Residual neuromuscular blockade in the immediate postoperative period may impair a patient’s ventilation and ability to protect his or her airway. Respiratory complications are the most frequently encountered problems in the immediate postanesthetic period; they are major contributors to mortality and morbidity associated with anesthesia. Airway obstruction, hypoventilation, and hypoxemia are the foremost manifestations of airway compromise. Apnea and hypoventilation are usually caused by either central depression or peripheral neuromuscular blockade. Early diagnosis and treatment can greatly increase the likelihood of a positive patient outcome.

Case summary
An 82-year-old woman presented to the emergency department for treatment of a left hip fracture that occurred from a fall 2 hours prior to arrival at the hospital. Her vital signs during triage in the emergency department were as follows: blood pressure, 139/85 mm Hg; heart rate, 83 beats per minute; respiratory rate, 17 breaths per minute; temperature, 97.0°F; and SaO₂, 97%. She rated her pain at 10 on a 10-point scale and explained that it was localized to her left hip. Routine laboratory data were obtained and revealed the following abnormal values: hemoglobin, 11.9 g/dL; hematocrit, 35.4%; international normalized ratio, 1.48; potassium 3.2 mmol/L; blood urea nitrogen, 51 mg/dL; and creatinine 1.9 mg/dL. A 12-lead electrocardiogram showed a paced ventricular rhythm capturing at 70 beats per minute. A chest radiograph revealed mild pulmonary congestion that was unchanged from a report 4 years earlier. Intravenous access was secured with a 20-gauge peripheral intravenous catheter inserted into the right antecubital vein.

The patient’s medical history was significant for hypertension, hypothyroidism, seasonal allergies, mild osteoporosis, anemia, atrial fibrillation treated by placement of an atrioventricular universal (DDD) pacemaker set at a rate of 70 heart beats per minute, and a urinary tract infection that began almost 1 week prior to her admission. Prior surgical history included an umbilical hernia repair in the 1980s and a radiofrequency ablation of the sinus node followed by placement of a permanent artificial cardiac pacemaker. The patient denied both tobacco and alcohol use. Her only known drug allergy was to sulfa that caused nausea and vomiting. Regular medications included valsartan, amiodarone, coumadin, furosemide, docusate sodium, alendronate sodium, levofloxacin, levethyroid, alprazolam, potassium supplement, ketoralac eye drops, and estrogen replacement therapy.

After admission into the hospital, surgery was delayed because of low potassium levels and the need for a cardiac clearance for surgery. Potassium, 20 mEq, was given intravenously over 4 hours with potassium, 20 mEq, by mouth to be given daily thereafter. At the end of the first day of admission, however, serum potassium was found to be 2.6 mEq/L, so another 20 mEq of potassium was given intravenously over 4
hours and followed by maintenance intravenous fluids (composed of dextrose, 5%; 0.45% normal saline; and potassium, 20 mEq/L) at 100 mL/h. On the second day of admission laboratory samples were drawn shortly after midnight and serum potassium was 4.3 mEq/L. Cardiac clearance was obtained after a cardiac consultation and an echocardiogram revealed an ejection fraction of 63%.

On the second day of admission the patient was scheduled for placement of a dynamic hip screw into the left hip. The patient’s morning dose of furosemide was withheld in accordance with the routine preanesthesia medical orders, but the patient received her oral potassium supplementation prior to transport to the preoperative holding area. The patient had received a total of approximately 100 mEq of oral and intravenous potassium supplementation over 42 hours prior to the surgery. General endotracheal anesthesia was started at 9:07 AM and achieved with 75 µg fentanyl, 0.5 mg midazolam, 20 mg etomidate, and 4 mg vecuronium. The intraoperative period proceeded uneventfully with minimal blood loss and no hemodynamic instability. Vecuronium was readministered twice with 2 mg each given at approximately 9:30 AM and 10:00 AM. A peripheral nerve stimulator was used to guide administration of muscle relaxants, a full train-of-four (TOF) was present before each additional dosage. Anesthesia was maintained with isoflurane and nitrous oxide. No additional narcotics were administered.

Following skin closure at 10:29 AM, the muscle relaxation was reversed with 3 mg neostigmine and 0.6 mg glycopyrrolate after a full TOF with no fade was observed. The patient was placed on 100% oxygen and an apneic oxygenation technique was used to increase ETCO2 and aid in the return of spontaneous respirations. After approximately 5 minutes, ETCO2 was at 50 mm Hg. Respirations were shallow at 36 breaths per minute. TOF was reassessed and had decreased to only 1 twitch. Ventilations were assisted and 25 mg of edrophonium and 0.2 mg of atropine where administered intravenously. No TOF improvement was appreciated and at 10:51 AM the patient was transferred to the recovery unit using a transport anesthesia bag with 100% oxygen through her orotracheal tube. She remained nonresponsive to both verbal and noxious stimuli with no observable TOF upon application of 4 supramaximal impulses from a peripheral nerve stimulator. Ventilatory assistance was required throughout emergence and pulse oximetry revealed that SpO2 remained at 100%. ETCO2 was maintained between 40 and 50 mm Hg.

