Pediatric Anesthesia and Critical Care Journal 2021;9(2):85-93
doi:10.14587/paccj.2021.15

PACCJ

Anesthetic care of a child receiving a ketogenic diet

R. Kidwell[1], J. D. Tobias[2]

[1]Heritage College of Osteopathic Medicine – Dublin Campus, Dublin, Ohio and Ohio University, USA
[2]Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital and the Department of Anesthesiology & Pain Medicine, The Ohio State University College of Medicine, Columbus, Ohio, USA

Corresponding author: J. D. Tobias, Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital and the Department of Anesthesiology & Pain Medicine, The Ohio State University College of Medicine, Columbus, Ohio, USA. E-mail: Joseph.Tobias@nationwidechildrens.org

Keypoints

1. The ketogenic diet (KD) is used in the treatment of medically refractory epilepsy. The high fat and low carbohydrate intake induces a state of ketosis which may result in anticonvulsant effects through enhanced neuronal energy reserves, antioxidant properties, and anti-inflammatory actions.
2. Specific perioperative concerns of patients on a KD include the impact of the KD on acid-base status and serum electrolytes, the choice of intravenous fluids and their impact on acid-base status, alteration of the ketogenic state by the administration of glucose in intravenous fluids or medications, the risk of hypoglycemia, and the impact of the ketosis and acidosis on cardiovascular function.
3. The acidosis established by the KD is generally mild and does not impact physiologic function or perioperative care. However, long term adverse effects of chronic acidosis can include altered serum electrolytes, renal stone production, and reduced bone mineralization.
4. Severe acidosis may occasionally be seen during prolonged surgical procedures or if other stresses are imposed on the patient including dilutional acidosis from the administration of non-buffer containing intravenous fluids, the administration of medications that inhibit carbonic anhydrase (topiramate or zonisamide) or metformin.

Abstract

The ketogenic diet (KD) is an alternative or supplementary treatment to medically refractory epilepsy and has been used successfully in pediatric patients for more than 100 years. The high fat, low carbohydrate intake of the KD induces a state of ketosis which may result in anticonvulsant effects through enhanced neuronal energy reserves, antioxidant activity, and anti-inflammatory actions. Pediatric patients following the KD for seizure management may require anesthetic care during surgery for various comorbid or associated conditions.

Perioperative adherence to the KD remains an integral component of perioperative care to prevent an increase in seizure burden. We present a 14-year-old adolescent on a KD who required anesthetic care during surgical treatment of neuromuscular thoracic scoliosis. The basic principles of the KD are reviewed, potential end-organ effects and their impact on anesthetic care discussed, and

techniques for general anesthesia presented.

Keywords

ketogenic diet; seizures; metabolic acidosis; ketosis

Introduction

The ketogenic diet (KD) is an alternative or supplementary treatment to medically refractory epilepsy, which has been used successfully in pediatric patients since the 1920s.[1] It includes a high fat, adequate protein, and limited or low carbohydrate intake meant to induce a state of ketosis, which has been shown to be effective in the control of refractory seizures.[2,3] Increased levels of ketones achieved on the KD may produce an anticonvulsant effect, presumably due to changes in cerebral energy metabolism, cellular stabilizing properties decreasing neuronal excitability, effects on neurotransmitter function, circulating factors acting as neuromodulators, and alterations in the extracellular mileu of the central nervous sytem.[3] Although the exact mechanisms have not been clearly delineated, neuroprotection may also result from enhanced neuronal energy reserves, antioxidant properties, and anti-inflammatory effects.[4] Pediatric patients following the KD for seizure management may require anesthetic care during surgery for various comorbid or associated conditions. Perioperative adherence to the KD remains an integral component of perioperative care to prevent an increase in perioperative seizure burden. We present a 14-year-old adolescent on a KD who required anesthetic care during surgical treatment of neuromuscular thoracic scoliosis. The basic principles of the ketogenic diet are reviewed, potential end-organ effects and their impact on anesthetic care discussed, and techniques for general anesthesia are presented.

