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Hyperkalemic periodic paralysis with paramyotonia and the anaesthetic implications

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Accepted 1 December 2022

SUMMARY

Hyperkalemic periodic paralysis (HyperKPP) is a rare disease with significant anaesthetic implications. We compare two perioperative courses in the same patient. The first surgery resulted in paralysis and a protracted hospitalisation, while the second surgery resulted in a same-day discharge. Various anaesthetic techniques may be used; however, clear communication surrounding optimisation both for home medications (eg, continuing potassium wasting diuretics) and avoidance of triggering medications (primarily: depolarising neuromuscular blockers), along with thermoregulation and glucose management plans, is critical and best performed early by an anaesthetic precare clinic. Our cases highlight the physiological underpinnings in managing patients with HyperKPP.

BACKGROUND

The patient is a woman in her 50s with a history of hypertension, morbid obesity, body mass index 46 kg/m², gastro-oesophageal reflux disease, obstructive sleep apnoea requiring continuous positive airway pressure and hyperkalemic periodic paralysis (HyperKPP) with paramyotonia confirmed by genetic testing (SCN4A Thr704Met mutation), and no family history of malignant hyperthermia who presented for an incision, drainage and washout of a left ankle wound. Twenty-five days prior, she had undergone surgical repair for a left foot tarsal tunnel release, posterior tibial repair and peroneal brevis tendon repair.

In the preoperative surgical unit, she was extremely anxious about 'not being able to move' following the surgery due to having experienced neuromuscular weakness and paralysis following her last surgery and several times during previous hospitalisations, with the most significant occurrences resulting in intensive care unit admissions. After these experiences, the patient had become highly attuned to her triggering factors. She informed the team that if her potassium rises above 3.6 mmol/L, she will start to experience symptoms. Additionally, she had previously had HyperKPP events in response to stress, pain, glucose excursions and temperature extremes. Both cases reported are the same patient. Case 1 resulted in a HyperKPP with paramyotonia exacerbation, and hospitalisation. Case 2 did not, and the patient was discharged home the same day.

CASE PRESENTATION**First case**

During the initial surgery on her ankle, she was treated with a preoperative nerve block and intraoperative sedation. Of note, she was informed as per standard protocol not to take her diuretics

(acetazolamide, hydrochlorothiazide) on the day of surgery (DOS). In preoperative holding, she was sedated with midazolam 2 mg, fentanyl 50 µg and dexmedetomidine 75 µg and then given a preoperative femoral and popliteal sciatic peripheral nerve block with 40 mL of ropivacaine 0.5%. She was then transferred to the operating room and given sedation totaling: midazolam 5 mg, fentanyl 50 µg, dexmedetomidine infusion of 133 µg, ketamine 20 mg and propofol 173 mg. She also received glycopyrrolate 0.2 mg, regular insulin 10 units and 20 mL of dextrose 50% during the case for a potassium of 5.7 mmol/L. She later reported that she was intermittently awake and in extreme discomfort during the surgery and that the nerve block was ineffectual.

In the post anaesthesia care unit, she was haemodynamically stable and able to move all four extremities but was profoundly weak, experiencing muscle stiffness and unable to bear weight. Her potassium fluctuated from 5.0 to 6.2 mmol/L and 3.2 mmol/L after treatment. She was transferred to the floor with hourly nursing checks. By postoperative day 2, she was able to sit at the side of the bed with assistance.

On postoperative day 3, she could ambulate a few steps with a rolling walker aided by her husband. She was discharged to home on postoperative day 4, after physical therapy review with home health visits. During postoperative days 5–11, she continued to have decreased strength of 3/5 globally.

Second case

Her second surgery was an incision, drainage and washout of the wound. Given her account of the failed nerve block and her subsequent complicated postoperative course, we elected not to sedate her with a nerve block for concerns of hypercarbia with resultant hyperkalemia. Instead, she received a total intravenous general anaesthetic (TIVA) with controlled ventilation and malignant hyperthermia precautions, despite no family history of malignant hyperthermia. She took her diuretics, and her starting potassium was 3.6 mmol/L. She was given nebulised albuterol 2.5 mg, oral acetaminophen . 1 g, oral celecoxib 200 mg, and intravenous midazolam 2 mg in preoperative period, then transferred to the operating room where she was induced with 100 mcg fentanyl, 100 mg lidocaine, 250 mg propofol, 50 mg rocuronium and then intubated. An arterial line was placed for frequent checks of her potassium and started a 5% dextrose containing normal saline solution. Forced air warming was



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To cite: Sender D, Doyal A. *BMJ Case Rep* 2023;**16**:e251699. doi:10.1136/bcr-2022-251699

Case report

used to keep the patient euthermic. During the case, she received a propofol infusion of 100–150 µg/kg/min, ondansetron 4 mg, cefepime 2 g, surgically infiltrated 0.25% bupivacaine 30 mL and was fully reversed with 300 mg sugammadex. Her potassium during the case was monitored by arterial blood gases and was 2.9 and 3.0 mmol/L. She was then extubated awake and transferred to the post anaesthesia care unit.

