Title: Case Report: General Anesthetic Management for Laparoscopic Cholecystectomy in Paramyotonia Congenita

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Highlights:

- In this case report, we describe general anesthetic induction and management for a patient with paramyotonia congenita, a rare disorder affecting skeletal muscle. Patients with this condition experience intermittent episodes of sustained myotonia, though the disease is non-progressive.
- Due to the predisposition for prolonged muscle contraction, special attention must be paid to anesthetic management during operative procedures to prevent complications similar to those seen in patients with malignant hyperthermia. To date, however, limited reports of anesthetic management in paramyotonia congenita are available.
- Our report describes successful anesthetic management using non-depolarizing muscle relaxant rocuronium, bolus propofol, ketamine, and continuous IV propofol with nitrous oxide in a patient with paramyotonia congenita. This provides a potential management plan that may be applied to PC patients undergoing a variety of surgical procedures and eliminates risk associated with succinylcholine and volatile anesthetics.

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Discussion Points:

1. What are the similarities and differences between paramyotonia congenita and malignant hyperthermia?
2. What impact may prescription mexiletine have had on determining the patient's intra-operative risk?
3. Is the risk associated with the use of volatile anesthetics significant in patients with paramyotonia congenita, as it is in patients with malignant hyperthermia?
4. Areas of future research should include determining whether this approach is superior to previously reported techniques, and should also aim to identify which agents may be effectively utilized to reverse a myotonic episode in PC patients should one occur intra-operatively.
5. Areas of future research should include whether this approach is applicable to other surgical procedures of longer duration.

ABSTRACT.

Background: Paramyotonia congenita (PC) is a rare disorder affecting skeletal muscle. Patients with this non-progressive condition experience intermittent episodes of sustained myotonia. Due to the predisposition for prolonged muscle contraction, special attention must be paid to anesthetic management during operative procedures to prevent complications similar to those seen in patients with malignant hyperthermia. To date, however, limited reports of anesthetic management in paramyotonia congenita are available.

The Case: The present report describes successful general anesthetic management in a patient with paramyotonia congenita using propofol and ketamine for induction, non-depolarizing rocuronium for muscle paralysis, and continuous nitrous oxide and IV propofol infusion for sedation. The patient remained stable throughout the case without myotonic episodes or other complications.

Conclusion: Our report describes successful anesthetic management in a patient with paramyotonia congenita. This provides a potential management plan that may be applied to PC patients undergoing a variety of surgical procedures and eliminates risk associated with succinylcholine and possibly volatile anesthetics. Further research is needed to determine whether this approach is superior to previously reported techniques, and should also aim to identify which agents may be effectively utilized to reverse a myotonic episode in PC patients should one occur intra-operatively.

Key Words: anesthesia; paramyotonia congenita; cholecystectomy, laparoscopic; sodium channel muscle disease; general anesthesia, malignant hyperthermia

INTRODUCTION.

Paramyotonia congenita (PC) is a rare muscular disorder with an estimated prevalence between 1/100,000 to 1/200,000.[1] The disorder is characterized by periodic muscle contraction, or myotonia, followed by flaccid paralysis.[1] It is caused by an autosomal-dominant mutation in the SCN4A gene, which is normally responsible for regulating the amount of sodium and potassium ions present across the skeletal muscle cell membrane. Therefore, the mutation in this gene is thought to interfere directly with normal muscle contraction and relaxation.[1] Most patients with paramyotonia congenita experience periodic myotonic contraction and paralysis by adolescence. However, in contrast to some other muscular disorders it is non-progressive and patients have a normal life expectancy.[1] Many patients with paramyotonia congenita do not require pharmacologic intervention and treatment is primarily symptomatic, including reduction of cold exposure, which may act as a trigger for myotonic episodes.[1] Patients who do receive pharmacologic treatment may be treated with mexiletine for muscle relaxation.[1]

Patients with paramyotonia congenita experience a spectrum of symptom severity, though they are all at increased risk when undergoing general anesthetic management, especially with succinylcholine (Figure 1).[1-2] While this is similar to the better-known presentation of malignant hyperthermia (MH), it is important to note that patients with PC are not at an increased risk for malignant hyperthermia.[3]

