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Anesthesia for videoscopic left cardiac sympathetic denervation in children with congenital long QT syndrome and catecholaminergic polymorphic ventricular tachycardia – a case series

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Summary

Objective—To describe our experience in the anesthetic management of pediatric patients who have undergone left cardiac sympathetic denervation (LCSD) for congenital long QT syndrome (LQTS) and catecholaminergic polymorphic ventricular tachycardia (CPVT).

Background—Long QT syndrome and CPVT predispose patients to ventricular arrhythmias and sudden death. One treatment option for these patients is LCSD. When these patients present for LCSD or other surgical procedures, anesthetic management is challenging, as many medications may exacerbate QT prolongation.

Methods—Retrospective review of the electronic medical records of 22 pediatric patients who underwent LCSD between November 2005 and December 2008.

Results—Six patients (27%) received midazolam as a premedication. Eleven patients (50%) underwent inhalation induction with sevoflurane. Eighty-six percent received either sevoflurane or isoflurane for maintenance of anesthesia, while the remaining 14% received a propofol infusion. Nine patients (41%) received esmolol infusions intraoperatively, while one patient (4.5%) received a labetalol infusion. Three patients (14%) received lidocaine infusions. No significant cardiac or other events occurred in any of these patients in the perioperative period.

Conclusions—Important anesthetic considerations in this population include avoidance of sympathetic stimulation, correction of any abnormal electrolytes, and the immediate availability of a defibrillator and magnesium sulfate to treat arrhythmias. Anxious patients may benefit from premedication to reduce sympathetic tone. We have safely used both volatile agents and propofol for induction and maintenance of anesthesia. In our experience, intraoperative infusions of β -

blockers and lidocaine seem to be helpful in reducing arrhythmogenic potential, especially in patients with profound QT prolongation.

Keywords

long QT syndrome; left cardiac sympathetic denervation; anesthetic management

Introduction

Congenital long QT syndrome (LQTS) is caused by a dysfunction of cardiac ion channels, which leads to impaired ventricular repolarization. This delayed and heterogeneous repolarization predisposes to arrhythmias, most commonly torsades de pointes (TdP), a polymorphic ventricular tachyarrhythmia (1). Patients with LQTS may present with a history of syncope, seizures, or sudden death because of TdP. These episodes are often triggered by sympathetic stimulation (e.g., exertion, stress, and auditory stimulation). Several different genetic mutations have been implicated in causing LQTS, and most are inherited in an autosomal dominant pattern (2). Rarely, patients present with a prolonged QT interval in association with congenital deafness, also known as Jervell and Lange-Nielsen syndrome (JLNS). JLNS is inherited in an autosomal recessive pattern (3). The prevalence of LQTS is approximately 1 in 2500 persons (4). Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a syndrome typically presenting with exertional syncope or sudden death. Its mortality rate ranges from 30% up to 50% by age 35 that makes it the most malignant cardiac channelopathy in young patients with structurally normal hearts (5). In contrast to patients with LQTS, those with CPVT have normal resting electrocardiograms. Bidirectional ventricular tachycardia that may be present during exercise, emotional stress, and catecholamine stress testing has been considered the hallmark arrhythmia for CPVT. There is recent evidence that mutations in the myocardial ryanodine receptor gene, which encodes the ryanodine receptor 2, are responsible for at least a subclass of patients with CPVT (5).

Therapeutic options for patients with LQTS and CPVT include pharmacotherapy (β -blockade for LQTS and CPVT, calcium channel blockers and/or flecainide for CPVT), implantable cardioverter defibrillators (ICDs), and left cardiac sympathetic denervation (LCSD). For patients who continue to have cardiac events while taking β -blockers, receive frequent shocks from ICDs, or cannot tolerate pharmacotherapy, LCSD is another therapeutic option with strong antifibrillatory effects (6,7). In a retrospective study, Schwartz *et al.* (6) showed a dramatic >90% decrease in the yearly number of cardiac events per patient following LCSD. Collura *et al.* recently published the Mayo Clinic experience with videoscopic LCSD in 20 pediatric and adult patients. Appropriate ICD shocks have been completely eliminated so far in eight of 11 patients who presented with a history of ICD shocks or aborted cardiac arrest. One patient, who received 15 ICD shocks in the year prior to surgery, has had only one shock in the 36 months since her procedure. The two remaining patients have had less successful results with a minimal reduction in the frequency of cardiac events/ICD shocks postoperatively. The mean follow-up time was 16.6 ± 9.5 months (7).