On arrival to PACU the patient became hypotensive and required repeat boluses of 100 µg of neosynephrine to maintain blood pressure, but adequate spontaneous ventilation was achieved. Bilateral breath sounds were equal and present over all lung fields. Mucous membranes remained pink and no signs of cyanosis were present. Pulse oximetry continued to display a SpO2 of 100%. At 11:29 AM the electrocardiogram showed that the pacemaker was capturing only every other beat with a rate of 35 beats per minute and a blood pressure of 81/39 mm Hg. The patient was given 0.2 mg of atropine intravenously, and a dopamine drip was started at 5 µg/kg per minute. The patient was placed on a ventilator to control respirations with a tidal volume of 600 mL and an intermittent mandatory ventilator rate of 10 breaths per minute. Laboratory values were as follows: arterial blood gas PH, 7.46; PaCO2, 29.2; PaO2, 46 mm Hg; NaHCO3, 22 mEq/L; base excess, 3; SaO2, 94%; potassium, greater than 7.6 mEq/L; glucose, 232 mg/dL; and hematocrit, 33%.

After laboratory values were verified with a second blood sample, treatment for hyperkalemia was instituted with intravenous administration of 5 units regular insulin, 50 mEq NaHCO3, and 1 g calcium chloride. The ventilator rate was increased to 14 breaths per minute. Ten minutes later the patient’s blood pressure stabilized and the electrocardiogram once again revealed a 100% paced rhythm at a rate of 70 beats per minute. Vasopressors were discontinued at 11:55 AM and blood potassium level was 5.7 mEq/L. The patient became responsive to verbal stimuli at this time. She was placed on a T-piece to an orotracheal tube with 60% oxygen and a Kayexalate enema was ordered.

At 4:30 PM, the patient’s blood potassium was 3.9 mEq/L and she was awake and alert. She was transferred to an intensive care unit and extubated later that night. The patient was subsequently diagnosed with chronic renal insufficiency. The rest of her stay was uneventful and no permanent complications were evidenced. She was discharged to a rehabilitation care facility on postoperative day 6.

Discussion
The anesthesia provider often uses an external peripheral nerve stimulator to monitor neuromuscular blockade and the recovery from blockade. When nerve fibers are stimulated by an electrical impulse, they release acetylcholine into the synaptic cleft of the neuromuscular junction. A subsequent sustained stimulation of the same neuromuscular junction results in a much stronger contractile response because a higher concentration of acetylcholine is achieved within the synaptic cleft; more acetylcholine is released into the synaptic cleft before all of the previously released acetylcholine molecules can be
Potassium regulation is a function of potassium ingestion, potassium excretion, and redistribution of potassium between intracellular and extracellular fluid compartments. The first line of defense against extracellular fluid (ECF) increases in potassium concentration is redistribution among internal compartments. The long-term maintenance of potassium homeostasis is dependant on renal excretion.6

Potassium in the ECF is tightly regulated within a narrow range, which is approximately 3.5 to 5.0 mEq/L.6 Variations from this range result in changes in the excitability of neuromuscular membranes as a direct result of the alterations in the resting membrane potential. See Figure 2 for the factors that alter potassium balance in the ECF and intracellular fluid (ICF) compartments. Potassium ingestion is controlled entirely by an individual's dietary intake. Potassium excretion occurs solely in the renal system.

There are 7 variables involved in redistribution of potassium among internal compartments.6 These variables include insulin, aldosterone, β-adrenergic stimulation, acid-base abnormalities, cell lysis, strenuous exercise, and extracellular fluid osmolarity.

Managing the treatment for hyperkalemia has 3 aspects:7 (1) determine and treat reversible causes, (2) initiate measures to reduce membrane excitability to counteract the adverse effects of hyperkalemia, and (3) initiate measures to lower potassium levels.

Determining reversible causes requires that a thorough preoperative assessment be completed. Many disease processes and medications can contribute to hyperkalemia. Reversible causes cannot be easily identified with an incomplete or inaccurate health history. Renal function, nutritional status, and recent medications are particularly important to ascertain during a preoperative assessment in order to adequately evaluate electrolyte status.

Treatment of hypokalemia with potassium supplementation must be closely monitored using laboratory quantification of serum potassium levels to prevent overtreatment. Aggressive or inappropriate treatment of hypokalemia may result in lethal complications due to the deleterious changes in cellular electrical physiology caused by potassium imbalances. A decrease of serum potassium from 4.0 mEq/L to 3.0 mEq/L is associated with an approximate total body potassium deficit of 300 to 400 mEq.6 Many different guidelines for potassium supplementation are available for clinical use with the major differences between them being the various suggested dosages for potassium administration and the maximum rate of infusion.

The total body potassium deficit is ideally corrected over several days through oral supplementation, but if clinical cardiac symptoms are present then quicker

metabolized. A stronger contraction occurs because the total number of acetylcholine molecules available to bind to nicotinic receptors is increased. This is termed either post-tetanic potentiation or the staircase phenomenon. This response often makes subsequent neuromuscular assessments with a nerve stimulator used on the same site inaccurate, so overestimation of recovery from paralytics can occur.

