Perioperative Considerations in A Child with Zellweger Syndrome: A Case Report

Case Report

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ABSTRACT

Background: Zellweger spectrum disorder is a heterogenous group of genetic disorders inherited in autosomal recessive pattern presenting in paediatric age group with symptoms of cerebrohepatorenal degeneration. Clinically, children present with features of hepatic dysfunction, seizures, developmental delay, hearing/visual impairment, and adrenocortical dysfunction.

Case presentation: A developmentally challenged 3 years, 8.7 kg girl was admitted in paediatric emergency ward with nine months history of frequent seizures, poor feeding, and repeated episodes of non-bilious vomiting. She had significantly delayed milestones followed by developmental regression over one year. The child was planned for feeding Jejunostomy in view of poor general condition and to avoid discomfort of nasogastric tube. There was focal neurological deficit, reduced vision and hearing. Airway examination showed short neck and poor dentition. MRI brain revealed diffuse cerebral atrophy and CE-MRI abdomen reported mild hepatomegaly, choledochal cyst with cholelithiasis. Prior to surgery, nasogastric feed was withheld for eight hours. Premedication administered was aspiration and antiepileptic prophylaxis. In addition to the standard monitoring, entropy and PVI using multiwavelength pulse-oximetry masimo was monitored. Anaesthesia was induced with intravenous thiopentone titrated to effect. Neuromuscular blocking agent was not administered in view of hypotonia involving oro-laryngo-pharyngeal musculature. 4% lignocaine was sprayed into airway and endotracheal intubation was accomplished using videolaryngoscopy. Procedure performed was Roux-en Y feeding jejunostomy. Analgesia was given using intravenous paracetamol and local infiltration of 0.2% ropivacaine at surgical site. Child was extubated when fully awake maintaining normal haemodynamic parameters and SpO_2. Post extubation monitoring was continued in PACU and she was shifted to the ward after two hours. Patient was discharged home after 10 days and on a follow up after 6 months, she has gained weight and clinically improved.

Conclusions: Children with ZS have multiple perioperative challenges especially compromised respiratory status due to severe hypotonia and recurrent aspirations. Hypoalbuminemia and antiepileptic medications alter pharmacodynamics and pharmacokinetics of most of the anaesthetics. However, judicious titration of anaesthetics, optimum intravenous fluid administration, vigilant monitoring and thoughtfully planned surgical technique is essential to improve perioperative outcomes.

Key Words: Anesthesia, congenital disorders, case report, genetic, pediatric, zellweger syndrome.

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BACKGROUND

Zellweger spectrum disorder is a heterogenous group of genetic disorders inherited in autosomal recessive pattern presenting in paediatric age group with symptoms of cerebrohepatorenal degeneration.[1,2] Clinically, children present with features of hepatic dysfunction, seizures, developmental delay, hearing/visual impairment, and adrenocortical dysfunction. These are a family of peroxisomal biogenesis disorders having impaired peroxisomal function. Peroxisomes are intracellular organelles playing important role in intracellular fatty acid metabolism pathway that are constituents of nearly all membranes including myelin. Hypotonia is an important presenting symptom which poses many anaesthetic challenges.

CASE PRESENTATION:

A developmentally challenged 3 years, 8.7 kg girl was admitted in paediatric emergency ward with nine months history of frequent seizures, poor feeding, and repeated episodes of non-bilious vomiting. Antenatal history was uneventful, and baby was born at full term through normal

