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Hyperkalemia during surgery: is it an early warning of propofol infusion syndrome?

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Abstract
We present a case of severe hyperkalemia in a 48-year-old man after short-term infusion of an average dose of propofol. We suspected that the hyperkalemia in this patient was a sign of propofol infusion syndrome. The patient was undergoing a video-assisted esophagectomy, for which one-lung ventilation, with air/oxygen, isoflurane, and continuous epidural analgesia was supplemented with propofol infusion. In the intraoperative period, the patient developed severe hyperkalemia with mild acidosis but no cardiovascular failure. There were no other evident causes of hyperkalemia as documented by laboratory data. The procedure was abandoned and the patient was taken to postoperative recovery, where his potassium levels returned to normal at the end of 10 h.

Key words Hyperkalemia · Propofol infusion syndrome

Introduction

High doses of propofol are known to cause hyperkalemia, rhabdomyolysis, acute renal failure, lactic acidosis, arrhythmia, and death, termed the "propofol infusion syndrome (PRIS)." Evidence suggests a dose-dependent association between propofol use and PRIS. Recent case reports describe PRIS after short-term (3–6 h) infusions, if infusion rates are high [1–3]. Here we describe a case of severe hyperkalemia in an adult after short-term propofol infusion of an average dose of 3 $mg \cdot kg^{-1} \cdot h^{-1}$.

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Case report

A 48-year-old man, a known diabetic, was scheduled for video-assisted thoracoscopic esophagectomy for carcinoma of the esophagus. His preoperative hemoglobin was 6.8 $g \cdot dL^{-1}$ for which he had received two units of packed cells on the day prior to surgery. He was converted to insulin treatment for surgery. Preoperative laboratory investigations were normal. His electrolytes on the morning of surgery were: sodium, 137 $mmol \cdot L^{-1}$; potassium, 4·1 $mmol \cdot L^{-1}$; and chloride, 106 $mmol \cdot L^{-1}$; blood sugar was 7.8 $mmol \cdot L^{-1}$. Continuous monitoring of ECG, peripheral oxygen saturation (Sp_{O_2}), and blood pressure (BP) was instituted.

A thoracic epidural catheter was inserted in the T9–10 space before anesthesia. After confirmation of the catheter position, 8 mL of 0.25% bupivacaine was administered through the catheter and 0.125% bupivacaine was infused at the rate of 5 $mL \cdot h^{-1}$. Anesthesia was achieved with 200 µg fentanyl and 300 mg thiopentone sodium, and muscle relaxation was achieved with 6 mg vecuronium. Lung isolation was achieved using a no. 37 left Robertshaw-type double-lumen tube. Placement of the tube was confirmed clinically and with a bronchoscope. Central venous access was obtained through the right subclavian vein, and the left radial artery was cannulated.

The initial part of the operation was performed with the patient in the left lateral position. One-lung ventilation, along with air/oxygen, isoflurane (1% dialed concentration), and continuous epidural analgesia was supplemented with propofol infusion. Propofol infusion was started at the rate of 3 $mg \cdot kg^{-1} \cdot h^{-1}$ (50 $\mu g \cdot kg^{-1} \cdot min^{-1}$) after a bolus of 1 $mg \cdot kg^{-1}$. The patient received controlled ventilation with a tidal volume of 5 $mL \cdot kg^{-1}$ and a rate appropriate to maintain end-tidal CO_2 (Et_{CO_2}) between 30 and 35 mmHg. Fluid therapy during the procedure included 1 L lactated Ringer solution and 500 mL of gelofusine. Blood sugar after induction was

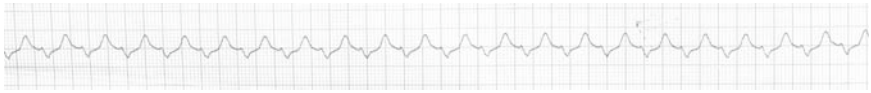

Fig. 1. ECG at 11:30 a.m. Potassium, 8.2 mmol·L^{-1}

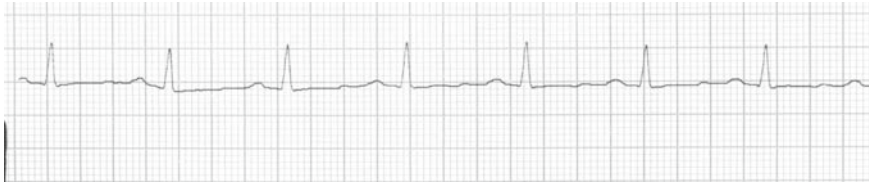

Fig. 2. ECG at 10:30 p.m. Potassium, 4.1 mmol·L^{-1}

12.56 mmol·L^{-1}, for which insulin infusion was started at 2 units·h^{-1}. Two hours after the start of surgery, ECG showed tall T waves, flattened P waves, and slightly widened QRS complex. These changes were attributed to inappropriate electrode placement The patient had one episode of bradycardia (heart rate [HR], 47 beats·min^{-1}) which responded to atropine 0.3 mg. During this entire period the patient remained hemodynamically stable with normal temperature.