Case report

Review of this case and presentation in this format followed the guidelines of the Institutional Review Board of Nationwide Children's Hospital (Columbus, Ohio). The patient was a 14-year-old, 49.1 kg adolescent male presenting for posterior spinal fusion to correct neuromuscular thoracic scoliosis. Past medical history included hypoxic-ischemic encephalopathy (HIE), quadriplegic cerebral palsy, and intractable Lennox-Gastaut seizure disorder. The patient's seizure treatment consisted of anticonvulsant medications (levetiracetam, topiramate, and rufinamide) as well as nutritional treatment with a KD, which had been initiated 8 months prior to surgery. Additional past medical history included reactive airway disease, obstructive sleep apnea (OSA) with nocturnal BiPAP requirement, and GJ tube dependence with previous aspiration pneumonia. Other medications at the time of surgery included diazepam, clobazam, glycopyrrolate, albuterol, ferrous sulfate, guaifenesin, lansoprazole, acetaminophen, cholecalciferol, and allergy drugs. The patient was held *nil per os* for 6 hours prior to the surgical procedure. All routine seizure medications were administered prior to surgery. The patient was transported to the operating room and routine American Society of Anesthesiologists' monitors were placed. Following the inhalation induction of anesthesia with sevoflurane in air and oxygen, a peripheral intravenous cannula was placed. Fentanyl (50 µg) and rocuronium (10 mg) were administered and his trachea was intubated. After anesthetic induction and endotracheal intubation, a second peripheral intravenous cannula and a right radial arterial cannula were placed. Per our usual practice to allow for neurophysiological monitoring during spinal surgery, anesthesia was maintained with desflurane titrated to maintain the bispectral index (BIS) at 50-60 and methadone with a remifentanil infusion at 0.3-0.5 µg/kg/hour, adjusted to maintain the mean arterial pressure at 55-65 mmHg.[5] Additional blood pressure control was provided by the administration of a clevidipine infusion at 1-5 µg/kg/min. Baseline neurophysiological monitoring including motor and somatosensory evoked potentials were obtained. The patient was turned and positioned prone. Tranexamic acid was administered to limit intraoperative blood loss (50 mg/kg bolus dose followed by an infusion at 5 mg/kg/hour). Forced air warming and the infusion of warmed intravenous fluids was used to maintain normothermia. Arterial blood gas analysis, glucose levels, and hemoglobin concentrations were measured intermittently

during the surgical procedure. The base deficit ranged from -3.8 to -7.6 mMol/L during the procedure. The surgical procedure was completed in 8 hours 15 minutes with an estimated blood loss of 1050 mL which was washed and returned via the cell saver. Intraoperative fluids included 1700 mL of Normosol-R® and 1750 mL of 5% albumin. Acetaminophen (1000 mg) and ketorolac (30 mg) were administered intravenously to supplement postoperative analgesia. Ondansetron (4 mg) and dexamethasone (4 mg) were administered for postoperative nausea and vomiting prophylaxis. At the completion of surgery, the patient was turned supine and sugammadex was administered to reverse residual neuromuscular blockade. The patient's trachea was extubated, and he was transferred to the post-anesthesia care unit (PACU). Upon transport to the PACU, the patient experienced worse than normal upper airway obstruction post-extubation with poor inspiratory effort even after that application of BiPAP. The patient's trachea was reintubated following the administration of propofol and rocuronium due to arterial blood gas levels consistent with hypercapnic respiratory failure. Following stabilization, the patient was transferred to the intensive care unit (ICU). On postoperative day 1, the patient's trachea was extubated to their home BiPAP settings. The postoperative hemoglobin was 10.0 gm/dL. No allogeneic blood products were administered during the intraoperative or postoperative course. KetoVie peptide feeds were restarted following tracheal extubation along with the patient's chronic home gastrointestinal and anticonvulsant medications. Due to an ileus, the feeds were paused on postoperative day 3 and the bowel regimen maximized. The KD was restarted on postoperative day 5. Urinary ketones were measured daily per the home routine. Due to progressive respiratory insufficiency and increasing BiPAP settings, the patient's trachea was reintubated again on postoperative day 6. On postoperative day 10, the patient had a second trial of tracheal extubation. Trials off the BiPAP began the day after tracheal extubation and were subsequently continued with increasing duration. On postoperative day 19, the patient was transferred to the pediatric pulmonology service and resumed to his normal respiratory regimen with night-time BiPAP. The patient was discharged home on postoperative day 25.

