Dexmedetomidine as the primary anesthetic agent during cardiac surgery in an infant with a family history of malignant hyperthermia

Aymen Naguib,
Chris McKee,
Alistair Phillips,
Joseph D. Tobias
Departments of Anesthesiology, and Pediatrics, "The Heart Center, Nationwide Children’s Hospital and the Ohio State University, Columbus, Ohio

ABSTRACT
Malignant hyperthermia (MH) is an acute hypermetabolic crisis triggered in susceptible patients by the administration of succinylcholine or a volatile anesthetic agent. When providing anesthetic care for MH-susceptible agents, a total intravenous anesthetic (TIVA) technique is frequently chosen. When choosing the components for TIVA, several options exist including the combination of propofol or dexmedetomidine with an opioid. We present our experience with the use of dexmedetomidine as a key component of the anesthetic regimen in a 5-month-old infant with a family history of MH. Previous reports of the use of dexmedetomidine in MH-susceptible patients are reviewed and its benefits in such patients discussed.

Key words: Congenital heart disease, dexmedetomidine, malignant hyperthermia

INTRODUCTION
The management of patients who are susceptible to malignant hyperthermia (MH) represents a challenge to the anesthesia provider. Although its incidence is only 1 in 15,000 in infants and children, if untreated, the mortality exceeds 80%.[1] The primary defect responsible for MH is the ryanodine receptor of the sarcoplasmic reticulum which regulates calcium release.[2] Triggering agents for MH include the volatile anesthetic agents and the depolarizing neuromuscular blocking agent, succinylcholine. The cellular defect of MH results in the excessive and ongoing release of calcium into the cytoplasm, producing myofibrillar contraction, depletion of high-energy phosphate compounds in the muscle, accelerated lactic acid and carbon dioxide production, increased oxygen consumption, metabolic acidosis, and the generation of heat. Damage to cell membranes results in rhabdomyolysis with the release of potassium and myoglobin. Treatment includes elimination of the triggering agent, administration of dantrolene, and treatment of the physiologic changes of the hypermetabolic state.[3]

Given its low incidence, most anesthesia providers will never be faced with an acute episode of MH. More commonly, anesthesia providers are confronted by a patient who has a family history of MH. In such cases, total intravenous anesthesia (TIVA) with a combination of various intravenous anesthesia agents can be provided. Alternatively, in selected surgical procedures, the need for general anesthesia can be avoided by the use of a regional anesthetic technique.

Dexmedetomidine is an α₂-adrenergic agonist which initially received Food and Drug Administration (FDA) approval in the United States in 1999 for the sedation of adults during mechanical ventilation and then in...
CASE REPORT

A 5-month-old, 5.5 kg infant presented for surgical repair of a perimembranous VSD and pulmonary stenosis. There was a strong maternal family history of MH (maternal grandmother, aunt and cousin diagnosed by muscle biopsy). The patient was scheduled as the first case of the day, the anesthesia machine was flushed with a high flow of oxygen, the soda lime canister was replaced, and the vaporizers were removed. After obtaining the appropriate consents, the patient was brought to the operating room where standard American Society of Anesthesiologists’ monitors were placed. Cerebral oxygen saturation was measured with a probe placed on the right forehead. In addition, depth of anesthesia was monitored using the bispectral index probe (BIS). After breathing 50% nitrous oxide in oxygen, an intramuscular injection was administered containing midazolam (0.1 mg/kg), ketamine (1 mg/kg), glycopyrrolate (10 µg/kg), and rocuronium (1 mg/kg). After the intramuscular injection, the nitrous oxide was discontinued. After anesthetic induction, two peripheral intravenous catheters and an arterial cannula were placed and the airway was secured with a 3.5-mm cuffed endotracheal tube. Dexmedetomidine was administered as a loading dose of 1 µg/kg followed by an infusion of 1 µg/kg/hr. This was followed by a caudal block with 1 µg/kg of clonidine and 35 µg/kg of preservative free morphine in a total of 6 mL of preservative free normal saline. During the surgical procedure, maintenance anesthesia included a total of 45 µg of fentanyl, 1 mg of midazolam, and the dexmedetomidine infusion in a dose ranging from 1 to 2 µg/kg/hr. The dexmedetomidine infusion was titrated to maintain the patient’s vital signs within 20% of baseline and to maintain the BIS at 40–60. The patient’s heart rate and blood pressure remained stable (within 20% of baseline values) and appropriate for age. The BIS values remained between 30 and 45 during the case, and the cerebral oxygen saturation was greater than 60% during the entire case. The total CPB time was 86 minutes and the aortic cross-clamp time was 51 minutes. The starting blood lactate concentration was 0.83 mmol/L, the highest lactate level was 1.23 mmol/L, and the ending level was 1.05 mmol/L. The starting blood glucose concentration was 85 mg/dL, the highest blood glucose was 156 mg/dL, and the ending blood glucose was 127 mg/dL. Before separation from CPB, a milrinone loading dose of 25 µg/kg was administered and followed by an infusion at a rate of 0.25 µg/kg/minute. Separation from CPB was uneventful. The dexmedetomidine infusion was decreased to 0.5 µg/kg/hr and the patient’s trachea was extubated at the completion of the surgical procedure. The patient was transported to the cardiothoracic intensive care unit (CTICU) with standard monitors, receiving supplemental oxygen at 0.5 L/minute via nasal cannula. Postoperative analgesia was provided as per our usual routine with fentanyl administered via nurse-controlled analgesia (NCA) with a bolus of 3 µg, lock-out interval of 15 minutes, and no basal infusion rate. During the initial 48 postoperative hours, the median Face, Legs, Activity, Cry & Consoleability (FLACC) score was 0 (range: 0–5) with a total dose of fentanyl of 0.4 µg/kg/hr. The average NCA use for the first 48 postoperative hours was 1–2 doses every 2 hrs. The patient was discharged home on postoperative day 4.