While this report by Collura *et al.* (7) examines the surgical technique, perioperative complications, and short-term outcomes in the Mayo Clinic experience, it does not describe the details of anesthetic care. Anesthesia for patients with these sudden death-predisposing cardiac channelopathies, particularly LQTS, is challenging, as many medications, including anesthetics, may exacerbate QT prolongation (8). In addition, most reports on the effects of anesthetics on the QT interval have been either case reports or studies done in healthy individuals. In this case series, we have examined and summarized our recent experience

with patients undergoing LCSD, focusing on pediatric patients and limiting our review to the immediate perioperative period.

Materials and methods

After Institutional Review Board approval, the medical records of 22 pediatric patients who underwent LCSD between November 2005 and December 2008 were reviewed. Two patients had been diagnosed with CPVT, while the remaining 20 patients had LQTS. Two patients underwent open thoracotomies and 20 patients had video-assisted thoracoscopic surgery. A detailed medical record review was performed, examining preoperative medications, intraoperative anesthetic management, postoperative pain, and perioperative complications. Assessment of postoperative pain was performed using a 0–10 numeric pain scale or FLACC scale. All continuous variables are reported as mean $\pm$ standard deviation (SD).

Results

Preoperative characteristics

Twelve patients (55%) were male, while ten (45%) were female. The patients ranged in age from 1 month to 17 years with a median of 14.7 years (IQR 1.75–14.75 years). The average QTc was 530 ± 81 ms, range 430–687 ms. Table 1 shows a summary of the patients' characteristics. Ten patients (45%) underwent LCSD for primary prevention of cardiac events, mostly secondary to pharmacotherapy intolerance or perceived high risk, while twelve patients (55%) underwent LCSD for secondary prevention because of a history of aborted cardiac arrest or appropriate VF-terminating ICD shocks. Twenty patients (91%) were taking β -blockers preoperatively. Six patients (27%) were treated with mexiletine, a class I antiarrhythmic drug. Seven patients (32%) had ICDs preoperatively, and two patients (9.1%) underwent ICD placement at the time of their LCSD surgery.

Intraoperative management

Upon arrival in the operating room, all patients had external defibrillator pads placed, and any ICDs were inactivated. Depending on the age and size of the patient, single-lung ventilation was achieved with a double-lumen endotracheal tube, a bronchial blocker, or a standard endotracheal tube advanced into the right mainstem bronchus. Monitoring included electrocardiogram (recording leads II and V5), noninvasive blood pressure, and pulse oximetry in all patients. An arterial line was placed in 20 patients (91%). Table 2 provides a summary of anesthetic techniques used.

For premedication, six patients (27%) received midazolam prior to entering the operating room, while an additional seven patients (32%) who entered the preoperative area with i.v. access in place received midazolam either in the preoperative area or upon entry to the operating room. Eleven patients (50%) underwent inhalation induction with sevoflurane. Other induction agents included propofol (10 patients, 45%) and thiopental (1 patient, 4.5%). Twenty patients (91%) received fentanyl prior to intubation. For maintenance of anesthesia, 86% of patients received either sevoflurane (4.5%) or isoflurane (82%). The remaining 14% received a propofol infusion. The majority (21 patients, 95%) received fentanyl for intraoperative pain control. The mean dose of fentanyl was 6.1 ± 6.4 mcg·kg⁻¹. Two patients received oxymorphone (8.8 and 17 mcg·kg⁻¹), along with fentanyl. One patient received a remifentanyl infusion at $0.1\text{--}0.5$ mcg·kg⁻¹·min⁻¹, as well as ketorolac, intraoperatively. Table 3 provides a summary of pain medications that were given in the operating room and recovery room. To improve surgical conditions, muscle relaxation was achieved with vecuronium (17 patients, 77%), rocuronium (1 patient, 4.5%), or atracurium

(3 patients, 14%). All patients were mechanically ventilated. Seven patients (32%) received glycopyrrolate and neostigmine for reversal of paralysis.

For nausea prophylaxis or treatment, eight patients (36%) were given ondansetron perioperatively, and six patients (27%) received dexamethasone. To reduce the risk of arrhythmias in the subset of patients perceived at highest clinical risk secondary to profound QT prolongation, nine patients (41%) received esmolol infusions ($7\text{--}667\text{ mcg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) intraoperatively, while one patient (4.5%) received a labetalol infusion ($4.4\text{--}17\text{ mcg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). Titration was determined by the anesthesiologist. These were titrated to maintain heart rate and blood pressure parameters as determined by the anesthesiologist. Three patients (14%) received lidocaine infusions at doses of $15\text{--}21\text{ mcg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$.