Discussion

Fasting and forcing the body to rely on its endogenous fat sources was suggested by Hippocrates as a means of treating various illnesses and was the one therapeutic measure for epilepsy included in their Hippocratic archives noted in the history of epilepsy from Greek culture.[6] Ancient biblical records including excerpts from the book of Mark in the New Testament suggested the potential therapeutic effect of fasting as he proclaimed that a sick boy could only be cured by prayer and fasting (Mark 9:14-29 New King James Version). In the United States, reports of fasting were first suggested to provide relief from diseases including asthma, diabetes, paralysis, epilepsy, and more in the 1920s by physical fitness fanatic, Bernard MacFadden and his assistant, Dr. Hugh Conklin.[6] These practices were supported by several different hypotheses and postulated mechanisms by which abstaining from food could have potential health benefits. As the processing of food requires energy, MacFadden reasoned that without the presence of food, the body could harness energy towards healing itself from disease. Conklin suggested that the digestion of food released toxic substances into the blood that could cause numerous health problems; however with water alone, one could restore their natural health. Specifically, he applied this idea in the treatment of an epileptic patient with the hopes of decreasing seizure activity. Conklin's promising outcomes inspired Dr. Rawle Geyelin to attempt similar methods in a large cohort. Geyelin subsequently presented the successful results of fasting in patients with epilepsy to the American Medical Association in 1921.[7] Following the release of his analysis, several other studies emerged supporting the potential therapeutic benefit of fasting in patients with epilepsy.

The first large cohort study of fasting as a treatment for epilepsy was performed in France in 1911.[8] Twenty

patients of various ages with epilepsy were "detoxified" by consuming a low-calorie vegetarian diet, combined with periods of fasting and purging. Two patients saw significant clinical improvement with improved seizure control without the adverse effects of sedation that were commonplace with the only available anticonvulsant medications of the time, potassium bromide and phenobarbital. However, most of the patients failed to maintain compliance with the significant dietary restrictions imposed by the diet.

In the 1920's, biochemical research into the metabolic changes induced by fasting or consuming a low carbohydrate diet identified the presence of ketone bodies (water-soluble compounds including β-hydroxybutyrate, acetoacetate, and acetone) produced by the liver. Dr. Russell Morse Wilder, at the Mayo Clinic, built on this research and coined the term "ketogenic diet" to describe a diet that produced a high level of ketone bodies in the blood (ketonemia) through an intake that included an excess of fat and limited carbohydrate. This work led to the more widespread use of the KD as treatment for patients with epilepsy. Wilder's colleague, pediatrician Mynie Gustav Peterman, later formulated the classic KD in children, with a ratio of one gram of protein per kilogram of body weight, 10–15 grams of carbohydrates per day, and the remainder of calories from fat. Peterman's work in the 1920s established the techniques for induction and maintenance of the KD as well as demonstrating the clinical benefits when compared to conventional therapies available at the time. However, with the introduction of phenytoin into clinical practice in 1938, there was a decline in the use of the KD as more effective pharmacologic agents became available.

Despite the growing number of medications available to control epilepsy and seizure disorders, there are still a significant number of patients who fail medical regimens even those including multiple medications. Other patients, although they achieve adequate seizure control, have significant adverse effects related to the need for multi-drug regimens. In the 1990s, the KD reemerged after the televising of a documentary about a young child with seizures, unmanageable by medications, who experienced seizure control after institution of the KD. The parents of the child would later establish the Charlie Foundation that would repopularize the KD for seizure treatment.