MH is usually triggered by succinylcholine and/or halogenated volatile anesthetics and presents with hypercarbia, muscle rigidity, hyperthermia, and rhabdomyolysis following anesthetic induction. [3] In patients with paramyotonia congenita, the only symptom is myotonia, typically in the hands, face, or neck.[4] Nevertheless, there is clear risk for patients with paramyotonia congenita who undergo anesthesia.[1-2] Despite the known risk associated with the use of common agents such as succinylcholine and some volatile anesthetics for general anesthesia in patients with paramyotonia congenita, there are few reports of anesthetic management for this condition. Previously reported techniques included intubation without neuromuscular relaxant for pylorotomy and continuous IV anesthesia with intercostal nerve block for repair of congenital nasal dysplasia using autologous costal cartilage.[5-6]

Although successful anesthetic induction has been reported in patients with myotonic dystrophy (a similar disorder), using rocuronium, a non-depolarizing muscle relaxant, , there are no reports of anesthetic management using rocuronium for paralysis in patients with paramyotonia congenita, to the authors' knowledge. [7] Thus, the present report describes successful management of anesthesia in a patient undergoing laparoscopic cholecystectomy, a common surgical procedure, using non-depolarizing rocuronium for muscle paralysis, propofol and ketamine for induction, and propofol infusion/nitrous oxide for general anesthesia maintenance. Written HIPPA authorization was obtained from the patient.

THE CASE.

A 36-year-old Caucasian female presented to the outpatient general surgery office with complaints of recurrent nausea following meals over a period of several months. Upper endoscopy did not reveal an obvious etiology for post-prandial nausea. Subsequent diagnostic testing, including cholescintigraphy scan, was pursued and revealed a reduced gallbladder ejection fraction, diagnostic for biliary dyskinesia. Thus, it was recommended that the patient undergo elective laparoscopic cholecystectomy for symptomatic relief. The patient underwent pre- and peri-operative anesthesia exam, which revealed a past medical history of paramyotonia congenita, chronic cholecystitis, GERD, hypertension, asthma, hypothyroidism, and anxiety. The patient had not previously undergone general anesthesia, though she was aware of the risk associated with anesthesia due to her underlying paramyotonia congenita.

Current medications at the time of surgery included mexiletine 150 mg q 12 hours, omeprazole 40 mg qd, montelukast 10 mg qhs, azelastine hydrochloride-fluticasone propionate 137 mcg-50 mcg nasal spray bid, levothyroxine 50 mcg qd, clonazepam 0.5 mg QHS, eszopiclone 3 mg prn, and propranolol 10 mg prn. Cardiovascular and respiratory review of systems was negative, aside from history of asthma as stated (mexiletine used for chronic pain and muscle relaxation) and the patient was npo for over 8 hours. She had not used propranolol (for anxiety) prior to surgery.

Airway exam revealed Mallampati score of 1, thyromental distance > 3 fingerbreadths, and mouth opening > 3 fingerbreadths. Cardiorespiratory exam revealed a regular rate and rhythm, no murmurs, rubs, or gallops, and non-labored respirations. Pre-operative labs including CBC and electrolytes were within normal limits and pregnancy test was negative. Vital signs prior to anesthetic induction included temperature = 37 C, heart rate = 96 bpm, respiratory rate = 18 breaths/minute, blood pressure = 112/65 bpm, and O2 = 100% on 2L nasal cannula. To maintain normothermia, the patient was covered with heated blankets in the preoperative area and in the operating room. A Bair Hugger system was also utilized throughout the duration of the case.

