

CASE REPORTS

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Prolonged Loss of Consciousness and Elevated Porphyrins following Propofol Administrations

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PORPHYRIA is an ecogenic disorder, often with pharmacologic agents playing an important role in its exacerbation. Propofol is a widely used anesthetic agent and is considered safe when administered to patients with porphyria.^{1,12} Consciousness usually returns promptly after discontinuation of propofol administration.² We report a patient who had a prolonged alteration in consciousness, with multiple transient neurologic deficits and neuropathic pain after intravenous propofol administration. Urinary porphyrins were markedly elevated, including δ -aminolevulinic acid (ALA), porphobilinogen, and coproporphyrin III. The likely possibility of propofol exacerbating previously undiagnosed coproporphyrin is discussed.

Case Report

A 23-yr-old man with a history of a tetralogy of Fallot repaired at 2 yr of age was referred for catheter ablation of right ventricular tachycardia. He was in good health except for one episode of exercise-related ventricular tachycardia. The ablation procedure lasted approximately 16 h. In the first 7 h, monitored-anesthesia-care sedation was achieved with an average dose of $106 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ intravenous propofol while the patient was breathing spontaneously. Arterial blood gas tests, performed during ventricular tachycardia 8 h into the procedure,

revealed a pH of 7.15, a P_{CO_2} of 81 mmHg, and a P_{O_2} of 160 mmHg. At this point, a decision was made to intubate the patient and administer mechanical ventilation. He was intubated with a 7.5-mm internal diameter endotracheal tube without muscle relaxation. Subsequent arterial blood gas tests showed a pH of 7.39, a P_{CO_2} of 36 mmHg, and an O_2 of 310 mmHg. For the next 9 h, an average dose of $95 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ propofol was used. He received a total dosage of 6.75 g propofol. The patient was aware of the risk of recall with this technique. Caffeine and isoproterenol were used to induce tachycardia during the procedure. Ventricular tachycardia was induced several times during the procedure, but the patient was never significantly hypoxic, with oxygen saturations at 99 to 100% throughout the procedure. After discontinuation of propofol, the patient could not be aroused or extubated for 10 h. Although he was extubated the next day, he remained minimally arousable and markedly stuporous. A neurologic examination revealed profound weakness in the patient's right arm and left leg without cranial nerve, cerebellar, or consistent reflex deficits during this 3-day period. As the patient became more awake, he complained of severe lancinating pain in the right shoulder and right side of the abdomen. Laboratory tests revealed normal electrolytes and elevated liver enzymes thought to be from passive hepatic congestion because the patient had incessant right ventricular tachycardia causing elevated right-sided pressures. Serum ammonia concentration was normal. Serial computed tomography and magnetic resonance imaging scans of the brain were normal. Serial electroencephalography did not reveal seizure activity. Because of the motor deficits that did not fit a vascular pattern, neuropathic pain, and negative central nervous system and spinal imaging studies, the possibility of porphyria was considered. The patient was treated with 300 g/day dextrose, with a plan to administer panhematin if symptoms persisted. Blood glucose concentrations before dextrose administration were 110 mg/dl. After this treatment, neurologic deficits showed a marked improvement, with normalization of motor strength in the right arm and the left leg. Neuropathic pain abated, and the patient returned to baseline state 2 days later. Serum propofol concentration, drawn during his state of altered consciousness, was $0.07 \mu\text{g}/\text{ml}$ (level of $1.0 \mu\text{g}/\text{ml}$ is associated with normal coherence). Urinary porphyrins measured during a 24-h period were markedly elevated, with an aminolevulinic acid concentration of 175 mm (8-50 mm), porphobilinogen concentration of 310 mm (0-18 mm) and coproporphyrin III of 346 mm (50-100 mm).

Discussion

Porphyrias are a group of metabolic disorders with specific enzyme deficiencies in the heme biosynthetic pathway.³ Porphyrias of interest to anesthesiologists are he-

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patic porphyrias, including acute intermittent porphyria, variegate porphyria, and hereditary coproporphyria. Hepatic porphyrias are characterized by neurologic symptoms, including neuropathic pain, especially in the abdomen and the proximal limbs, and mental disturbances. This disease is categorized with ecogenic disorders in which environmental, physiologic, and genetic factors interact to cause manifestations of the disease. Drugs, especially anesthetic agents, often are cited as precipitating agents for this disease. Prolonged starvation and surgery have been known to cause clinical deterioration in porphyric patients and may have exacerbated our patients' clinical findings, as discussed herein.^{4,5}

Propofol has been suggested to be the induction agent of choice in porphyric patients.^{6,7} However, tissue models and clinical data yielded mixed results.^{1,6,7} There has been a case report of elevated urinary porphyrins without clinical symptoms in acute intermittent and variegate porphyria after propofol administration.⁶ There is a reported case of safe propofol use in a patient with known hereditary coproporphyria.⁸ To our knowledge, this is the first report of clinically significant deficits putatively resulting from propofol-exacerbated porphyria. Our patient did not have a previous diagnosis of porphyria, and no known family members have this disorder. The amount of propofol used is not unusual in ventricular tachycardia ablation procedures. Because of its neutral electrophysiologic effects, propofol increasingly is being used for anesthesia in these procedures. The amount of propofol used, the duration of the procedure, hepatic congestion, and prolonged *non per os* state may have contributed to the porphyrin increase. Our patient's clinical features and urine porphyrin data are most consistent with a diagnosis of coproporphyria.⁹ The confirmatory test for this disorder, namely coproporphyrin oxidase activity, is not widely available and was not performed. This pattern of porphyrin increase also has been seen in the so-called multiple chemical sensitivity syndrome.¹⁰ However, the extent and the nature of the patient's clinical features preclude this diagnosis. The possibility of persistence of propofol in the blood causing his symptoms was excluded by the near-undetectable level of propofol during severe symptoms.¹¹ This level also helped to rule out the possibility of propofol interfering with the porphyrin measurement. The high lipid load with a propofol infusion is unlikely to elevate urine porphyrins, as decreased caloric intake is what may exacerbate abnormal porphyrin metabolism. Although various colored substances akin to azodyes appear in the urine after propofol infusions, none are

related to the porphyrins. In our patient, because of the very low propofol level measured, the likelihood of any byproduct interfering with the porphyrin measurement is very low.

This patient received *non per os* from midnight before the procedure, except for maintenance fluids of D5NS. Starvation is known to exacerbate porphyria but is unlikely to have been the sole trigger in this case because the patient underwent a previous attempt at ablation and previous cardiac surgery, both necessitating prolonged *non per os* status without neurologic consequence. This was, however, his first exposure to propofol. Cardiac ablation procedures may be complicated by vascular embolization to the central nervous system, producing neurologic symptoms, but the patient's neurologic findings did not conform to a vascular territory and subsequent neurologic imaging studies were negative.

Caffeine and isoproterenol are not known to increase urinary porphyrin levels. The patient routinely drank caffeinated beverages. Caffeine and isoproterenol were used in his previous ablation procedures without clinical repercussions.

Although several factors in this patient potentially may have contributed to the elevated urinary porphyrins and the clinical presentation, it appears that the prolonged propofol infusion must be seriously considered as the most likely cause.

Conclusion

To our knowledge, this is the first report of clinically significant elevation of urinary porphyrins associated with the use of propofol, an agent considered to be safe to use with porphyria. Further study is necessary to assess the safety of propofol, especially when used in high doses, with porphyric patients.

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