Mean surgical time was 49 ± 15 min, and mean anesthesia time was 140 ± 23 min (the two patients who underwent ICD placement at the time of LCSD are excluded). One infant, who was hospitalized in the intensive care unit prior to surgery, required a transfusion of packed red blood cells postoperatively. His anemia was most likely related to frequent phlebotomy during his hospitalization.

Postoperative management

Following the conclusion of surgery, all patients received a chest x-ray while still in the operating room, and no significant pneumothoraces requiring chest tube placement were identified. After evaluation of the chest x-ray, 19 patients (86%) were extubated either in the operating room or in the recovery room, while three patients were taken to the intensive care unit intubated. In patients with ICDs in place, these devices were reactivated before the patients left the operating room. All patients were monitored in the intensive care unit. One patient, who had just experienced out-of-hospital cardiac arrest and was receiving a lidocaine infusion preoperatively for refractory arrhythmias, required a prolonged 9-day wean of this medication postoperatively because of ventricular ectopy. No other significant ventricular arrhythmias occurred in any patient during hospitalization. The mean length of hospital stay was 6.5 ± 6.3 days. Nine patients (41%) were discharged on the day following surgery.

Among the 16 patients who were taken to the recovery room postoperatively, pain scores ranged from 0 to 10, with a mean of 2.7 ± 3.2 , on the 10-point numeric pain scale or FLACC scale. Nine of 16 patients (56%) received additional fentanyl for pain control with a mean dose of $0.82 \pm 0.50\text{ mcg}\cdot\text{kg}^{-1}$. One patient received oxymorphone ($17\text{ mcg}\cdot\text{kg}^{-1}$) and ketorolac for pain, along with meperidine for postoperative shivering. Another patient received ketorolac and hydromorphone ($6.7\text{ mcg}\cdot\text{kg}^{-1}$), as well as fentanyl, in the recovery room.

Pain scores on the day of surgery ranged from 0 to 8, with a mean of 1.9 ± 2.3 . On the first postoperative day, pain scores ranged from 0 to 9, with a mean of 1.3 ± 1.8 . After admission to the intensive care unit, postoperative pain control was achieved with morphine in 13 patients (59%), fentanyl in seven patients (32%), and acetaminophen alone in three patients (14%). A total of 17 patients (77%) received acetaminophen during their hospitalization. Other pain medications given during the first three postoperative days included ketorolac (4 patients, 18%), oxycodone (6 patients, 27%), tramadol (1 patient, 4.5%), hydromorphone (1 patient, 4.5%), acetaminophen/oxycodone (1 patient, 4.5%), acetaminophen with codeine (1 patient, 4.5%), and ibuprofen (3 patients, 14%).

Discussion

We have described the anesthetic management of 22 patients who underwent LCSD, which is a valuable therapeutic option for patients with LQTS and patients with CPVT. These patients present a challenge to the anesthesiologist, as they are predisposed to cardiac arrhythmias, and many anesthetic agents can increase this risk. Careful planning and monitoring are crucial to ensure a safe perioperative course.

As TdP can be triggered by sympathetic stimulation, including loud noises, the operating room should be a calm, quiet environment, especially during induction. Care should be taken to avoid light anesthesia, hypertension, profound bradycardia causing hypotension, tachycardia, hypothermia, hypoxemia, hypercapnia, and hypocapnia, because these conditions can affect cardiac repolarization and increase sympathetic tone (8). Serum electrolytes should be measured and corrected preoperatively, as hypokalemia, hypomagnesemia, and hypocalcemia can contribute to delayed myocardial repolarization. Magnesium sulfate is the treatment of choice for TdP and should be readily available in the operating room (8). An external defibrillator should also be present in the operating room, and pads should be placed on the patient prior to inactivating an existing ICD. Invasive blood pressure monitoring with an arterial line is indicated during this procedure to immediately detect any hemodynamic instability related to arrhythmias.

To avoid increased sympathetic tone, anxious patients may benefit from a premedication. Midazolam does not cause any prolongation in the QT interval (9,10) and should be considered to alleviate preoperative anxiety. Premedication with ketamine is probably best avoided in patients with LQTS because it stimulates sympathetic nervous system activity (8).