At the end of the thoracic part of the surgery, 4 h after the start of surgery, the propofol infusion was stopped. When the patient was turned to the supine position, the ECG showed taller T waves, a wide QRS complex and absent P waves, but the patient was hemodynamically stable (Fig. 1). Arterial blood gas analysis showed a pH of 7.33, and serum potassium was 8.2 mmol·L^{-1}. The patient received 20 mL of 10% calcium gluconate given over 10 min, followed by 1 mmol·kg^{-1} sodium bicarbonate given over 15 min. Samples were collected for a peripheral blood smear and serum CPK, and a urine sample was processed for the presence of myoglobin. At 4.5 h after the start of surgery, potassium was 7.8 mmol·L^{-1}. A further 10 mL of calcium gluconate was given, followed by 50 mL of 50% glucose, along with 10 units insulin over 15 min; and continued with 10% glucose 50 mL·h^{-1} with insulin infusion of 3 units·h^{-1}. At 5 h after the start of the surgery, the QRS widening had decreased, and serum potassium was 7.0 mmol·L^{-1}.

Thorough clinical examination was carried out to rule out compartment syndrome. Meanwhile it was confirmed that the patient was maintaining good urine output (375 mL at the end of 4 h, 120 mL the next hour, and 80–100 mL·h^{-1}in subsequent hours). The peripheral smear did not reveal any fragmented RBCs, CPK was 362 IU·L^{-1}, and repeat serum potassium was 6.2 mmol·L^{-1}. At this point a decision was taken to postpone the abdominal part of the operation. The patient was given 4 mg midazolam IV with a repeat dose of antibiotic and was taken to postoperative recovery for elective ventilation. Late in the evening, 9 h after the start of surgery and 7 h after the onset of the ECG changes, serum potassium was still 6.9 mmol·L^{-1}, and it normalized to 4.1 mmol·L^{-1} late at night (Fig. 2). Next day in the morning the remaining surgery was completed successfully. As the epidural catheter had been accidently dislodged, the patient was given IV morphine as an analgesic. Except for the omission of propofol, the rest of the anesthetic management was same as that in the first surgery. Intraoperative serum electrolytes revealed potassium 4.2 mmol·L^{-1}. The patient was extubated on the table after adequate recovery from anesthesia. He had an uneventful recovery and was discharged home after 10 days.

Discussion

There are many causes of intraoperative hyperkalemia: the use of succinylcholine, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II blockers, or potassium-sparing diuretics; malignant hyperthermia (MH); accidental potassium injection; rhabdomyolysis; intravascular hemolysis; acute renal failure; and severe acidosis. We did not use succinylcholine, nor was our patient on any drugs that could impair potassium excretion. Temperature and Et_{CO_2} in our patient were maintained at normal levels throughout the course of surgery, ruling out MH. His hemoglobin dropped from a preoperative value of 9.1 g·dL^{-1} to 7.8 g·dL^{-1} with a blood loss of around 450 ml during surgery. The rise in the serum CPK level was appropriate for his surgery and the amount of muscle retraction. The absence of fragmented RBCs on the peripheral smear, the appropriate drop in hemoglobin for the amount of blood loss, and the absence of myoglobinurea ruled out rhabdomyolysis and intravascular hemolysis as causes of the hyperkalemia. The patient had normal renal function with good urine output throughout the surgery.

Having excluded all other known causes, we postulate that the hyperkalemia in our patient may have resulted from the propofol infusion. The course of intraoperative events in our patient was unusual for PRIS. The most prominent and only sign was acute hyperkalemia, with corresponding ECG changes. The acute

increase in serum potassium from 4.1 to 8.2 mmol·L^{-1} in our patient occurred in the absence of acidosis.

Propofol infusion syndrome (PRIS) was first documented in 1992 in a five-case series in the United Kingdom. Five children developed increasing metabolic acidosis, bradyarrhythmia, and fatal progressive myocardial failure following propofol infusion [4]. In 1996, the first case of PRIS in an adult was reported [5]. This syndrome consists of cardiac failure, rhabdomyolysis, severe metabolic acidosis, and renal failure [6].

The mechanism responsible for PRIS has yet to be ascertained. Possible explanations include inhibition of enzymes in the mitochondrial respiratory chain, impaired fatty-acid oxidation, diversion of carbohydrate metabolism to fat substrates, antagonism of ß-receptors, impaired myocardial oxygen use, and the presence of an unidentified metabolite. Although prolonged high-dose propofol infusions are typically required to produce PRIS, it has also been observed during average-dose propofol anesthesia. It has been postulated that propofol might act as a trigger substrate in the presence of priming factors such as poor oxygen delivery, sepsis, and serious cerebral injury.

Recently various authors have reported cases of PRIS with the use of short-duration propofol infusion at various doses [1–3,7]. Most of the reports in the literature have found metabolic acidosis, due to raised lactates; hypotension; cardiogenic shock; and acute renal failure as presenting features of PRIS. We found none of the above features, but we found isolated hyperkalemia and believe that this unexplained severe hyperkalemia represented an episode of early PRIS.

Anesthetists and intensivists using propofol for the maintenance of anesthesia or sedation should be aware of the potential occurrence of the syndrome even when average doses are used briefly. European regulatory authorities suggest that patients on propofol infusion should be monitored for metabolic acidosis, hyperkalemia, rhabdomyolysis, and an elevated creatine kinase level, and/or the progression of heart failure [8]. If the development of PRIS is suspected, the propofol infusion should be stopped, cardiorespiratory and metabolic support should be started promptly, and hemodialysis or hemoperfusion should be initiated, given the potentially fatal side effects of propofol and its metabolites.

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