The mechanisms responsible for the therapeutic effect of the KD remain speculative. To ensure therapeutic effective, specific initiation, maintenance, and monitoring protocols have been suggested to safely start and maintain ketogenesis. Nutritional and medical support is essential when beginning KD therapy to ensure appropriate KD ratios, safe blood pH levels, and adequate seizure management. For successful treatment, patient compliance and routine monitoring is imperative. Although the exact blood ketone level required to reduce seizure activity has not yet been determined, the presence of +4 urinary ketone bodies (160 mmol/L) is generally cited as the therapeutic threshold.[9] Laboratory values that are followed routinely include electrolytes, blood glucose, albumin, lipid profiles, and hepatic enzymes.[9] Once a proper regimen has been identified, home monitoring of urine ketone levels is instituted to verify that an appropriate therapeutic effect is being maintained.

During the perioperative period, appropriate care for patients with refractory epilepsy receiving a KD begins during the preoperative preparation of the patient. In addition to preparations to maintain and resume the KD during the perioperative period, attention should be directed at identifying the patient's current anticonvulsant regimen. Maneuvers to limit the potential for perioperative seizures include a documentation of therapeutic anticonvulsant levels prior to the surgical procedure with optimization of therapy by the pediatric neurology service as well as the administration of routine anticonvulsant medications the day of the procedure.[10] These should be administered despite the patient's nil per os status. When enteral administration is not feasible, alternative routes of delivery including intravenous administration is feasible for many of these agents. Consultation with the neurology or

pharmacology service is suggested when questions arise concerning dosing conversion from enteral to intravenous or per rectum administration. In addition to their administration the morning of the surgery, for prolonged procedures, the continued redosing of anticonvulsants intraoperatively is suggested to maintain therapeutic levels during prolonged surgical procedures.

Due to the unique requirements of the KD, ongoing consultation with a licensed dietitian and the patient's pediatric neurologist is suggested during the perioperative period. KD patients should follow routine nil per os guidelines leading up to surgery, with the exception that although clear liquids should be encouraged up to 2 hours prior to surgery, they should be glucose free. Additional perioperative concerns include the impact of the KD on acid-base status and serum electrolytes, anesthetic agents increasing the occurrence of seizures, the choice of intravenous fluids, altering the patient's ketogenic state by the inadvertent administration of glucose in intravenous fluids or the diluent of medications, the risk of hypoglycemia, and the potential impact of the ketosis and acidosis on cardiovascular responses including the autonomic nervous responses to general anesthetic agents and hypovolemia or blood loss.

The ultimate success of the KD in managing seizures is dependent on sustaining a ketogenic state. However, the biochemical changes induced by the KD may pose potential risks especially during the perioperative period such as chronic metabolic acidosis, dehydration, and altered serum electrolytes due to increased urinary losses of potassium, magnesium, and calcium. These cations are excreted in the urine to balance the loss of negatively charged ketones. Chronic hypercalciuria may result in renal stone formation and decreased bone mineralization due to calcium losses.[11,12] Preoperative measurement of serum electrolytes, magnesium, and calcium should be considered, especially early on after the start of the KD.

The acidosis established by the KD has generally been described as a low-grade metabolic acidosis, having only a small effect on acid-base balance. Despite the increase in serum and urine ketones, the changes in serum pH and bicarbonate levels are limited in most patients.[13] Serum β-hydroxybutyrate levels vary from 4-6 mMol/L (normal ≤ 1.5 mMol/L), indicating a mild degree of ketosis.[14,15] The ketosis experienced by these patients is significantly less than the values that occur with diabetic keto-acidosis. However, significant metabolic acidosis may occur during prolonged surgical procedures or if other stresses are imposed on the patient including dilutional acidosis from the administration of non-buffer containing intravenous fluids, the administration of anticonvulsants that inhibit carbonic anhydrase (topiramate or zonisamide) or the concomitant administration of metformin. Valencia et al. noted the development of metabolic acidosis in 3 of 9 patients on a KD for the treatment of medically intractable epilepsy during procedures lasting longer than 3 hours.[16] Intravenous bicarbonate can be administered intraoperatively or oral citrate and electrolyte supplementation may be prescribed when initiating the KD.