In the post anaesthesia care unit, she experienced moderate pain that was treated with intravenous fentanyl and hydro-morphone, and she did not endorse any weakness or stiffness throughout her postoperative course. She had 5/5 strength throughout her body and could ambulate without difficulty. She was discharged home from the post anaesthesia care unit without any complications.

OUTCOME AND FOLLOW-UP

After case 1, it took the patient's 2 weeks to return to baseline strength levels. After case 2, the patient experienced no residual weakness after discharge. The variations between these two events had a substantially different impact on the patient's quality of life and ability to participate in activities of daily living.

DISCUSSION

HyperKPP is an autosomal dominant neuromuscular disorder caused by a mutation to the SCN4A gene that encodes for the alpha subunit of the skeletal muscle voltage-gated sodium channel (NaV 1.4).¹ It is a rare disease with an incidence between 1:200 000 and 500 000.²

Excitable cells at the motor endplate have a resting membrane potential of -70 mV and a threshold potential of -55 mV. These gross voltages are predominantly due to the resting potentials of potassium ($E_k -75$ mV) and sodium ($E_{Na} +55$ mV).

In hyperkalemia physiology, the resting membrane potential is more positive at baseline due to a lessened concentration gradient between intracellular and extracellular K⁺.³ However, the threshold potential for NaV channels remain the same. This results in a lessened Na⁺ influx requirement to generate an action potential. These effects are seen most readily in the cardiac excitatory effects of hyperkalemia.⁴

HyperKPP pathophysiology is triggered by a slight increase in extracellular K⁺, most commonly resulting from the ingestion of potassium-rich food, rest after a heavy workout, periods of fasting, emotional stress, pregnancy, exposure to cold, surgery and anaesthesia.⁵ This slight K⁺ increase may still be within normal laboratory values but causes a minor membrane depolarisation. If an impulse is generated, an unknown percentage of mutated NaV 1.4 channels may fail to inactivate, leading to a prolonged increase in intracellular Na⁺ and persistent cell depolarisation.⁶ If intervention occurs at this point, often paralysis can be avoided, and weakness will be transient. If this continues, the cycle undergoes a pathologic feedback loop with worsening membrane excitability at baseline from (1) the higher intracellular Na⁺ concentration driving K⁺ extracellularly and (2) continuation of the initial hyperkalemic trigger event. The net result of this cycle is the subsequent loss of electrical excitability and thus paralysis.⁷

Considerations for anaesthesia

The number of HyperKPP patients undergoing general anaesthesia (GA) and suffering a postoperative attack of either weakness or paralysis is approximately 30%.⁵ Using our case reports as a crossover of two different anaesthetics in the same person allows for some broad anaesthetic principles to

be considered, and the physiology underpinning HyperKPP to be examined: (1) Preanaesthetic evaluation of these patients can prevent the inadvertent holding of medications such as diuretics on the DOS. In case 1, both acetazolamide and hydrochlorothiazide were held; however, in case 2 both were given. HyperKPP patients often require K⁺ wasting diuretics as a prophylactic treatment, and these medications are occasionally flagged to be held per protocol. (2) In neither case did our patient receive preoperative carbohydrate loading. Fasting is a known trigger and preoperative nothing by mouth (NPO) guidelines may need augmentation with carbohydrate drink loading and careful intraoperative glucose monitoring.⁸ The mechanism behind fasting as a trigger is poorly understood. The current thought is that counter-regulatory hormones such as glucagon, cortisol and epinephrine raise blood glucose in response to the fasting or stress state, driving K⁺ extracellularly.⁹ (3) Extracellular potassium monitoring and management are of paramount importance. During case 1, only preoperative and postoperative chemistries were sent. Comparatively, in case 2, an arterial line was placed for close monitoring of potassium and glucose. Additionally, preoperative albuterol was administered in case 2 to prophylactically decrease potassium by driving the electrolyte intracellularly.

Our crossover comparing TIVA with endotracheal tube intubation and regional techniques with sedation cannot be used to generalise a preference for one technique over the other. Previous case studies in pregnancy examined labour epidural versus GA.¹⁰ Their findings are suggestive that either technique can be safely administered, but if any concerns for weakness exist preoperatively, then GA with/without paralysis using a non-depolarising neuromuscular blocker such as rocuronium is preferable. Complete reversal of neuromuscular blockade is essential, as weakness following regional or neuraxial anaesthesia could be indistinguishable from periodic paralysis in the postoperative period. One disadvantage of using GA is the inability to ask patients about subjective weakness in upper extremities or peribulbar musculature. Additionally, hypothermia is a known trigger, and approximately 45% of HyperKPP patients have coexisting paramyotonia presenting as muscle stiffness in response to cold as does our patient.¹¹ Thermoregulation during GA is impaired to a more significant degree than neuraxial, which is worse than regional.¹² Fluid warming may also be used to optimise thermoregulation, as suggested in a previous case.¹³ Preoperatively warming the patient in case 2 likely prevented the paramyotonia seen during case 1.

