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Anesthetic management of a pediatric patient on a ketogenic diet

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Abstract
There are several specific considerations regarding seizure control during the perioperative period in patients who have been placed on a ketogenic diet (KD). A KD is high in fat and low in protein and carbohydrates and has a long history of use for the treatment of intractable seizures in children. Maintaining therapeutic ketosis and modifying the acid–base balance are particularly important for preventing seizures in patients on a KD. We report changes in the biochemical parameters of a patient with double cortex syndrome who was on a KD and who had been scheduled for the treatment of dental caries under sevoflurane anesthesia and acetate Ringer administration. Inhalation induction with a high concentration of sevoflurane should be reconsidered in view of recent reports describing the epileptogenic potential of sevoflurane.

Key words Ketogenic diet · Ketosis · Metabolic acidosis · Double cortex syndrome

Introduction

A ketogenic diet (KD), which is high in fat and low in protein and carbohydrate, has been used to treat seizures refractory to multiple antiepileptic drugs (AEDs) [1]. A perioperative strategy for the prevention of seizures is required; therefore, maintaining therapeutic ketosis and modifying the acid–base balance are particularly important for patients on a KD [2–4]. We describe the perioperative management of a patient on a KD in terms of seizure control and report changes in biochemical parameters, such as the level of ketone bodies, during minor surgery.

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Case report

A 7-year-old boy on a KD underwent treatment for dental caries. He had experienced tonic-clonic seizures at the age of 4 years and 9 months and had been diagnosed as having double cortex syndrome on the basis of a computed tomography study of his brain. At the age of 5 years and 9 months, a 4:1 (fat:protein + carbohydrate), 1200-kcal classic KD based on medium-chain triglycerides was introduced because his generalized seizures were being poorly controlled with the AEDs phenytoin, zonisamide, and sodium valproate. Nineteen months later, the diet and AEDs had contributed to a 50%–90% decrease in seizure frequency and intensity. The patient's height and weight were 104 cm and 18.2 kg at the age of 7 years. These data correspond to –2 standard deviations on a normal growth curve (according to the National Center for Health Statistics), although the child's weight-to-length proportion was appropriate for his age.

The preoperative total ketone body level in the patient's blood serum was 3746 μmol·l^{-1} (normal range, 12.7–294 μmol·l^{-1}), and the level of acetone bodies in his urine was 2+, demonstrating ketosis. The level of blood glucose was kept between 65 and 90 mg·dl^{-1} Electroencephalography (EEG) monitoring for 24 h showed polyspikes and waves in certain phases of sleep and wakefulness. The KD was continued with no increase in daily caloric intake and with a fluid restriction of 600 ml·day^{-1} until 1 day before the operation.

Premedication consisted of only 0.3 mg of atropine intramuscularly, and preoperative sedation was not used. The preoperative fasting period was 9 h. Following the placement of standard monitoring, general anesthesia was induced with the use of sevoflurane inhalation; tracheal intubation was facilitated by 4 mg of vecuronium. Anesthesia was maintained with sevoflurane (1%–2% end tidal concentration) in a nitrous oxide–oxygen mixture ($F_{I_{O_2}}$ = 0.5). During the

Table 1. Variations in perioperative glucose, plasma ketones, urine ketones, pH, and base excess levels

			Postoperative			
	Preinduction	Postinduction	30 min	60 min	90 min	1 h
Glucose ($mg \cdot dl^{-1}$)	65	113	105	103	122	78
Plasma ketones ($\mu mol \cdot l^{-1}$)	3746		4627		5793	
Urine ketones ($mg \cdot dl^{-1}$)	40	40	15	15	15	40
pH	7.498	7.397	7.445	7.4	7.432	
Base excess ($mmol \cdot l^{-1}$)	–3.2	2.1	1.8	0.7	1	

