Propofol Infusion Syndrome (PRIS) and Critical Care Considerations

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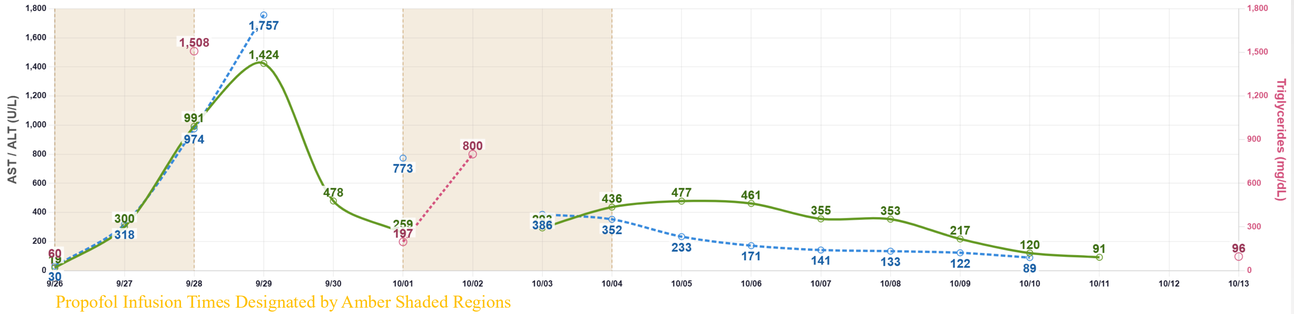
Introduction

- **Definition**: PRIS is a rare but life-threatening complication of propofol characterized by metabolic acidosis, cardiac dysfunction, rhabdomyolysis, renal failure, and hyperlipidemia[2,5].
- **Incidence**: In a large prospective multicenter ICU study (n=1,017), PRIS occurred in ~1.1% of patients receiving ≥24 hours of propofol infusion[4].
- **Mortality**: Reported mortality remains high: ~30 to 50% in cohort studies and case series, with one structured review reporting ~51% mortality across published cases[4].
- **Dose and duration threshold**: Risk increases significantly with doses >4 mg/kg/hr (~67 mcg/kg/min) and duration >48 hours, though cases have been reported below these thresholds[3].
- **Time course**: PRIS typically develops after 2–6 days of infusion, with one study showing a mean onset around 3 days after initiation[4].
- **Pathophysiology**: Experimental and clinical data support mitochondrial respiratory chain inhibition and impaired fatty acid oxidation, leading to cellular energy failure. Early lactic acidosis is dose-related, while later rhabdomyolysis is duration-related[1,3,5].
- **Key clinical signature**: Early findings include otherwise unexplained lactic acidosis, transaminitis, and cardiac dysfunction, with later progression to rhabdomyolysis, arrhythmias, and renal failure[2,3].
- **Risk factors**: Independent or commonly associated risk factors include critical illness severity, vasopressor use (~91% in one cohort), traumatic brain injury, fever, and catecholamine/steroid exposure[2,3,4].
- **Diagnostic challenge**: PRIS is frequently underrecognized due to overlap with critical illness (e.g., sepsis, shock) and may occur even at moderate doses, making vigilance essential[2].
- **Clinical importance**: Despite its low incidence, PRIS carries disproportionately high morbidity and mortality, and early recognition with prompt discontinuation of propofol remains the most effective intervention[1,3].