Core temperature monitoring was established via the esophagus and recorded periodically. Normal sinus rhythm was confirmed with EKG. Anesthetic management began with 100 mcg fentanyl, 4 mg odansetron, and 2 mg midazolam for pain, nausea, and anxiety. Antibiotic prophylaxis with 900 mg clindamycin was given. Next, 200 mg propofol and 20 mg ketamine were used for induction. Rocuronium (35 mg) was given for non-depolarizing muscle paralysis. The trachea was smoothly intubated by video laryngoscope. This was performed by a registered nurse anesthetist under the supervision of an attending anesthesiologist. Nitrous oxide and continuous propofol infusion with 10 mg/mL IV emulsion 100 mL at 7.59 mg/hr were used for maintenance of general anesthesia for the remainder of the case.

Pre-operative and post-operative electrolytes were within normal limits. Intraoperative electrocardiogram (EKG) monitoring was performed throughout the entire procedure and the patient maintained normal sinus rhythm. No indication of hyperkalemia (such as peaked T waves, flattening of P waves, or prolongation of the PR interval) was apparent for the entirety of EKG monitoring. Thirty minutes after anesthetic initiation, an additional 50-mcg fentanyl and 20 mg ketamine was given for pain management and sedation. Dexamethasone 4 mg and glycopyrrolate 0.6 mg were given just prior to the end of anesthesia (Table 1). The patient's vitals remained

stable throughout the case, with an increase in systolic blood pressure prompting further pain management at 30 minutes. Total anesthetic time was 85 minutes. The patient awoke from anesthesia without complications and was discharged home on the same day, approximately 2 hours after the case concluded. She was seen for follow up in the general surgery office one week later. She reported some mental fatigue following surgery and did experience a delayed return to work secondary to this. She otherwise recovered well without complications.

DISCUSSION.

The present case describes successful general anesthetic management in a patient with paramyotonia congenita using propofol and ketamine for induction andnon-depolarizing rocuronium for muscle paralysis, with continuous nitrous oxide and IV propofol infusion for anesthesia maintenance. The patient remained stable throughout the case without myotonic episodes, evidence of hyperkalemia, or other complications. Given the clear contraindication to succinylcholine, this suggests that the use of non-depolarizing agents during intubation is a viable alternative strategy in patients with paramyotonia congenita when general anesthesia is necessitated. . Moreover, it is known that use of volatile anesthetics for maintenance anesthesia poses a risk for patients with malignant hyperthermia. There are minimal reports regarding the use of volatile anesthetics in patients with paramyotonia congenita and thus, we did not use sevoflurane for maintenance in our patient to avoid unnecessary risk.

Regardless of anesthetic strategy used, hypothermia and hyperkalemia are the two biggest perioperative risks for a myotonic episode and should be monitored accordingly with a temperature probe, EKG, and electrolyte panels. Unfortunately, there is slim evidence available to date regarding agents that could potentially reverse an acute myotonic episode, should one occur. There is only one reported case study in the literature that describes an acute reversal of a myotonic episode in PC during surgery.[8] The patient was a 40-year-old female who did not know that she had paramyotonia congenita and was given succinylcholine during induction. Immediately, she was noted to have rigidity of her upper extremities, neck, and masseter muscles to the point that her mouth could not be opened for intubation. Mask ventilation was performed and a 100 mg IV propofol bolus was given and within 4-5 minutes her myotonia receded allowing for intubation. The surgery was then performed without complications.

Additional research has suggested that the successful reversal may be secondary to the ability of propofol to block not only wild-type sodium channels, but also mutant sodium channels in a patient with PC.[9] Moreover, Matsumoto et al. (2019) reported a case that suggested the class 1B anti-arrhythmic drug mexiletine could potentially be used as a reversal agent due to its sodium channel inhibition.[7] If considered from a purely mechanistic view, this is logical since paramyotonia is caused by a derangement in sodium deactivation and mexiletine blocks sodium channels. However, the cited randomized control trial is somewhat limited because it reports that mexiletine is superior to placebo in reducing stiffness symptoms over a four-week period, not reversing an acute myotonic episode immediately.[10] Interestingly, our patient was taking mexiletine at the time of surgery for chronic pain and muscle rigidity. Although it is unclear if this lowered her risk of myotonia intra-operatively, this fact represents an important limitation of the present report. There were no indications for holding this medication pre-operatively, and, given the beneficial effect of mexiletine in paramyotonia congenita, doing so may not have been in the patient's best interest. It is therefore unknown, however, whether paralysis with the non-depolarizing agent rocuronium, as described in this report, would have been successful without the patient's prior prescription of mexiletine. Therefore, additional research is needed to examine anesthetic management with rocuronium in patients with paramyotonia congenita who are not taking mexiletine. Additional areas of focus may also include whether starting mexiletine in the pre-operative period (i.e. one month prior to surgery) in patients with paramyotonia congenita shows benefit in reducing intra-operative complications for patients undergoing elective procedures.