perioperative period, a carbohydrate-free solution, acetate Ringer, was used. Glucose, arterial blood gas, and the ketone levels in blood and urine were examined every 30 min. The patient's blood sugar level increased gradually from 65 to 122 $mg \cdot dl^{-1}$. The blood ketone level also increased from 3746 to 5793 $\mu mol \cdot l^{-1}$, whereas the urine ketone level decreased from 40 to 15 $mg \cdot dl^{-1}$ (Table 1). The ranges of arterial blood gases during the operation were as follows: pH, 7.397–7.498; HCO^{3-}, 25–28 $mEq \cdot l^{-1}$; anion gap, 13–15 $mmol \cdot l^{-1}$; and base excess, –3.2 to 2.1 $mEq \cdot l^{-1}$. At the end of surgery, the patient was administered 10 mg of diazepam rectally and extubated without causing any seizures. The duration of the general anesthesia was 115 min. The amount of intravenous fluids (acetate Ringer) administered was 165 ml, the urine volume was 32 ml, and the surgical blood loss was 10 ml. He was restarted on a full KD on postoperative day 1 and was discharged without experiencing a seizure on postoperative day 2.

Discussion

A KD has been considered an alternative therapy for children with seizures that are difficult to control since Wilder's original report in 1921 [1]. This dietary therapy has been gaining popularity in recent years because of its efficacy and safety, while numerous AEDs and surgical treatments have also been introduced [5,6]. The diet restricts the quantity of protein and carbohydrate consumed, and most calories are provided as fat. This causes a state of chronic ketosis, which is an essential aspect of this therapeutic regimen.

The anesthetic management of patients on a KD must be carefully considered to prevent seizures. There are several specific considerations for perioperative seizure control in pediatric patients on a KD. First, the plasma ketone body concentration should be similar to that in the preoperative period. Sedative syrups containing amino acids and sugars for premedication should be avoided because the infusion of amino acids and/or glucose is associated with a fall in plasma ketones [2–4]. When amino acid or glucose utilization is low or deficient, the rates of fatty acid oxidation will be high, resulting in the synthesis of ketone bodies. Perioperative intravenous fluids must also be amino acid- and carbohydrate-free. In this patient, acetate Ringer solution was chosen, and moderate ketosis and normoglycemia were maintained practically throughout the anesthesia and 1 h postoperatively (Table 1).

The patient's urinary ketone levels ranged from moderate to small (20–40 $mg \cdot dl^{-1}$). The reason for the discrepancy between the high level of ketone bodies in the blood and the low level of ketone bodies in the urine is not known. During ketosis, urinary ketons may represent 10%–20% of ketone body production, although the kidney conserves ketone bodies by increasing the reabsorption rate [7].

Secondly, acid–base imbalances should be carefully monitored and treated immediately, because ketone bodies have the potential to lead to metabolic acidosis. Acidosis influences the threshold for seizures. We believe that acetate Ringer solution may be useful as an indirect exogenous buffer in these patients. The metabolism of acetate in the liver results in the consumption of H^+ and the regeneration of the bicarbonate buffer [8]. Valencia et al. [4] suggested that intravenous bicarbonate should be used unreservedly if a child develops acidosis. In our case, the arterial blood gases were maintained within the desired pH 7 range (7.397–7.445) during the operation without the use of intravenous bicarbonate. The use of sodium bicarbonate Ringer solution might also have been profitable as a direct bicarbonate source. That solution would correct metabolic acidosis promptly without being metabolized in the liver.

Thirdly, propofol anesthesia may be a relatively safer method for seizure-prone patients because sevoflurane has been suspected of having an epileptogenic potential. Several studies have indicated that inhalation induction using high concentrations of sevoflurane can cause seizure-like changes in the EEG [9,10]. On the other hand, propofol reduces seizure duration during electroconvulsive therapy and thus seems to possess antiepileptic properties [11]. Sedation with propofol in children, however, remains controversial [12]. In the present

case, sevoflurane was chosen for the inhalation induction and maintenance of anesthesia, because it is a nonirritant, it acts and emerges quickly based on a lower blood-to-gas coefficient, and it stabilizes the hemodynamic state. Unfortunately, an EEG recording was not made in this patient.