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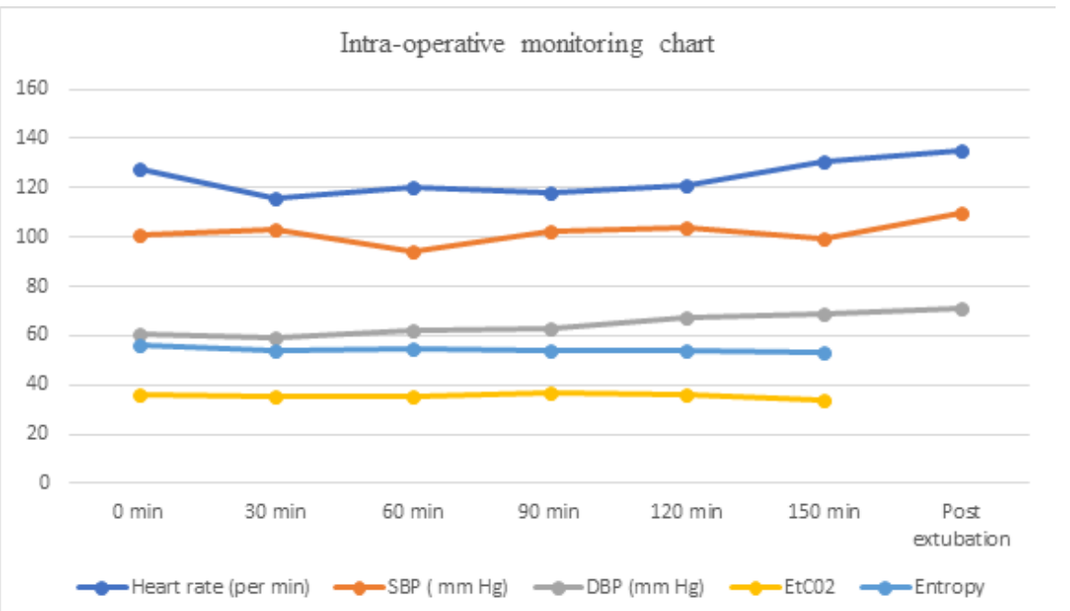
vaginal delivery, birth weight 2.5 kg. During neonatal period, she was exclusively breast fed for two weeks after birth and afterwards top feeds were added due to poor suckling. She had significantly delayed milestones followed by developmental regression over one year.

The child was planned for feeding Jejunostomy in view of poor general condition and to avoid discomfort of nasogastric tube. Preoperatively, she was afebrile, lethargic, had facial dysmorphism, microcephaly and pectus excavatum. There was focal neurological deficit, reduced vision and hearing. Airway examination showed short neck and poor dentition. Blood investigations revealed normal complete blood count and renal function test. The liver enzymes were elevated - AST 276 U/l, ALP 368 U/l, bilirubin 0.43 mg/dl. Coagulogram was derranged- INR 1.63, PTI 75%.MRI brain revealed diffuse cerebral atrophy and CE-MRI abdomen reported mild hepatomegaly, choledochal cyst with cholelithiasis. Previous endoscopic examination had diagnosed a polyp at gastroesophageal junction.

Prior to surgery, nasogastric feed was withheld for eight hours. High risk written informed consent was taken with special mention of need for postoperative mechanical ventilatory support.

Premedication administered was aspiration and antiepileptic prophylaxis. Monitoring consisted of Heart Rate, $EtCO_2$, NIBP, ECG, SpO_2, temperature and entropy.[3] (Table 1). PVI, PI were also recorded using multiwavelength pulse oximetry masimo monitor.[4,5] Nasogastric suction was done, and no aspirate was found. Anaesthesia was induced with intravenous thiopentone titrated to effect. Neuromuscular blocking agent was not administered in view of hypotonia involving oro-laryngo-pharyngeal musculature. 4% lignocaine was sprayed into airway to prevent intubation response. Endotracheal intubation was accomplished using videolaryngoscopy (C-MAC). We decided to use video-laryngoscope as the child had short neck and because we planned to intubate without neuromuscular blockade. Airway was secured with 4.5 mm cuffed endotracheal tube and child was ventilated using an assisted pressure control mode of ventilation. Anaesthesia was maintained using a mixture of Sevoflurane and air-oxygen mixture in ratio of 1:1. Depth of anaesthesia was monitored using entropy and end-tidal concentration of inhalational agents. Intravenous paracetamol 100 mg was administered for analgesia. Injection dexamethasone (1 gram) was also given intravenously for its antiemetic and anti-inflammatory properties. Local anaesthetic 5ml of 1% lignocaine was injected at the surgical site. Unavailability of remifentanil along with unpredictable sedative effects of opioids on maldeveloped brain of a child with a syndrome associated with hepatic and renal impairment, and availability of other options for analgesia prompted us to avoid opioids. Procedure performed was Roux-en Y feeding jejunostomy. Intraoperative period was uneventful. At the completion of surgical procedure skin was infiltrated with 5ml of 0.2% ropivacaine. Blood sugar and venous blood gas sampling revealed normal values. Child was extubated when fully awake maintaining normal haemodynamic parameters and SpO_2. Post extubation monitoring was continued in PACU and she was shifted to ward after two hours. Patient was discharged home after 10 days and on a follow up after 6 months, she has gained weight and clinically improved.

