

# A Death Associated with Possible Propofol Infusion Syndrome

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**Abstract** Propofol, an intravenously administered, centrally acting sedative/hypnotic, is a popular medication for anesthesia and sedation due to rapid onset, controllability and short recovery time. Prolonged propofol infusions, (>48 h) with elevated doses (>67 mcg/kg/min) may result in a rare but fatal condition known as the Propofol Related Infusion Syndrome (PRIS). This is a case of severe metabolic acidosis and refractory hyperkalemia in a 53 year old female with polytrauma on a continuous propofol infusion that was associated with fatal outcome.

**Keywords** Propofol infusion syndrome · Head injury

## Introduction

Propofol, an intravenously administered, centrally acting sedative/hypnotic, is a popular medication for anesthesia and sedation due to rapid onset, controllability and short recovery time. Prolonged propofol infusions (>48 h) with elevated doses (>67 µg/kg/min) may result in a rare but fatal condition known as the propofol-related infusion syndrome (PRIS).

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This is a case of severe metabolic acidosis and refractory hyperkalemia in a 53-year-old female with polytrauma on a continuous propofol infusion that was associated with fatal outcome.

## Case Report

A 53-year-old female pedestrian was involved in a high-speed motor vehicle accident. She was resuscitated and intubated in the emergency department. She sustained subarachnoid hemorrhages, intraparenchymal contusions, right humeral neck fracture, grade 3 liver lacerations with active bleeding, comminuted right superior and inferior pubic rami fractures, right sacral ala fracture with active bleeding in the pelvis, as documented on CT scanning. She underwent angiogram embolization of right hepatic arterial branch and right internal iliac artery for the hepatic and pelvic bleeding. After embolization, she was admitted to the intensive care unit.

Her treatment included invasive intracranial pressures (ICP) monitoring. Mechanical ventilation and sedation were continued with intravenous morphine (0.5–4 mg/h), midazolam (0.3 mg/kg/h), propofol (20–65 µg/kg/min). The patient had intermittent episodes of hypotension and was started on adrenaline (0.05–0.25 µg/kg/min). Her ICP elevated steadily to 56 mmHg (normal 5–15 mmHg) on day 5. Medical management continued with (propofol 85–95 µg/kg/min, morphine and midazolam), active cooling (32–34 °C) and hyperventilation (ETCO<sub>2</sub> of 20–25 mmHg). Her ICP remained high and noradrenaline requirements increased to 16 µg/250 ml dextrose 5 % in water to support the hypotension.

The patient developed recurrent episodes of ventricular tachycardia felt to be secondary to hyperkalemia and worsening lactic acidosis (arterial pH 7.19, normal 7.35–7.45),

(K7.8 mmol/L, normal 3.4–5 mmol/L), (lactate 7.3 mmol/L, normal <1.3 mmol/L).

In view of the escalating noradrenaline requirements and worsening acidosis, surgical consult was done for suspected bowel ischemia. The patient underwent an exploratory laparotomy that showed evidence of hypoperfused small bowel, large bowel, stomach and liver with no evidence of ischemia or gangrene; liver laceration was also noted with no signs of active bleeding. Intraoperatively, her metabolic acidosis (pH 7.03, lactate 11.5 mmol/L) and hyperkalemia (K9.3 mmol/L) worsened. The patient suffered a cardiac arrest with pulseless electrical activity. The patient had chest compressions, adrenaline boluses and insulin infusion to correct her hyperkalemia, which was ineffective, and the patient died in the operating room. An autopsy was done that supported death due to complications from her original trauma. The management of the case was reviewed in the monthly mortality audit by an intensivist, anesthetist, neurosurgeon and trauma surgeon; it was agreed that the patient's clinical course and postmortem exam supported the diagnosis of fatal PRIS.

## Discussion

Propofol is a short-acting intravenous sedative/hypnotic agent used for anesthesia induction and maintenance as well as sedation in intensive care units and for invasive procedures. High dose infusions (>67 µg/kg/min) and long-term (>48 h) use of propofol have been associated with serious adverse effects, and when combined, a rare but fatal condition called PRIS may develop [1]. This condition is characterized by the development of lactic acidosis, rhabdomyolysis, acute renal failure and hyperkalemia. Patients with traumatic brain injury are at elevated risk because high doses of propofol are frequently used to control elevated ICP, and concurrently, vasoactive medications are used to maintain blood pressure [2]. PRIS was first reported in 1992 in a pediatric population, describing the potentially fatal complications after prolonged administration of the drug [3]. Unexplained lactic acidosis has been the first manifestation of this syndrome [4, 5]. There have been reported cases of PRIS without lactic acidosis. In this patient, the first sign of lactic acidosis was evident approximately 12 h after commencement of propofol. Serum triglyceride levels also have been reported to rise in these patients with hypertriglyceridemia, lactic acidosis and Brugada-type electrocardiogram changes (coved ST segment elevation in right precordial leads V1–V3) associated. A rise in serum triglycerides may be seen in healthy individuals following propofol infusions who do not subsequently develop any adverse events [6]. This patient also had a rise in the serum triglyceride level, which was evident on hospital day 5.

Propofol impairs utilization of free fatty acids and mitochondrial activity. The metabolic demand of the body

increases with critical illness, but with the inability to generate fuel, catabolism occurs, leading to cardiac and skeletal muscle necrosis with accumulation of free fatty acids. Clinically, this accumulation is evidenced by elevated levels of serum creatine kinase, troponin I and myoglobin.

The interaction of propofol and catecholamine has previously been described [7]. Propofol has a negative inotropic effect due to the antagonism of beta-adrenoceptor and calcium channels, hence higher doses of catecholamine are required in patients on propofol to maintain hemodynamic stability. As catecholamine requirement increases, the amount of propofol necessary to maintain sedation increases to provide the same sedative effect. Thus, a vicious cycle is created, resulting in the hypercatabolic state. This leads to rhabdomyolysis, metabolic acidosis, acute renal failure and ultimately cardiac failure. This was clearly evident in this patient as her propofol requirements were increased in order to control the ICP and concurrently noradrenaline requirements were also increased.

## Conclusion

The occurrence of PRIS has yet to have a well-understood cause. We present this report for surgeons who are frequently consulted for bowel ischemia as a probable cause of these symptoms. They should consider PRIS as a differential diagnosis in patients receiving high doses of propofol and requiring increasing inotropic support and develops unexplained lactic acidosis. Intensive care units strictly adhere to not exceeding the recommended infusion rate of 20–65 µg/kg/min.

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