Morbidity from HyperKPP results from chronic progressive myopathy and skeletal muscle atrophy, although secondary to HyperKPP immobility, diabetes mellitus, obesity, hypertension and hyperlipidaemia all contribute to a significant cardiovascular burden.

CONCLUSION

HyperKPP with paramyotonia is an exceedingly rare condition, but various anaesthetic approaches may be used to prevent morbidity or mortality. Our observations reinforce that a pre-anaesthetic clinic should evaluate these patients to optimise DOS medications, promote carbohydrate drink loading preoperatively, use glucose-containing intravenous fluids, ensure a robust thermoregulation plan is in place and prevent the use of triggering medications (eg, depolarising neuromuscular blockers). As prevention of hyperkalemia is foundational in the management of these patients, previous studies have focused on vigilant

Patient's perspective

For the first surgery, I was told that it was best for me to have a nerve block and sedation. I thought this was not a good idea, as I had a block in a surgery for carpal tunnel release years ago where I felt intense pain and distress. I was overruled and was given full leg block. Throughout the surgery, I was sedated but kept feeling cutting pain and kept saying and crying out that I was in distress. They would give me more sedation but still felt terrible pain. When waking in recovery, I felt as though I was paralysed and it was getting worse every moment. My blood sugars were on target but my potassium was severely elevated. I ended up completely paralysed and was in pain from surgery. I was admitted to hospital under observation. I didn't receive physical therapy for several days, which was a very important component to getting my movement back. After receiving physical therapy, I was able to stand and then went home. I had residual stiffness, weakness and pain in my muscles for a week after surgery.

I think that there was a lot of fear to give me general anaesthesia in the first surgery. The stress of constant pain enabled my cortisol levels to increase, which is always a trigger for paralysis. I was so dismayed in the recovery room and kept asking if my potassium was checked intraoperatively. I was given a huge amount of insulin to bring my potassium level down in recovery after discovering it was 6.7 mmol/L. Being admitted to the hospital as a paraplegic, and with surgical pain is a horrible experience.

Finding out after weeks of severe pain that I had an infection, and needed more surgery was very scary.

After speaking to my anaesthesiologist, I felt he actually understood my needs more than first time. The suggestion of using albuterol to bring down my potassium level before surgery I think helped. General anaesthesia took away the distress of monitoring potassium levels throughout surgery and enabled me to wake up and not have paralysis. Of course this surgery was much shorter than first and I have had short surgeries without paralysis in the past. Monitoring potassium consistently seems to be the only way to avoid paralysis. Blood glucose monitoring is easier now with my continuous pump and must be monitored in conjunction with my potassium.

I believe the second surgery was more successful due to monitoring potassium levels and after the first surgery, my anaesthesiologist had a better understanding of the mechanisms of the disease. I feel the proactive rather than reactive approach is what makes the difference. The first anaesthesiologist was trying their best but was acting reactively to each thing that went wrong. Once paralysis sets in, it is very hard to reverse. Plus having a flaccid leg from the nerve block didn't allow me to have any movement making it more difficult to gauge paralysis and attempt to start moving. The second surgery I had postoperative pain but was able to go home not paralysed.

Hyperkalemic periodic paralysis with paramyotonia is a very rare condition with discreet needs for each patient. Listening to my experience is important to figure out how to solve the complexity of keeping my potassium and glucose at a level I know is right for me. I do not meet any standard notion of proper potassium levels. Every minute counts when correcting my potassium to avoid complete paralysis.

monitoring of electrocardiogram changes during the procedure as a sign of hyperkalemia. However, our case highlights that even small K⁺ shifts within normal ranges can trigger attacks.¹⁴ Attention to these details in the perioperative period and a high level of vigilance can help to prevent exacerbations of HyperKPP.

Learning points

- ▶ Preanaesthetic clinic evaluation is vital for this population.
- ▶ Prevention of depolarising neuromuscular blocking medications.
- ▶ Prevent hypoglycaemia with dextrose fluids and preoperative carbohydrate loading.
- ▶ Manage surgical stressors be that pain, temperature or psychological stress.
- ▶ The anaesthetic approach general versus regional is less important than preparing for known triggers.

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Contributors DS wrote discussion, conclusion, formatted paper, cared for patient in post anaesthesia care unit and interviewed and consented patient for their portion. AD wrote the case portion, interviewed staff, patient, supervisory guidance writing a case report.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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