While generally well tolerated, significant acidosis (pH ≤ 7.20) may result in direct depression of myocardial contractility and systemic vasodilatation resulting in hypotension. Additionally, acidosis may depress the normal response to vasoactive agents. Other cardiovascular complications including arrhythmias with QT interval prolongation, ST-T wave changes, and even cardiac arrest have all been anecdotally noted as potential adverse effects associated with acidosis.[17] Additionally, cardiomyopathy related to selenium deficiency has been reported in a patient on the KD.[18,19] At the tissue and cellular level, acidosis stimulates the pro-inflammatory cascade with the release of tumor necrosis factor and nitric oxide and impairs tissue oxygenation resulting in reduced ATP production. Defects in coagulation function may occur related to prolongation of thrombin generation and increasing fibrinogen breakdown. The severity of these potential complications further underlines the necessity of perioperative serum electrolyte and acid-base monitoring during the perioperative period. Additional preoperative testing including an echocardiogram, electrocardiogram,

coagulation function, and urinalysis should be considered when there are clinical signs and symptoms or additional comorbid conditions are present.

Several agents used to induce and maintain general anesthesia may alter seizure activity through their effects at $GABA_A$ receptor. The majority of anesthetic agents including propofol, benzodiazepines, and the inhalational anesthetic agents lower the seizure threshold, acting as anticonvulsants and even being used in the treatment of status epilepticus.[20-22] Although motor movements resembling seizure activity and even occasional spike and wave activity on the EEG have been reported with sevoflurane, these effects generally occur only when the inspired concentration is rapidly increased during anesthetic induction when there is accompanying hypocarbia.[23] In clinical practice, there does not appear to be any contraindication to the use of sevoflurane or any of the inhalational anesthetic agents in patients with underlying seizure disorders. Other commonly used agents such as nitrous oxide and opioids have no effect on seizure activity and can be safely administered. Etomidate and methohexital may activate the EEG and even stimulate seizure activity.[24] Although the exact mechanisms responsible are not fully understood, the use of these agents in patients with seizure disorders should be avoided. The noncompetitive NMDA receptor antagonist, ketamine, may cause seizures at lower doses, but it has anticonvulsant effects at anesthetic doses, and has been used in the treatment of refractory status epilepticus.[25]

Pediatric patients with refractory epilepsy are often treated with a variety of medications in combination with the KD. To maintain the KD, all perioperative medications must contain little to no carbohydrate. The addition of even small amounts of glucose to the patients' predetermined allowance may impact the efficacy of the KD on seizure control. This aspect of care can be challenging as the exact diluents used and its specific composition may be difficult to verify as pharmaceutical companies are not required by the Food and Drug Administration to supply this information. Conover et al. present the carbohydrate content of commonly used perioperative medications including those that are safe and those that should be used with caution or avoided completely.[12] Oral suspensions often contain larger amounts of carbohydrates, although the carbohydrate content of all oral and intravenous medications must be considered. The reader is referred to reference 12 for an excellent review of specific medication use, their carbohydrate content, and impact on the KD.

Intravenous fluids and fluid used for the dilution of intravenous infusions can also impact the metabolic changes induced by KD by providing substrate for gluconeogenesis thereby altering the ketogenic state or resulting in dilutional acidosis and increasing the impact of the ketosis-induced metabolic acidosis. Commonly used isotonic fluids for intraoperative maintenance and replacement of 3rd space and insensible losses include 0.9% normal saline, lactated Ringer's, as well as the balanced salt solutions Plasmalyte® and Normosol-R®. Clinical reports have documented the safe use of both lactated Ringer's and normal saline in patients receiving a KD. In larger quantities, normal saline solutions may lead to a dilutional acidosis with an increase in base deficit.[26] Although the impact on overall acid-base status is generally limited, the addition of the dilutional acidosis to the underlying chronic acidosis from ketosis may be clinically significant during intraoperative care. Given this concern, use of an isotonic solution with buffering capabilities including lactate, acetate or gluconate may be preferable. The lactate of lactated Ringer's has the potential to disrupt ketosis by increasing the production of glucose, and as a result may be theoretically contraindicated in patients on a KD.[27] The effect on glucose occurs through the hepatic oxidation of lactate to pyruvate by lactate dehydrogenase, thus initiating the first step of gluconeogenesis. While lactate may be shunted into gluconeogenic pathways during metabolism, the actual effect on blood glucose is negligible. Alternatively, both acetate and gluconate have been used as buffers in isotonic fluids. Acetate is converted to acetyl CoA by the enzyme acetyl CoA