Table 1: Intra-operative monitoring. (SBP- Systolic blood pressure, DBP-Diastolic blood pressure)



DISCUSSION

Zellweger spectrum disorders is a heterogenous group of genetic disorders inherited in autosomal recessive pattern presenting in paediatric age group with symptoms of cerebrohepatorenal degeneration.[1] Presenting clinical features include- neonatal jaundice, seizures, hypotonia, global developmental delay, auditory and visual disability, and adrenocortical dysfunction. This is most severe form of peroxisomal biogenesis disorders with short life span.[2] This child had attained age of three years with good parental care and timely medical interventions.

Children with ZS have multiple perioperative challenges especially compromised respiratory status due to severe hypotonia and recurrent aspirations. Hypoalbuminemia and antiepileptic medications alter pharmacodynamics and pharmacokinetics of most of the anaesthetics. Sedative pre-medication is avoided as these children have pre-existing respiratory depression due to hypotonia. Anyhow, after spending time with the patient she could be brought to operating room without parental separation anxiety. Aspiration prophylaxis and modified rapid sequence intubation is recommended as these children are prone for gastro-oesophageal reflux. In this case, the child had nasogastric tube in-situ which helped us to aspirate gastric contents before induction. Involvement of musculoskeletal system needs special focus from anaesthesia point of view.

Thiopentone was preferred over propofol as induction agent as recent ongoing studies have shown detrimental effect of propofol on neuronal mitochondrial function. Propofol suppresses PGC-1a (Peroxisome proliferator-activated receptor-y coactivator-1a) which in turn leads to reduced mitochondrial function and neurotoxicity which may further deteriorate pre-existing impaired peroxisomal function.[6] The decision to avoid neuromuscular blocking agents was taken based upon the type of surgery and appropriate surgical conditions could be provided with local anaesthetic infiltration and inhalational anaesthesia. Use of succinylcholine in children with this syndrome can cause hyperkalemia and hence it's use is not recommended. Due to increased sensitivity to neuromuscular blocking agents, neuromuscular monitoring has been advised. Considering deranged hepatic and renal functions in these patients we minimized use of anaesthetic agents. Entropy monitoring helped us to maintain adequate depth of anaesthesia.

Hepatic impairment with associated coagulopathy precludes central-neuraxial techniques in these children. Ultrasound guided transverse abdominis plane block might have been useful but considering poor muscle mass and laxity of abdominal muscle due to poor nutritional status we preferred to use local infiltration anaesthesia. This child could be managed successfully without opioids and neuromuscular blocking agents. Thus, she returned to her preoperative status without need for postoperative ventilatory support. PVI guided intraoperative fluid management ensured optimum intraoperative hydration.

CONCLUSION

In such high-risk children with Zellweger syndrome, judicious titration of anaesthetics, optimum intravenous fluid administration, vigilant monitoring and thoughtfully planned surgical technique is essential to improve perioperative outcomes.

ABBREVIATIONS

1. CE MRI: Contrast-enhanced Magnetic Resonance Imaging

2. C-MAC: Karl Storz Video Macintosh laryngoscope

3. ECG: Electrocardiogram

4. SpO2: Oxygen saturation

5. MRI: Magnetic Resonance Imaging

6. NIBP: Non-invasive blood pressure

7. PACU: Post Anesthesia Care Unit

8. PI: Perfusion Index

9. PVI: Pleth Variability index

CONFLICT OF INTEREST

There are no conflicts of interest.

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