Although sevoflurane and isoflurane prolong the QT interval (11–15), they have been used successfully in patients with LQTS (14,16). This is consistent with our experience: both isoflurane and sevoflurane were used without adverse effects. Propofol does not prolong the QT interval and actually has been shown to reverse sevoflurane-induced QT prolongation in healthy patients (11,15,17). Propofol was the most common intravenous induction medication used in our patients. For muscle relaxation, the majority of our patients received vecuronium or atracurium, which have not been found to affect the QT interval (9). Succinylcholine is best avoided in patients with LQTS because of its potential for vagal stimulation and potassium shifts (8). It has been reported that the combination of an anticholinergic medication and anticholinesterase agent prolongs the QT interval (18,19). While this combination was used safely in seven of our patients, caution is warranted if neuromuscular reversal agents are used in this patient population.

Postoperative nausea and vomiting prophylaxis can be difficult in these patients. It has been widely known that droperidol has the potential to prolong the QT interval. Recently, Charbit *et al.* (20) reported that ondansetron also prolongs the QT interval in healthy patients. Ondansetron was used in 36% of our patients without adverse effects; nevertheless, caution is warranted with this medication in patients with LQTS.

Among the subset of patients with LQTS/CPVT with malignant phenotypic expression, intraoperative β -blockade may help minimize the arrhythmogenic potential. Furthermore, among patients who are receiving combination therapy with a β -blocker and mexiletine, intraoperative use of intravenous lidocaine with a postoperative wean and transition back to oral mexiletine may help stabilize myocardial function.

Pain following videoscopic LCSD was well controlled with a combination of opioids, acetaminophen, and ketorolac. There were no significant adverse perioperative events. In

summary, successful perioperative management of patients with LQTS or CPVT requires a thorough understanding of potential risks, careful monitoring of cardiac status, and close communication within the care team.

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Table 1

Patient demographics and preoperative characteristics. Patients who underwent LCSD for primary prevention had not experienced cardiac events but were felt to be at high risk and/or had intolerance to pharmacotherapy. Patients in the secondary prevention group had a history of aborted cardiac arrest or appropriate VF-terminating ICD shocks. Continuous variables are reported as mean $\pm$ standard deviation

Age (years)	8.3 $\pm$ 6.3
Sex	
Male	55%
Female	45%
Preoperative QTc (ms)	530 $\pm$ 81
Preoperative β -blocker therapy	91%
Presence of ICD	
Existing ICD preoperatively	32%
ICD placed during LCSD	9.1%
Indication for LCSD	
Primary prevention	45%
Secondary prevention	55%

ICD, implantable cardioverter defibrillators, LCSD, left cardiac sympathetic denervation.

Table 2

Anesthetic agents used during left cardiac sympathetic denervation surgery

Anesthetic management	No of patients (%)
Premedication with midazolam	6 (27)
IV induction	11 (50)
Propofol	10 (45)
Thiopental	1 (4.5)
Inhalation induction with sevoflurane	11 (50)
Maintenance with volatile agents	
Sevoflurane	1 (4.5)
Isoflurane	18 (82)
TIVA	
Propofol/Fentanyl	2 (9.1)
Propofol/Remifentanyl	1 (4.5)
Muscle relaxant	21 (95)
Vecuronium	17 (77)
Rocuronium	1 (4.5)
Atracurium	3 (14)
Reversal with neostigmine/glycopyrrolate	7 (32)
Antiemetics	
Ondansetron	8 (36)
Dexamethasone	6 (27)
Intraoperative Infusions	
Esmolol (7–667 mcg·kg ⁻¹ ·min ⁻¹)	9 (41)
Labetalol (4.4–17 mcg·kg ⁻¹ ·min ⁻¹)	1 (4.5)
Lidocaine (15–21 mcg·kg ⁻¹ ·min ⁻¹)	3 (14)

Table 3

Pain medications given in the operating room and recovery room. Continuous variables are reported as mean $\pm$ standard deviation

No of patients (%)		Dose
Intraoperative pain medications		
Fentanyl	21 (95)	$6.1 \pm 6.4 \text{ mcg}\cdot\text{kg}^{-1}$
Remifentanyl	1 (4.5)	$0.1\text{--}0.5 \text{ mcg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$
Oxymorphone	2 (9.1)	$13 \pm 5.8 \text{ mcg}\cdot\text{kg}^{-1}$ (also received fentanyl)
Recovery room pain medications (16 patients went to the recovery room)		
Fentanyl	9 (56)	$0.82 \pm 0.5 \text{ mcg}\cdot\text{kg}^{-1}$
Oxymorphone	1 (6.3)	$17 \text{ mcg}\cdot\text{kg}^{-1}$
Hydromorphone	1 (6.3)	$6.7 \text{ mcg}\cdot\text{kg}^{-1}$
Ketorolac	2 (13)	$0.39 \pm 0.19 \text{ mg}\cdot\text{kg}^{-1}$