Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked recessive genetic disease, caused by deficiency of this enzyme in the hexose monophosphate (HMP) shunt pathway that results in decreased production of nicotinamide adenine dinucleotide phosphate hydrogenase (NADPH). The G6PD enzyme catalyses the first step in the pentose phosphate pathway, leading to anti-oxidants that protect cells against oxidative damage. Ingestion of certain drugs, infections, and metabolic conditions which may cause oxidative stress can result in haemolysis in patients with G6PD deficiency and may lead to permanent neurologic damage or death.

The Arnold-Chiari Malformation (ACM) consists of a downward displacement of the cerebellar tonsils through the foramen magnum, causing non-communicating hydrocephalus. Management of anaesthesia must consider the possibility of increases in intracranial pressure (ICP). There are very few case reports of surgery in patients with G6PD deficiency in association with ACM.

We report a case of 25-day-old male child with G6PD deficiency associated with ACM posted for meningo-myelocele repair.

CASE REPORT

An 11-day newborn male child, weighing 2.9 kgs was admitted with the complaints of swelling on back, bilateral foot deformity, seizure, fever, poor intake and decreased urine output. On examination, child had ruptured MMC on lumbar region. He was diagnosed to have ventriculitis with hydrocephalus, ACM and G6PD deficiency. The patient was put on anti-epileptics and antibiotics. Meanwhile, the child developed hypotonia, intermittent episodes of stridor, desaturation, bradycardia, apnoea and respiratory acidosis for which he was intubated and taken on ventilator. He was posted for lumbar MMC repair on 14th day of admission / 25th day of life. There was no history of haemolysis or jaundice and all investigations were within normal limits except haemoglobin (Hb) which was 11.8 g/dl. The total leukocyte count (TLC) was 13000/cumm, SGOT was 35, SGPT was 23, and S. bilirubin was 0.6 mg/dL. Chest X-ray was normal. Serum creatinine was 0.53 mg/dL. Patient`s G6PD levels were low (3.2 U/G Hb).

On the day of surgery, all investigations including serum electrolytes were within normal limit, and antibiotics and antiepileptic drugs were continued. The child was premedicated intravenously (IV) with glycopyrollate (15 µg) and fentanyl (4 µg). Child was induced with propofol and maintained on oxygen and nitrous oxide mixture and propofol infusion (6 mg/kg/hr), and intermittent boluses of atracurium were administered. The child was turned into prone position. To maintain normothermia, warming blankets and warm fluids were administered. The surgery lasted for 45 minutes; and at the end of procedure, rectal paracetamol (60 mg) suppository was put for postoperative analgesia. Residual neuromuscular blockage was not reversed and child was shifted back to neonatal intensive care unit (NICU). Child was posted for ventriculo-peritoneal (VP) shunt 11 days after the first surgery. Surgery lasted for 30 minutes and was uneventful. Later in his stay in NICU, patient developed fungemia due to fungal ball impaction at ureter bilaterally. Child was given several weaning trials but failed and was kept on ventilator for a long-time. Finally, he was discharged after 3 months. Unfortunately, his milestones were not upto the age and his lower limb weakness persisted.
DISCUSSION

Deficiency of G6PD is responsible for several pathologic processes, most common being haemolysis. The usual clinical expression of this disorder includes anaemia, jaundice, hepatosplenomegaly, and reticulocytosis, as a consequence of haemolysis in these patients. Various types of qualitative and quantitative tests are available for assessing G6PD deficiency. Two types of qualitative tests include fluorescent spot test and dye reduction test. We opted for quantitative test as this test is cheap and gold standard. Indication for performing test for G6PD deficiency was that the neonate was planned to give antibiotics (which could precipitate haemolysis in G6PD deficient patients) due to his recurrent urinary tract infection which developed due to urinary stasis as a result of paraplegia with bladder involvement. Other reason was low haemoglobin level.

Haemolysis usually occurs after exposure to drugs or to other substances that produce peroxides (e.g. \( \text{H}_2\text{O}_2 \)), resulting in oxidation of Hb and red blood cell membranes. Drugs implicated in causing haemolysis in G6PD deficiency are antimalarial drugs, sulphonamides, methylene blue, naphthalene, aspirin, nitrofurantoin, isoniazid, dapsone and furazolidine etc. In clinical practice, fever, infections, and diabetic ketosis, are the common precipitating factors. In this case, child was having fever and urinary tract infection, which were treated preoperatively to eliminate stress factors during surgery.

Altikat et al. studied the effects of halothane, isoflurane, sevoflurane, ketamine, prilocaine, diazepam, and midazolam on the enzymatic activity of G6PD. They found that isoflurane, sevoflurane, diazepam, and midazolam had an inhibitory effect on G6PD activity in vitro, while halothane, ketamine, and prilocaine had none. On the other hand, no documented cases were found to show that benzodiazepines, codeine, fentanyl or ketamine can cause haemolytic crisis in G6PD deficient patients in vivo. We could not find any literature on the effects of propofol and nitrous oxide in patients with G6PD deficiency. In this case, we used propofol and avoided inhalational agents for induction as well as maintenance of anaesthesia. Administration of propofol concomitantly with fentanyl has been reported to cause serious bradycardia in paediatric patients. However, this patient remained haemodynamically stable intraoperatively. Postoperatively, G6PD deficient patient should be monitored carefully as haemolysis is seen 1 - 3 days after contact with triggering agent. Acute haemolysis is self-limited; but in rare conditions, it can be severe enough to warrant a blood transfusion. Thiopentone and phenytoin are the two drugs that deserve special attention in context of neurosurgery. Tritated administration of phenytoin and maintenance of plasma level is necessary. Safety of using higher doses of these agents in patients presenting for neurosurgery with G6PD deficiency needs to be established.

ACM is a developmental malformation characterised by downward displacement of cerebellar tonsils into spinal canal. One of the most important goals during general anaesthesia is to avoid aggravating the already disturbed craniospinal pressure relationship. ACM may present with obstructive hydrocephalous and MMC, which were present in this case. Management of anaesthesia must consider the possibility of increases in intracranial pressure (ICP). We preferred propofol for induction rather than sevoflurane as it decreases ICP and was not a precipitating factor for haemolysis in G6PD deficient state. Ketamine is probably safe in G6PD deficient patients but increases ICP. Proper positioning and extremes of neck flexion and extension should be avoided, if hypotonia is associated. Neuromuscular monitoring should be done on the limb not affected by motor deficit to avoid overdose. However, it was not done in this case, as we planned to keep the baby on mechanical ventilation postoperatively. Caudal block is best avoided in the patients with ACM as there are case reports of worsening of pre-existing neurological symptoms due to wet tap during epidural block up to 2 weeks after dural puncture. We preferred rectal suppository of paracetamol for the immediate postoperative pain management. These patients should be evaluated for vocal cord dysfunction and breathing disorder even if ICP is well controlled; and preferably be shifted to ICU for signs of apnoea and compromised airway.

The patients of G6PD deficiency require careful workup in the preoperative period like history of jaundice, haemolysis, history of blood transfusion and investigations like haemogram, peripheral blood smear, serum bilirubin, haptoglobin level and tests to quantify enzyme deficiency of G6PD. One should avoid oxidising drugs for the safe anaesthesia management. One of the most important goals in patients with ACM during general anaesthesia is to avoid aggravating the already disturbed craniospinal pressure relationship. Propofol can be safely used for induction and maintenance of anaesthesia in such patients.

REFERENCES