The TOF stimulus and TOF ratio are 2 different tools that may be used to assess residual neuromuscular blockade and the return of neuromuscular function. Post-tetanic potentiation will increase each contractile response to a TOF stimulus; when 4 twitches are present each contractile response is increased by the same percentage. The TOF ratio is obtained by comparing the amplitude of the fourth TOF stimulus to the amplitude of the first TOF stimulus. The TOF ratio is not altered by the staircase phenomenon5 when 4 twitches are present. This is true because the amplitude of fourth and first contractile responses are increased by the same percentage, which allows the ratio of the amplitudes of the fourth to the first contractile response to remain unchanged even though each contractile response is greater in amplitude. The TOF ratio is perhaps the most reliable assessment of the presence of residual neuromuscular blockade because of its ability to not be altered by post-tetanic potentiation like the basic TOF stimuli may be altered. Other sensitive indicators of the return of neuromuscular function is either a sustained head lift or hand grasp for at least 5 seconds.4

Central depression and peripheral neuromuscular blockade are the 2 major possible causes of postoperative apnea and hypoventilation. Other factors that contribute to residual neuromuscular weakness are delineated in Figure 1.

Electrolyte imbalances can have a profound effect on electrical conduction that controls motor and cardiac function. One of the most deleterious electrolyte disorders is hyperkalemia.9 Initially hyperkalemia causes hyperexcitability of cellular membranes by moving the resting membrane potential closer to threshold potential, a smaller stimuli is needed to initiate a contraction. Eventually the Na,K-ATPase pumps begin to fatigue from the excessive depolarizations, and cellular membranes become less excitable. Hyperkalemia potentiates the neuromuscular blockade induced by muscle relaxants by decreasing the excitability of the skeletal muscle. Hyperkalemia initially affects cardiac muscle by increasing the excitability of the syncytium, resulting in ventricular tachycardia or ventricular fibrillation. Eventually the syncytium will become less excitable and demonstrate arrhythmias with slow heart rates (heart blocks, bradycardia, asystole, etc).
One of the human body’s homeostatic mechanisms to maintain normal physiologic acid-base balance is to exchange hydrogen and potassium ions for each other from ECF/ICF compartments to help maintain balance in each compartment. For example, if ECF fluid gains excess hydrogen ions—becomes acidic—then hydrogen will be transported into cells and potassium will be transported out of cells to compensate. The opposite of this process will occur if ECF becomes alkaline; potassium will be pumped into cells and hydrogen will be pumped out of cells. \(^\text{10}\)

This physiological process explains how altering the respiratory rate can have an impact on potassium ion concentrations throughout the body. Hyperventilation decreases ECF hydrogen ion concentrations and results in the net movement of potassium ions from the ECF into the ICF compartments, as hydrogen ions move in the opposite direction. Hypoventilation results in an
Excess of ECF hydrogen ions with a net movement of potassium ions from the ICF to the ECF compartment, as hydrogen ions move in the opposite direction.

There are multiple drug therapies that may be used in the treatment of hyperkalemia. The only treatment available to decrease membrane excitability is the intravenous administration of calcium, which helps to counteract the deleterious cardiac effects of hyperkalemia. Sodium bicarbonate, insulin, β2 agonists, and ion exchange resins are among the other most utilized pharmacological therapies. No one drug therapy has proved to be any more efficacious over the others.

Ion exchange resins are not appropriate as an initial treatment for acute symptomatic hyperkalemia because a couple of hours are needed to achieve a significant reduction in plasma potassium levels. Sodium bicarbonate, insulin, and β2 agonists are rapid acting and best suited for symptomatic hyperkalemia. Drug treatments work by hydrogen ion manipulation to alter potassium transport or by activation of potassium ion channels on cell membranes.

Hemodialysis can be used in the treatment of acute hyperkalemia. This modality is particularly useful for the rapid correction of life-threatening hyperkalemia after failure of pharmacological interventions. Peritoneal dialysis would take several hours to correct increased potassium levels, so this modality is reserved for patients with chronic hyperkalemia secondary to renal failure.

Conclusion

Major presentations of residual neuromuscular blockade are airway obstruction, hypoventilation, and hypoxemia; each of these responds quickly to prompt airway support. The anesthetist must be able to rapidly diagnose and treat postoperative residual neuromuscular weakness; late intervention is associated with very high mortality and morbidity rates. Many factors must be considered when determining the cause of residual neuromuscular weakness, such as coexisting diseases, physical factors, and drug-induced muscle weakness.

Hyperkalemia is an electrolyte disorder that can be difficult to diagnose in the presence of neuromuscular blocking drugs because the anesthesiology provider may attribute residual muscle weakness to the muscle relaxant and overlook electrolyte disturbances as a potential culprit. Anesthesia providers must be vigilant and consider all potential contributing factors to the prolonged effects of neuromuscular blocking drugs.

REFERENCES


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