Case Presentation

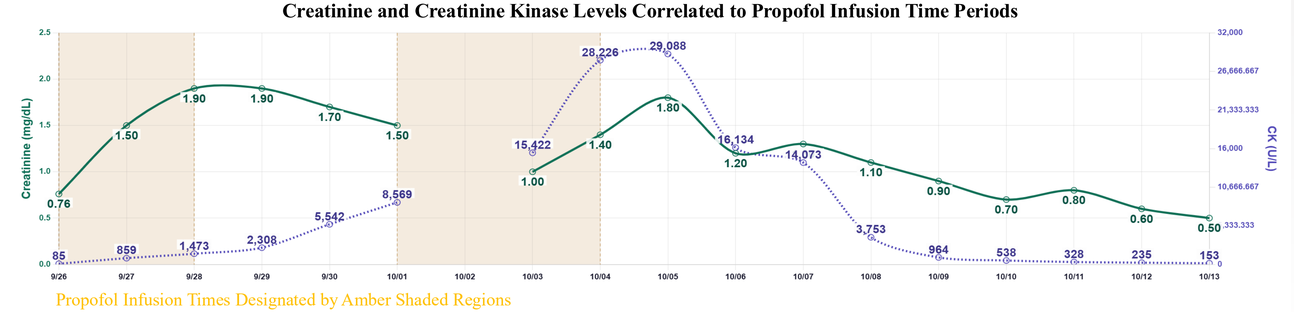
- 31-year-old male with morbid obesity (BMI 54.5), autism spectrum disorder, prediabetes, and metabolic syndrome initially presented to urgent care with bilateral conjunctivitis approximately 1 week prior to hospitalization.
- Presented to ED on 09/26/2025 with progressive dyspnea, acute hypoxic respiratory failure, and septic shock.
- Vitals: HR 117 bpm, BP 88/46 mmHg, Temp 101.3°F, RR 22 bpm, SpO_2 85–90% on room air.
- Chest radiograph demonstrated right lower lobe consolidation, with a differential for pneumonia.
- Met SIRS criteria with an additional qSOFA score of 3, ultimately determined to be in septic shock secondary to pneumonia.
- Received IV fluids, antibiotics, required vasopressor support, and required intubation with mechanical ventilation with ICU admission.
- Propofol infusion initiated for sedation at 20 mcg/kg/min and rapidly escalated to ~150 mcg/kg/min for ~48 hours (09/26–09/28).
- Within 24 hours of high-dose propofol therapy, patient developed: Transaminitis, acute kidney injury (AKI), hypertriglyceridemia, and an elevated creatinine kinase (CK)
- Initially, laboratory abnormalities were attributed to septic shock secondary to pneumonia.
- Approaching 48 hours of propofol therapy, labs continued worsening, with marked CK elevation concerning for rhabdomyolysis.
- Clinical course was further complicated by development of acute respiratory distress syndrome (ARDS).
- Propofol infusion syndrome (PRIS) became a significant differential consideration.
- Propofol discontinued and alternative sedation started.
- Within 48 hours of discontinuation, laboratory improvement was observed, including improving transaminitis and AKI.
- Due to worsening respiratory failure, patient was transferred to a tertiary care center on 10/01/2025 for ECMO evaluation.
- Propofol was restarted at the receiving institution (10/01–10/04) despite concern for evolving PRIS.
- Following re-exposure to propofol: CK increased from 8,569 (10/01) to peak 29,088 (10/05) and AKI also worsened.
- After final discontinuation of propofol on 10/04 labs began to normalize.
- Clinical course demonstrated strong temporal association between high-dose propofol exposure and metabolic/muscular injury, worsening with rechallenge and improving after discontinuation, strongly supporting a diagnosis of PRIS.

AST, ALT, and Triglyceride Levels Correlated to Propofol Infusion Time Periods



Propofol Infusion Times Designated by Amber Shaded Regions

Creatinine and Creatinine Kinase Levels Correlated to Propofol Infusion Time Periods



Propofol Infusion Times Designated by Amber Shaded Regions

Discussion

- Although rare, consider PRIS as a differential in patients who are on a propofol infusion who are experiencing lab abnormalities that fit the picture.
- Be mindful of PRIS risk factors when initiating propofol.
- Development of hypertriglyceridemia, transaminitis, acute kidney injury, and severe rhabdomyolysis closely aligned with the proposed pathophysiology of PRIS.
- PRIS should remain on the differential diagnosis even when alternative explanations for laboratory abnormalities exist.
- In this case, septic shock and evolving ARDS initially provided reasonable explanations for worsening hepatic injury, renal dysfunction, and hemodynamic instability.
- However, progressively worsening CK elevation and persistent metabolic injury despite treatment increased concern for PRIS.
- Clinicians should maintain suspicion for PRIS in patients receiving propofol who develop: Unexplained metabolic acidosis, rapidly rising creatine kinase, rhabdomyolysis, hypertriglyceridemia, hepatic injury, acute kidney injury, cardiovascular instability disproportionate to underlying illness.
- Strong temporal association supported the diagnosis: Laboratory abnormalities worsened during propofol exposure, improved after discontinuation, worsened again following rechallenge, subsequently normalized after final cessation.
- This case reinforces the importance of: Early recognition, routine laboratory surveillance during prolonged propofol infusions, prompt discontinuation of propofol when PRIS is suspected to prevent severe multiorgan dysfunction and death.

References

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