

Is acute severe asthma a risk factor for the propofol infusion syndrome?

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ABSTRACT

Propofol infusion syndrome (PRIS) is a rare but potentially fatal syndrome observed more commonly in young obese men receiving high dose (usually >4mg/kg/hr) or long term (>48 hrs) propofol. It can cause metabolic acidosis, renal failure, rhabdomyolysis, hyperkalemia, and cardiac failure. We report a case of possible PRIS in a 24-year-old obese Hispanic man admitted for acute severe asthma who developed PRIS in less than 12 hours on lower doses of propofol (3 mg/kg/hr tapered within 3 hrs) while on concurrent corticosteroids. Patients with acute asthma and subclinical myopathy may be at increased risk for propofol toxicity and need careful monitoring if this drug is used for sedation.

Key words: propofol, metabolic acidosis, rhabdomyolysis, acute kidney injury, asthma

INTRODUCTION

Propofol infusion syndrome (PRIS) is a rare but potentially fatal syndrome observed more commonly in young obese men receiving high dose (usually >4mg/kg/hr) or long term (>48 hrs) propofol.¹ It is more frequent in critically ill patients receiving catecholamines or corticosteroids, and it presents as severe unexplained metabolic acidosis, renal failure, rhabdomyolysis, hyperkalemia, and cardiac failure.^{2,3} The incidence of PRIS is unclear, and most information is based on case reports in the last two decades. We report a case of possible PRIS in a 24-year-old obese Hispanic man admitted for acute severe asthma who developed PRIS in less than 12 hours on lower doses of propofol (3 mg/kg/hr tapered within 3 hrs) while on concurrent corticosteroids.

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CASE

A 24-year-old obese Hispanic man with history of asthma since childhood presented with shortness of breath and chest tightness for one day. On presentation his heart rate was 120/min, BP 136/81 mmHg, respiratory rate 22/min, and oxygen saturation 93% on nasal cannula oxygen (FiO₂-36%). His BMI was 34 kg/mm². He was in severe respiratory distress, and his chest examination revealed diffuse wheezing bilaterally with prolonged expiration. Initial ABG showed pH 7.36, PaO₂ 66 mmHg on Fi O₂ 36%, and PaCO₂ 34 mmHg. He was intubated because of impending respiratory failure and put on ventilator support. He was started on propofol, fentanyl, methylprednisolone (100mg/day), bronchodilators, azithromycin, and enoxaparin. His labs showed an increased WBC count and serum potassium levels but normal renal function tests (Table). His hyperkalemia was treated with calcium gluconate, IV insulin/glucose, and inhaled albuterol. His urine was positive for cannabinoids. A CT scan of the thorax showed a

possible pulmonary embolism which was later ruled out by a VQ scan. On day two of admission, the patient started developing reddish colored urine and had deterioration in his renal function (creatinine increased from 0.7 mg/dl to 2.3 mg/dl). Arterial blood gases showed a metabolic acidosis with a pH of 7.18, his triglyceride level was 138 mg/dl, and his creatine kinase (CK) level was 2892 IU/L. The diagnosis of propofol infusion syndrome (PRIS) was entertained,

and propofol (total 2.937gm of propofol infused over 11hrs) was stopped. He was switched to dexmedetomidine, and IV fluids (normal saline, 1/2 normal saline + bicarbonate) were started to maintain urine output of >150 ml/hr and urine pH >6.5. His CK started to fall, and his renal function returned to the baseline in two days. He was extubated on day four of admission and discharged home on day eight.

Table Laboratory results

Labs	9/8/----- 1637	9/9/----- 0227	9/10/----- 0323	9/11/----- 0320	9/13/----- 0352	9/16/----- 0533
pH	7.36	7.18	7.28	7.42	7.41	ND*
PaCO ₂	34	46	50	45	45	ND
PaO ₂ /FiO ₂	182	264	305	262	249	ND
Lactate (mmol/L)	6.7	3.5	1.9	1.1	1.7	ND
Potassium (mmol/L)	7.4	7.6	5.1	4.4	4.2	4.3
BUN (mg/dl)	9	27	25	24	19	13
Creatinine (mg/dl)	0.7	2.3	1	0.7	0.6	0.7
Triglyceride (mg/dl)	ND	138	223	ND	ND	ND
Creatinine Kinase (IU/L)	ND	2892	4053	2275	906**	446

*ND-not done; ** 9/14/-----

DISCUSSION

Propofol infusion syndrome (PRIS) was first described by Bray in 1998 as the sudden onset of bradycardia progressing to asystole with one of the following: severe metabolic acidosis, hyperlipidemia, fatty infiltration of liver, or rhabdomyolysis.¹ A large multicentered study with 1017 patients reported the incidence of PRIS at 1.1% with an 18% mortality rate.⁴ Risk factors for PRIS include propofol doses >83 µg/kg/min, a duration of therapy >48 hrs, concomitant use of catecholamine vasopressors or glucocorticoids, and age <18 yrs.⁵

The exact pathophysiology has not been determined, but impaired tissue metabolism due to inhibition of mitochondrial respiratory chain or fatty acid metabolism, i.e., reduced mitochondrial entry of long chain fatty acylcarnitine esters due to inhibition of transport protein (carnitine palmitoyl transferase), appears to be the mechanism.⁶ Propofol can impair the mitochondrial electron transport in isolated heart preparations in laboratory animals.⁷ Diversion of metabolism from carbohydrates to fat substrates might cause PRIS; it is uncommon in adults compared to children since adults have higher carbohydrate reserves. A carbohydrate intake of 6-8mg/kg per minute should provide adequate calories to suppress fat metabolism in critically ill patients.⁸

Evidence for a dose-dependent association led to guidelines that recommend a maximum propofol infusion rate of 4.8 mg•kg⁻¹•h⁻¹ for long-term sedation in intensive care unit patients.⁹ Our patient had a relatively short term of infusion of 12 hours at a lower dose (3mg/kg/hr) than usually described in literature. He was critically ill with concomitant corticosteroid administration which may have predisposed him to develop PRIS. In addition, patients with acute severe asthma can develop an acute myopathy with elevated CK levels and abnormal muscle biopsies.^{9,10,11} This muscle injury is associated with high dose intravenous corticosteroids, neuromuscular blocking agents, and mechanical ventilation. However, patients with asthma can present with elevated CK and myoglobin levels prior to any in-patient treatment.¹⁰ Propofol

can inhibit the production of ATP, and muscles with increased workloads may develop necrosis without adequate energy. Consequently, this patient may have been at risk for PRIS secondary to subclinical muscle injury secondary to acute severe asthma. Clinicians should carefully monitor patients on propofol and keep the dose as low as possible. Monitoring electrocardiograms and arterial blood gases for unexplained metabolic acidosis and arrhythmias is helpful. Patients with acute severe asthma who require mechanical ventilation may be at increased risk to develop PRIS, and an alternative sedative, if needed, should be considered. To date there is no specific treatment for PRIS; therapeutic plasma exchange has been used in one case report.⁹ Alternative sedative agents are recommended by the American College of Critical Care Medicine for patients with escalating vasopressor or inotrope requirements or cardiac failure during high-dose propofol infusions.¹⁰

In summary, PRIS is an uncommon syndrome with severe metabolic consequences. It occurs more frequently in patients on propofol at higher doses for longer periods of time. Patients with muscle injury, including acute severe asthma, may be at increased risk and need careful monitoring.

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