DISCUSSION

Despite its widespread use during the perioperative period, there remain limited data regarding the use of dexmedetomidine in MH-susceptible patients. Given its mechanism of action and the pathophysiology of MH, dexmedetomidine would appear to be safe for use in MH-susceptible patients. There is also an increasing body of evidence regarding the possible advantages of dexmedetomidine during and after pediatric cardiac surgery. Mukhtar et al. examined the effects of dexmedetomidine on the surgical stress response following cardiac surgery in infants and children. Patients who received dexmedetomidine had lower plasma concentrations of several stress hormones including cortisol, epinephrine, and norepinephrine as well as lower plasma glucose concentrations. The blunting of catecholamine levels may be beneficial in MH-susceptible patients as norepinephrine and epinephrine may trigger MH.

To date, there are only three previous reports regarding the use of dexmedetomidine in MH-susceptible patients. Unger used a dexmedetomidine infusion along with propofol, nitrous oxide, and fentanyl to provide anesthesia for a 59-year-old woman with MH diagnosed by muscle biopsy. Dexmedetomidine dosing included a loading dose of 1 µg/kg over 10 minutes followed by an infusion of...
0.6 µg/kg/hr during the procedure and 0.4 µg/kg/hr for the initial 30 minutes in the PACU. Propofol was added to the dexmedetomidine infusion and titrated to maintain the BIS at 40–55. There were no adverse effects related to the anesthetic care and the patient had an uncomplicated perioperative course. Hudcova and Schumann reported the use of a dexmedetomidine infusion as part of the intraoperative anesthetic care of a 35-year-old woman with a positive family history of MH, during excision of two neuroendocrine tumors.[8] The authors were concerned regarding the potential for the development of the propofol infusion syndrome due to the expected prolonged operative time and the elevated catecholamine levels from the tumor. Dexmedetomidine was used as part of the intraoperative anesthetic care to limit the propofol dose. Following anesthetic induction, a dexmedetomidine infusion was started at 0.7 µg/kg/hr. Following the prolonged surgical procedure (10 hrs and 49 minutes), the propofol and dexmedetomidine infusions were discontinued and the patient’s trachea was extubated. The patient’s postoperative course was uneventful. The final report described the use of dexmedetomidine in three MH-susceptible pediatric patients with associated allergies which precluded the use of propofol.[9]

In our case, we used dexmedetomidine as the primary maintenance anesthetic, supplemented by caudal morphine and clonidine and intravenous midazolam and fentanyl (8–9 µg/kg). We noted no additive adverse hemodynamic or respiratory effects from the combined use of dexmedetomidine and caudal clonidine. The intraoperative benefit of this combination was illustrated by the minimal stress response during the surgical procedure and CPB with stable intraoperative plasma glucose and lactate concentrations. Additionally, the technique resulted in a reduction of the postoperative opioid requirements in our patient during the 48-hr postoperative CTICU admission.