synthetase while the metabolic fate of gluconate in the human body is not as well understood.[28] Evidence-based medicine on the use of solutions containing acetate and gluconate in patients on a KD are limited, however neither has shown to be have negative physiologic effects. In general, there is limited clinical or experimental evidence to demonstrate the superiority of any specific isotonic fluid over another. One may consider having the pharmacy prepare special isotonic fluids with 0.9% sodium (half as NaCl and half as sodium acetate) or 2% buffered hypertonic saline for volume resuscitation.

Exogenous glucose or carbohydrates may also present in blood and blood products. The standard anticoagulant in blood and blood products is CPD or a combination of citrate, phosphate, and dextrose. There is approximately 1.6 grams of dextrose in 1 unit of preserved whole blood.[29] In general, the impact of blood and blood products on blood glucose has been shown to be limited.[30] Although blood glucose levels may increase in some patients, anecdotal evidence has noted a limited impact overall on the efficacy of the KD. As there is the potential that these products may disrupt the ketogenic state of these patients, their administration should follow standard transfusion guidelines.

As glucose and carbohydrate administered is strictly limited, hypoglycemia remains a concern especially during general anesthesia where its signs and symptoms may be masked, and glucose administration is avoided. The potential for hypoglycemia may be partly dependent on the duration of the procedure and the amount of time the patient has fasted preoperatively. For major cases requiring an extended operative time, increasing the daily caloric intake prior to surgery may be considered as a means of preventing hypoglycemia. Regardless of the procedure type and length; blood glucose, monitoring throughout the perioperative period is suggested. The goal should be to maintain blood glucose levels of 50-80 mg/dL with intervention only for a levels below 40 mg/dL.

In summary, the KD remains an alternative or supplementary treatment to medically refractory epilepsy that has seen increased use over the past decade. The high fat, low carbohydrate diet induces a state of ketosis which may result in an anticonvulsant effect through enhanced neuronal energy reserves with antioxidant and anti-inflammatory actions. Perioperative concerns of these patients may include the impact of the KD on acid-base status and serum electrolytes, the impact of intravenous fluids on acid-base status and gluconeogenesis, maintaining the ketogenic state by avoiding glucose in intravenous fluids or medications, the potential for hypoglycemia, and the potential impact of the ketosis and acidosis on cardiovascular function.

References

1. Swink TD, Vining EPG, Freeman JM. The ketogenic diet: 1997. Adv Pediatr. 1997;44:297-329.
2. Kim JM. Ketogenic diet: Old treatment, new beginning. Clin Neurophysiol Pract. 2017;2:161-162.
3. Schwartzkroin, PA. Mechanisms underlying the anti-epileptic efficacy of the ketogenic diet. Epilepsy Res. 1999;37:171-80.
4. Gasior M, Rogawski MA, Hartman AL. Neuroprotective and disease-modifying effects of the ketogenic diet. Behav Pharmacol. 2006;17:431-9.
5. Martin DP, Bhalla T, Thung A, Rice J, Beebe A, Samora W, Klamar J, Tobias JD. A preliminary study of volatile agents or total intravenous anesthesia for neurophysiological monitoring during posterior spinal fusion in adolescents with idiopathic scoliosis. Spine. 2014;39E1318-24.
6. Wheless JW. History of the ketogenic diet. Epilepsia. 2008;49(Suppl 8):3-5.
7. Geyelin HR. Fasting as a method for treating epilepsy. Med Rec. 1921;99:1037-9.
8. Guelpa G, Marie A. The fight against epilepsy by detoxification and by the reeducation about food. Rev Ther Med-Chirurg. 1911;78:8-13.
9. Kossoff EH, Zupec-Kania BA, Amark PE, et al. Optimal clinical management of children receiving the ketogenic diet: recommendations of the

International Ketogenic Diet Study Group. Epilepsia. 2009;50:304-17.