In conclusion, our report describes successful anesthetic management using non-depolarizing muscle relaxant, rocuronium, bolus propofol, ketamine, and continuous IV propofol with nitrous oxide in a patient with paramyotonia congenita. This provides a potential management plan that may be applied to PC patients undergoing a variety of surgical procedures and eliminates risk associated with succinylcholine and possibly volatile anesthetics. Additionally, the use of rocuronium as a muscle relaxant may allow easier and more efficient intubations in these patients, reducing the risk associated with prolonged hypoxia that is occasionally observed in difficult intubations. Further research is needed to determine whether this approach is superior to previously reported techniques and should also aim to identify which agents may be effectively utilized to reverse a myotonic episode in PC patients should one occur intra-operatively.

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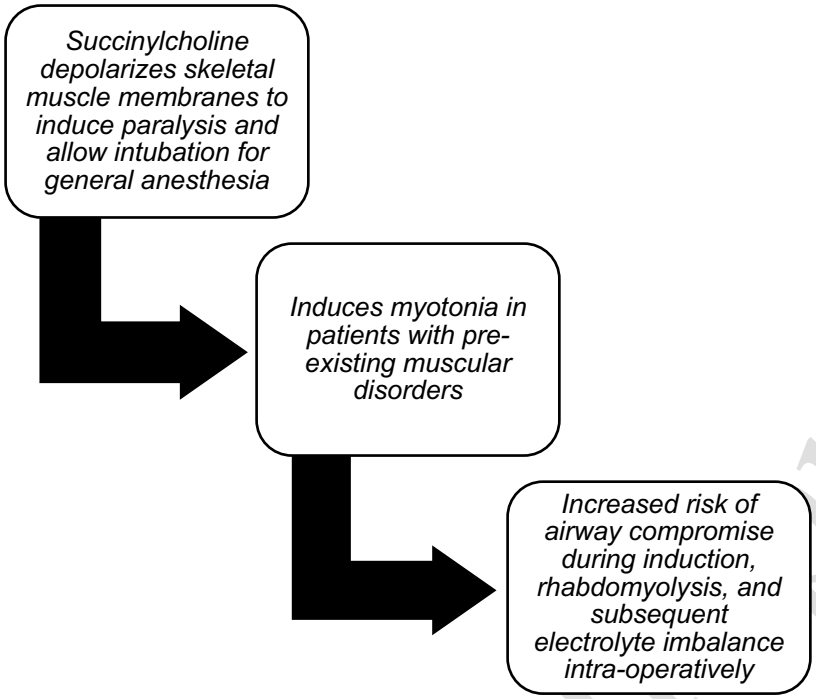
FIGURES AND TABLES.

Figure 1. Risk of Succinylcholine Utilization for Anesthetic Induction in Paramyotonia Congenita



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FIGURES AND TABLES.

Table 1. Medications Used for Anesthetic Management

Antibiotic Prophylaxis	900 mg clindamycin
Induction	200 mg propofol, 20 mg ketamine
Paralytic (Non-Depolarizing)	35 mg rocuronium
Anesthetic Maintenance	Nitrous oxide via nasal cannula, continuous propofol 10 mg/mL IV emulsion 100 mL @ 7.5 mg/hr
Intraoperative Monitoring	Potassium checks; electrocardiogram monitoring; temperature via esophagus
End of Sedation	4 mg dexamethasone, 0.6 mg glycopyrrolate