When considering the options for TIVA in the pediatric cardiac surgical patient, there are several potential alternatives including propofol, ketamine, and dexmedetomidine. Given our experience with the agent and its potential advantages over propofol, we chose to use dexmedetomidine as the primary intravenous anesthetic agent in our patient. Advantages of dexmedetomidine over propofol include more effective blunting of the surgical stress response related to its sympatholytic properties and the potentiation of opioid analgesia thereby limiting postoperative opioid requirements.[6,9] Like propofol, dexmedetomidine can have adverse hemodynamic effects including bradycardia and hypotension. However, these effects are less common in the pediatric population and generally respond to termination of the infusion, rarely requiring pharmacologic intervention.[8] Given its limited use as a primary anesthetic agent, there are relatively few data documenting its amnestic properties. However, in a cohort of eight healthy adult volunteers, Hall et al. demonstrated that dexmedetomidine at 0.6 µg/kg/hr resulted in an average BIS value of 66 with no recall as demonstrated by a comprehensive memory test using word recall.[11]

Although anecdotal, our case provides further evidence for the role of dexmedetomidine in pediatric cardiac surgery and its role as the primary agent of a non-triggering anesthetic for patients with history of MH. We used dexmedetomidine in doses up to 2 µg/kg/hr supplemented with moderate doses of fentanyl (8–9 µg/kg) and midazolam (0.2 mg/kg) to provide intraoperative anesthesia during cardiac surgery and CPB. Several factors must be considered in our case report. Although there is ample experience with its use in the pediatric population, dexmedetomidine is currently not approved by the United State’s FDA for use in the pediatric population. When used as an adjunct to general anesthesia, doses in the range of 0.4–0.7 µg/kg/hr have generally been reported. Given that dexmedetomidine was the primary agent in the anesthetic care of our patient, larger doses (up to 2 µg/kg/hr) were used to maintain hemodynamic stability and the BIS at 40–60. With such caveats in mind, we found that dexmedetomidine provided effective anesthesia and blunted the surgical stress response. In combination with caudal morphine and clonidine, these agents provided a stable postoperative course with a limited need for postoperative opioid administration. Future studies are needed to fully define the role of dexmedetomidine in pediatric cardiac surgery.

REFERENCES

1. Britt BA, Kalow W. Malignant hyperthermia: A statistical review. Can Anaesth Soc J 1970;17:293-315.
2. Mickelson JR, Gallant EM, Litterer LA, Johnson KM, Rempel WE, Louis CF. Abnormal sarcoplasmic reticulum ryanodine receptor in malignant hyperthermia. J Biochem Chem 1988;263:9310-5.
3. Harrison GG. Control of the malignant hyperthermic syndrome in MHS swine by dantrolene sodium. Br J Anaesth 1975;47:62-5.
4. Tobias JD. Dexmedetomidine: Applications in pediatric critical care and pediatric anesthesiology. Pediatr Crit Care Med 2007;8:115-31.
5. Mukhtar AM, Obayah EM, Hassona AM. The use of dexmedetomidine in pediatric cardiac surgery. Anesth Analg 2006;103:52-6.
6. Haggendal J, Jonsson L, Hohansson G, Bjurstrom S, Carlsten J. Disordered catecholamine release in pigs susceptible to malignant hyperthermia. PharmacoI Toxicol 1988;63:257-61.
7. Unger RJ. General anesthesia with dexmedetomidine in a malignant hyperthermia-susceptible woman. Acta Anaesthesiol Scand 2006;50:1312-3.
8. Hudcova J, Schumann R. Undiagnosed catecholamine-
Naguib, et al.: Dexmedetomidine and malignant hyperthermia

secreting paraganglioma and coexisting carcinoid in a patient with MH susceptibility: An unusual anesthetic challenge. J Anesth 2007;21:80-2.

9. Dewhirst E, Naguib A, Tobias JD. Dexmedetomidine as part of balanced anesthetic care in children with malignant hyperthermia. J Pediatr Pharm Therap (in press).

10. Sadhasivam S, Boat A, Mahmoud M. Comparison of patient-controlled analgesia with and without dexmedetomidine following spinal surgery in children. J Clin Anesth 2009;21:493-501.

11. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg 2000;90:699-705.

How to cite this article: Naguib A, McKee C, Phillips A, Tobias JD. Dexmedetomidine as the primary anesthetic agent during cardiac surgery in an infant with a family history of malignant hyperthermia. Saudi J Anaesth 2011;5:426-9.

Source of Support: Nil, Conflict of Interest: None declared.