10. Jones CT, Raman VT, DeVries S, Cole JW, Kelleher KJ, Tobias JD. Optimizing anticonvulsant administration for children before anesthesia: A quality improvement project. J Pediatr Neurol. 2014;51:632-40.
11. Carnauba RA, Baptistella AB, Paschoal V, Hübscher GH. Diet-induced low-grade metabolic acidosis and clinical outcomes: a review. Nutrients. 2017;9:538-43.
12. Conover ZR, Talai A, Klockau KS, Ing RJ, Chatterjee D. Perioperative management of children on ketogenic dietary therapies. Anesth Analg. 2020;131:1872-82.
13. Kurtz I, Maher T, Hutler HN, Schambelan M, Sebastian A. Effect of diet on plasma acid-base composition in normal humans. Kidney Int. 1983;24:670-80.
14. Neal EG, Chaffe H, Schwartz RH, Lawson MS, Edwards N, Fitzsimmons G, et al. A randomized trial of classical and medium-chain triglyceride ketogenic diets in the treatment of childhood epilepsy. Epilepsia. 2009;50:1109-17.
15. Fedorovich SV, Voronina PP, Waseem TV. Ketogenic diet versus ketoacidosis: what determines the influence of ketone bodies on neurons? Neural Regen Res. 2018;13:2060-3.
16. Valencia I, Pfeifer H, Thiele EA. General anesthesia and the ketogenic diet: clinical experience in 9 nine patients. Epilepsia. 2002;43:525-9.
17. Gupta L, Khandelwal D, Kalra S, Gupta P, Dutta D, Aggarwal S. Ketogenic diet in endocrine disorders: Current perspectives. J Postgrad Med. 2017;63:242-51.
18. Sirikonda NS, Patten WD, Phillips JR, Mullett CJ. Ketogenic diet: rapid onset of selenium deficiency-induced cardiac decompensation. Pediatr Cardiol. 2012;33:834-8.
19. Bergqvist AG, Chee CM, Lutchka L, Rychik J, Stallings VA. Selenium deficiency associated with cardiomyopathy: a complication of the ketogenic diet. Epilepsia. 2003;44:618-20
20. Shetty A, Pardeshi S, Shah VM, Kulkarni A. Anesthesia considerations in epilepsy surgery. Int J Surg. 2016;36(Part B):454-9.
21. Perks A, Cheema S, Mohanraj R. Anaesthesia and epilepsy. Br J Anaesth. 2012;108:562-71.
22. Mastrangelo M, Celato A. Diagnostic work-up and therapeutic options in management of pediatric status epilepticus. World J Pediatr 2012;8:109-15.
23. Constant I, Seeman R, Murat I. Sevoflurane and epileptiform EEG changes. Paediatr Anaesth. 2005;15:266-74.
24. Ebrahim ZY, DeBoer GE, Luders H, Hahn JF, Lesser RP. Effect of etomidate on the electroencephalogram of patients with epilepsy. Anesth Analg. 1986;65:1004-6.
25. Corssen G, Little SC, Tavakoli M. Ketamine and epilepsy. Anesth Analg. 1974;53:319-35.
26. King M, Martin D, Miketic R, Beebe A, Samora W, Klamar J, Tumin D, Tobias JD. Impact of intraoperative fluid management on electrolyte and acid-base variable during posterior spinal fusion in adults. Ortho Res Rev 2020;12:69-74.
27. Soysal E, Gries H, Wray C. Pediatric patients on ketogenic diet undergoing general anesthesia – a medical record review. J Clin Anesth. 2016;35:170-5.
28. Neavyn MJ, Boyer EW, Bird SB, Babu KM. Sodium acetate as a replacement for sodium bicarbonate in medical toxicology: a review. J Med Toxicol. 2013;9:250-4.
29. McNeely JK. Perioperative management of a paediatric patient on the ketogenic diet. Paediatr Anaesth. 2000;10:103-6.
30. Huang CJ, Chang CH, Cheng KW, Chen CL, Wu SC, Shih TH, Yang SC, Lee YE, Huang CE, Jawan B, Wang CH, Juang SE. Correlation between blood

transfusion and blood glucose levels in adult living donor liver transplantation. Transplant Proc. 2018;50:2645-7.