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ANESTHETIC MANAGEMENT OF A PATIENT WITH HEREDITARY FRUCTOSE INTOLERANCE AND PHENYLKETONURIA*

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This is a report of a five-year-old girl with phenylketonuria (PKU) and hereditary fructose intolerance (HFI) who underwent elective strabismus surgery. PKU and HFI are two inborn errors of metabolism which have an autosomal recessive mode of inheritance. This case report describes the anesthetic features of a patient with PKU and HFI, each defect requiring specific anesthetic management. *Key words: phenylketonuria, hereditary fructose intolerance, general anesthesia.*

Phenylketonuria (PKU) is an autosomal recessive disorder of amino acid metabolism characterized by a genetically determined absence of phenylalanine hydroxylase. If the disease is not diagnosed early and treated, it leads to mental retardation[1-3]. PKU occurs in 1 of 3954 newborn infants in Turkey[4]. In hereditary fructose intolerance (HFI), which is a genetic disorder of carbohydrate metabolism transmitted in an autosomal recessive pattern, there is a marked deficiency of fructose-1-phosphate aldolase B in the liver, renal cortex and in the small intestine[1,2].

According to reports from Switzerland, the incidence of HFI is presumed to be nearly 1 in 20,000 infants[4]. The statistical probability of both these defects occurring together is 1 in 75,080,000[4]. Both of these disorders were present in our patient, and each required specific anesthetic management.

Case Report

A five-year-old girl was previously diagnosed as having PKU and HFI because of an elevated blood phenylalanine level (>20 mg/dl) and sucrose and fructose intolerance. The patient has been receiving a low phenylalanine and sucrose/

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fructose free diet since she was one month-old[4]. The parents of the child are first cousins.

Since she had alternate exotrophia-hypertrophia, a right lateral rectus recession and a right medial rectus resection were planned under general anesthesia. There were no preoperative pathological findings except for molar hyperplasia. Liver and kidney function tests were within normal limits. There was no history of epileptogenic seizure.

After a six-hour period of no solid food, the patient was premedicated with atropine sulphate 0.015 mg/kg intramuscularly 45 minutes prior to surgery. She was given first priority on the elective surgery schedule and was infused with a 5% solution of dextrose in water. Anesthesia was induced by using intravenous thiopentone sodium 5 mg/kg and endotracheal intubation was facilitated with vecuronium bromide 0.1 mg/kg intravenously. Anesthesia was maintained with 0.5% halothane and 70% nitrous oxide in 30% oxygen. Towards the end of the operation, vecuronium bromide was reversed with neostigmine bromide 0.07 mg/kg and atropine 0.015 mg/kg intravenously. The operation lasted approximately 45 minutes. During the anesthesia the systolic blood pressure, heart rate, ECG, end tidal CO_2 (ET CO_2) and peripheral oxygen saturation (SaO_2) were monitored. Both hyper and hypocarbia were avoided. Approximately 24-hours postoperatively, nausea, drowsiness and weakness were observed because of the late feeding of the patient and she was transferred to the pediatric intensive care unit. She received a low phenylalanine and fructose/sucrose free diet. Since metabolic acidosis and hypoglycemia were present intravenous dextrose and bicarbonate therapy was initiated. She was discharged from the hospital on the third postoperative day.

Discussion

PKU may be associated with Charcot-Marie-Tooth disease, Down's syndrome, cystinuria, bilateral iris coloboma, cataract, and enamel hypoplasia. These patients may undergo elective surgery because of their primary pathology, as occurred in our case[1,4]. Untreated children may present clinically with eczema, decalcification of long bones, mental retardation, hyperreflexia, muscular hypertonicity, behavioral abnormalities, seizures and cataract[1-3,5]. There have been reports of increased incidences of congenital hyperthyroidism and pyloric stenosis in children with PKU who require specific anesthetic management[6-8].

In PKU patients, food should not be withheld for an extensive period preoperatively because it can result in a catabolic state characterized by the breakdown of tissue protein, and consequently, an elevated serum phenylalanine level. Therefore, these patients should be given first priority on elective surgery schedules. Minor surgery does not cause major long-lasting changes in the serum

phenylalanine level of PKU patients and, therefore, there is no need to alter the dietary regimen[2,9]. The effects of tranquilizers, narcotics and hypnotics used for preanesthetic sedation are quite unpredictable. A patient administered normal or abnormal doses of sedatives may develop severe respiratory depression which can persist into the postanesthetic period. A seizure-prone patient given preanesthetic agents, which induce respiratory depression, may develop seizures. Therefore, we suggest that anticholinergic drugs be used for preanesthetic sedation. Since glycopyrrolate does not easily cross the blood-brain barrier, as do atropine and scopolamine, it has less adverse effects than other drugs when administered to patients with abnormal brain metabolism and altered neurotransmitter activity[2,8]. If a patient has a history of eczema, care should be taken during the application of the face mask and the passage of the endotracheal tube because skin sensitivity may increase. After one year of age, if infants have not been treated for PKU, they may develop decalcification of the long bones. Therefore, a patient under general anesthesia should be carefully manipulated to avoid fracture of the extremities. In PKU patients with seizure disorders, bright lights and equipment such as electrocardiogram machines or other monitoring devices should be used with caution[2].

During anesthesia continuous measurement of body temperature, blood sugar determinations and, if available, continuous electroencephalographic monitoring should be carried out. Capnography and arterial blood gas analysis should be performed in seizure-prone patients for confirming continuous normothermia, normoglycemia and normocarbia[2]. In infants and children, halothane, oxygen and nitrous oxide may be employed in induction and maintenance of anesthesia. With inhalation agents, anesthesia is easily controlled and there is rapid recovery. The patient can receive an oral therapeutic regimen shortly after. In the patients who receive antiepileptic, or enzyme-inducing agents such as phenobarbital or carbamazepin, isoflurane may be used instead of halothane during anesthetic maintenance so as to assure not only a more rapid recovery, but perhaps more importantly a smaller degree of biotransformation of the inhalation agent to potentially toxic metabolites[2].

Hepatic intracellular concentration of fructose-1-phosphate becomes markedly elevated in HFI patients. The intracellular accumulation of fructose-1-phosphate causes renal tubular dysfunction and the inability to acidify urine which may result in generalized amino aciduria and albuminuria[1,2]. Patients who develop hypoglycemia, dehydration, or acid-base derangements due to both prolonged vomiting and renal alkaline losses should receive intravenous glucose and salt-containing solutions prior to surgery to achieve normoglycemia, normovolemia, a neutral blood pH and an adequate serum electrolyte concentration. In patients with hepatic dysfunction, anesthetic considerations are similar to those necessary in

any patient with a similar degree of hepatic dysfunction. An anesthetic agent which may be toxic to the liver should be avoided or used in minimal doses in HFI infants. These types of drugs may significantly impair drug conjugation functions and compounds that are biodegraded via this pathway which may have a prolonged effect on these patients. In patients with liver damage, the effect of succinylcholine is not prolonged if hypocholinesterasemia is not present. Except for vecuronium and pancuronium, the non-depolarizing muscle relaxants and decamethonium are unaffected by hepatocellular injury if there is no presence of renal dysfunction[2].

Systemic organ dysfunction did not occur in our patient who has been treated and followed up since the age of one. We complied with the principles of anesthesia, and therefore, our patient had a safe and effective anesthetic period. The development of hypoglycemia and acidosis because of late feeding postoperatively stresses that other than preoperative preparation and anesthetic management of the patient with metabolic disorders, postoperative care is equally as important.

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