube (ETT). The use of positive end-expiratory pressure (PEEP) can help prevent atelectasis and improve oxygenation. However, high ventilation pressures should be avoided as they can cause gastric distension and increase the risk of aspiration. Jet ventilation is an alternative ventilation technique that uses a high-velocity gas stream to deliver oxygen and remove carbon dioxide. Jet ventilation can reduce the risk of gastric distension, but requires special expertise and close monitoring. High-frequency ventilation (HFV) is a ventilation technique that uses a very high respiratory frequency and a very low tidal volume. HFV can reduce the risk of barotrauma and volutrauma to the lungs but requires special equipment and intensive monitoring. Selection of the appropriate ventilation technique must take into account the clinical condition of the baby, the type of esophageal atresia, and the experience of the anesthetist. Close monitoring of vital signs, oxygen saturation, and partial pressure of carbon dioxide ($PaCO_2$) is essential during ventilation to ensure adequate oxygenation and ventilation.[16,17]

The position of the baby during anesthesia is also an important factor in minimizing the risk of aspiration. Position tilted to the left or head elevated can help prevent regurgitation of stomach contents into the esophagus and trachea. Apart from that, this position can also improve respiratory function by reducing pressure on the diaphragm. During surgery, the baby's position must be adjusted periodically to ensure comfort and prevent complications such as pressure ulcers. Pillows and supports can be used to keep the baby's position stable and prevent nerve injury. Anesthetic management of neonates with esophageal atresia is a complex challenge, but with careful planning, selection of appropriate anesthetic agents and techniques, and close monitoring, the risk of complications can be minimized and optimal outcomes can be achieved. The surgical procedure for esophageal atresia depends on the type of atresia and the presence or absence of a tracheoesophageal fistula. In type C esophageal atresia, the most common procedure performed is thoracotomy with ligation of the tracheoesophageal fistula and primary esophageal anastomosis. During surgery, the surgeon will make an incision in the chest wall to reach the esophagus and trachea. The tracheoesophageal fistula is identified and ligated, then the two separate ends of the esophagus are connected with careful sutures. In some cases, additional procedures may be needed such as a gastrostomy to provide temporary nutrition or colon interposition if the distance between the two ends of the esophagus is too far.[16,17]

Intensive post-operative care in the neonatal intensive care unit (NICU) is essential to monitor complications and ensure optimal recovery. Babies usually remain on mechanical ventilation after surgery to maintain oxygenation and prevent atelectasis. Ventilation parameters are adjusted gradually according to the baby's condition. Parenteral nutrition is given to meet the baby's nutritional needs during the healing period of esophageal anastomosis. Enteral nutrition can be started gradually once esophageal

function recovers. Adequate analgesia is very important to reduce stress and pain in the baby. A combination of drugs such as opioids, paracetamol, and ketamine can be used for multimodal pain management. Infants are closely monitored for signs of complications such as aspiration pneumonia, anastomotic leak, esophageal stenosis, and gastroesophageal reflux. Periodic radiological examinations such as chest X-rays and esophagography can be performed to assess the integrity of the anastomosis and esophageal function. Once the baby is stable and can swallow adequately, rehabilitation programs such as physical therapy and speech therapy can be started to help the baby develop eating and drinking skills.[16,18]

Several factors can influence perioperative outcomes in neonates with esophageal atresia, including: Type of esophageal atresia: Type C esophageal atresia (with distal tracheoesophageal fistula) generally has a better prognosis than other types; Birth weight: Babies with low birth weight have a higher risk of complications; Concomitant disorders: The presence of concomitant disorders such as congenital heart defects can worsen the prognosis; Experience of the surgical team: The experience and expertise of the surgical team in treating esophageal atresia can influence the success of the operation and reduce complications; Postoperative care: Intensive post-operative care and close monitoring for complications are essential to ensure optimal recovery.[18]

Minimally invasive surgical techniques such as thoracoscopy are increasingly used to repair esophageal atresia. This technique offers several advantages such as less postoperative pain, shorter length of stay, and better cosmetic results. Stem cell therapy is being researched as an innovative approach to repair esophageal atresia without surgery. Although still in the experimental stage, stem cell therapy has the potential to regenerate damaged esophageal tissue and improve esophageal function. A multidisciplinary approach involving surgeons, anesthesiologists, neonatologists, nutritionists, and therapists is essential to providing comprehensive and integrated care for infants with esophageal atresia.[19]

4. Conclusion

Perioperative management of neonates with esophageal atresia is a complex process that requires attention to detail and interdisciplinary collaboration. Understanding the pathophysiology of esophageal atresia, implementing appropriate perioperative management strategies, and closely monitoring complications are key to achieving optimal outcomes.

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