Finally, anesthetic drugs that do not greatly disturb hepatic function should be chosen. Ballaban-Gil et al. [13] noted that hepatotoxicity develops as a result of interactions among a KD, valproate, and other AEDs. Ketone bodies are formed only in the liver and are utilized in extrahepatic tissues [14]. This means that the energy source of patients on a ketogenic diet depends on liver function. Sevoflurane rather than propofol might be better for maintenance of general anesthesia, considering the effect on hepatic metabolism [15]. In this patient, the level of extrahepatic enzyme was not elevated by the anesthetic drugs postoperatively.

Each biochemical parameter was controlled favorably during this minor surgery. It is well known that excessive surgical stress such as a long duration of surgery, massive blood loss, or an invasive surgical procedure tends to provoke catabolism, metabolic acidosis, and hyperglycemia. Therefore, proper depth of anesthesia and fluid infusion may also play an important role in regulating these stress responses.

In summary, we describe the anesthetic management of a pediatric patient on a KD from the prospective of seizure control. Inhalation induction with a high concentration of sevoflurane should be reconsidered in view of recent reports on the epileptogenic potential of sevoflurane.

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References

1. Wilder RM (1921) The effects of ketonemia on the course of epilepsy. Mayo Clin Proc 2:307–308
2. Hinton W, Schwartz RH, Loach AB (1982) Diet-induced ketosis in epilepsy and anaesthesia. Anaesthesia 37:39–42
3. McNeely JK (2000) Perioperative management of a paediatric patient on the ketogenic diet. Paediatr Anaesth 10:103–106
4. Valencia I, Pfeifer H, Thiele EA (2002) General anesthesia and the ketogenic diet: Cilnical experience in nine patients. Epilepsia 43:525–529
5. Kossoff EH, McGrogan JR (2005) Worldwide use of the ketogenic diet. Epilepsia 46:280–289
6. Thiele EA (2003) Assessing the efficacy of antiepileptic treatments: the ketogenic diet. Epilepsia 44:26–29
7. Garber AJ, Menzel PH, Boden G, Owen OE (1974) Hepatic ketogenesis and gluconeogenesis in humans. J Clin Invest 54:981–989
8. Burnier P, Tappy L, Jequier E, Schneeberger D, Chiolero R (1992) Metabolic and respiratory effects of infused sodium acetate in healthy human subjects. Am J Physiol 263:1271–1276
9. Chinzei M, Sawamura S, Hayashida M, Kitamura T, Tamai H, Hanaoka K (2004) Change in bispectral index during epileptifrom electrical activity under sevoflurane anesthesia in a patient with epilepsy. Anesth Analg 98:1734–1736
10. Constant I, Seeman R, Murat I (2005) Sevoflurane and epileptiform EEG changes. Paediatr Anaesth 15:266–274
11. Borgeat A (1997) Propofol: pro- or anticonvulsant? Eur J Anaesthesiol Suppl 15:17–20
12. Gottschling S, Meyer S, Krenn T, Kleinschmidt S, Reinhard H, Graf N, Shamdeen GM (2005) Effects of short-term propofol administration on pancreatic enzymes and triglyceride levels in children. Anaesthesia 60:660–663
13. Ballaban-Gil K, Callahan C, O'Dell C, Pappo M, Moshe S, Shinnar S (1998) Complications of the ketogenic diet. Epilepsia 39:744–748
14. Donald V et al. (1995) Lipid metabolism. In: Biochemistry. Wiley, New York, pp 678–680
15. Fukuda I, Uchihashi Y, Kira M, Ogura T, Shizukuishi M, Kazama T, Sugiura Y (2005) Effects of propofol on hepatic venous oxygen saturation—a comparison with isoflurane or sevoflurane anesthesia (in Japanese with English abstract). Masui (Jpn J Anesthesiol) 54:736–741