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Propofol Frenzy: Clinical Spectrum in 3 Patients

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Abstract

Postsedation neuroexcitation is sometimes attributed to intravenous injection of the sedative-hypnotic drug propofol. The movements associated with these events have strongly suggested convulsive activity, but they rarely have been comprehensively evaluated. We present video recordings of 3 healthy young patients who underwent elective surgery under conscious sedation and emerged from sedation with transient but repetitive violent motor activity and impaired consciousness. These manifestations required considerable mobilization of multiple health care workers to protect the patient from inflicting harm. All patients received propofol, and all fully recovered without adverse sequelae. We postulate that these movements are propofol related. Importantly, we found no evidence of seizures clinically or electrographically.

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Neurologists seldom see patients on an emergent basis following an outpatient procedure with conscious sedation. The purpose of this article is to call attention to the poorly understood occurrence of postsedation spells most likely associated with propofol administration. Although several authors have reported seizure-like movements following use of propofol,[1-6] the actual clinical presentation has rarely been presented visually.[7] We present a much broader spectrum of this potential propofol complication in video recordings of 3 healthy young patients who emerged from propofol sedation with transient but repetitive violent motor activity and impaired consciousness.

REPORT OF CASES

All 3 patients were sedated using our institutional conscious sedation protocol, which includes continuous monitoring of heart rate (HR), respiratory rate (RR), and pulse oximetry. Blood pressure (BP) was measured every 3 to 5 minutes. For the cases described in this report, the protocol was performed by a certified registered nurse anesthetist under the supervision of a board-certified anesthesiologist. The patients profiled herein have provided written consent for use of their medical records and the video recordings illustrating their condition.

Case 1

An 18-year-old woman with no notable medical history who was not taking any long-term medications had an outpatient surgical extraction of all third molars (wisdom teeth). At baseline, her HR was 82 beats/min, RR was 18 breaths/min, BP was 116/69 mm Hg, and arterial oxyhemoglobin saturation (Spo_2) measured by pulse oximetry was 100% while the patient breathed room air. The patient received 100 μg of intravenous (IV) fentanyl immediately followed by 3 mg of midazolam. A total of 200 mg of propofol was administered in divided doses over a period of approximately 30 minutes. The Richmond Agitation-Sedation Scale (RASS)[8] score [RASS] was −2 during the procedure, which denotes that the patient would awaken briefly to voice stimulus with eye opening and contact for less than 10 seconds (light sedation). There was no instability of measured physiologic variables. The postprocedure oral temperature was 36.3°C.

Soon after emergence from sedation, the patient became unresponsive with loud vocalizations and violent thrashing of both extremities (Supplemental Video, Left panel, available online at http://www.mayoclinicproceedings.org). She would localize to pain. The spells lasted 30 to 60 seconds and recurred after approximately 5 to 10 minutes, with recovery of awareness between spells. During the spells, HR was 111 to 185 beats/min and RR would increase to 40 to 50 breaths/min, but BP, temperature, and Spo_2 remained stable. She remained afebrile. After

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multiple spells, she received midazolam, 3 mg IV, with no improvement. For the next 2 hours, the spells continued despite trials with multiple medications. Intravenous meperidine, 25 mg, was administered to assess whether pain control could minimize her symptoms. When no response was seen, the opioid effect was reversed with naloxone, 0.16 mg. Flumazenil, 0.1 mg IV, was administered to reverse a potential toxicity from midazolam. She received an additional 70 mg of IV propofol to control her agitation, but movements would stop for only a few minutes. A trial of physostigmine, 1 mg IV, was administered to reverse a potential central anticholinergic syndrome without improvement. A repeated trial of propofol, 50 mg IV, did not resolve the spells, and the patient had progressively shorter periods of responsiveness between them.

Venous blood analysis revealed a pH of 7.25, lactate level of 5.86 mmol/L, bicarbonate level of 19 mmol/L, and a P_{CO_2} value of 51 mm Hg. There were no other electrolyte abnormalities. The increased lactate level was attributed to persistent muscle activity. The patient was already receiving 0.9% saline solution via IV infusion. A decision was made to intubate the trachea, not only to protect her airway but also to provide more sedation in order to avoid worsening lactic acidosis and rhabdomyolysis. The trachea was intubated following induction of general anesthesia with propofol, 180 mg IV, and succinylcholine, 100 mg IV, followed by continuous propofol infusion at 50 μg/kg per minute. Cranial computed tomography detected no abnormalities. Spot electroencephalography (EEG) was uninterpretable because of agitation-induced artifacts, but no obvious seizures were seen. Given the concern for possible propofol toxicity, sedation was switched to IV dexmedetomidine, 1.5 μg/kg per hour. Spells became infrequent and shorter within the first hour. When the spells recurred, immediate administration of a small bolus of fentanyl, 50 μg IV, caused attenuation of the spell (with persistence of very brief occasional lower-amplitude movements) within 1 minute of drug administration. This attenuation lasted about 20 to 30 minutes. Fentanyl infusion at 25 mcg per hour IV was also initiated, and the spells completely resolved. Within 10 hours, she was gradually weaned off dexmedetomidine by approximately 0.1 μg/kg per hour, and fentanyl was discontinued when the dexmedetomidine dose reached 0.7 μg/kg per hour. The endotracheal tube was then removed. Her condition returned to baseline, and the patient had no recollection of the episode.

Case 2

A 27-year-old woman with a history of depression treated with oral sertraline, 50 mg/d and duloxetine, 30 mg twice a day, presented for elective right wrist arthrodesis. Before the procedure, her HR was 80 beats/min, BP was 113/68 mm Hg, RR was 16 breaths/min, and Spo_2 was 98% while the patient breathed room air. Fentanyl, 50 μg, and midazolam, 2 mg, were administered IV at 8:42 AM. Subsequent doses of fentanyl were administered (200 μg in divided doses over 1 hour) in addition to subsequent doses of midazolam (4 mg in divided doses over 1 hour). Intravenous propofol, 40 mg, was loaded (9:10 AM), followed by an infusion at 200 μg/kg per minute (9:18 AM). The dose was gradually weaned during the procedure and stopped at 10:43 AM. The RASS score was −1 or −2 (ie, the patient awakened to voice stimulus with eye contact for more than or less than 10 seconds, respectively). Ondansetron, 4 mg IV, was administered for postoperative nausea prophylaxis. There was no instability of measured physiologic variables. The postprocedure oral temperature was 36.9°C.

At 11:14 AM, the patient began to have spells of whole-body jerking, flexion and extension of her legs, and side-to-side head movements (Supplemental Video, Center panel). These movements were associated with irregular eye movements, tachycardia (HR, 100-141 beats/min), and tachypnea (RR, 25-35 breaths/min). Blood pressure, Spo_2, and temperature remained normal and stable. The patient was awake but unable to interact with others. She would localize to pain. There was no rigidity or hyperreflexia. The spells lasted about 1 minute and would recur after 10 to 15 minutes or on stimulation (eg, loud noises, tactile stimulation) with return to quiescence between spells. Because of concern for possible dystonic reaction from ondansetron, diphenhydramine, 50 mg IV, was administered initially. Given the lack of response, benztropine, 2 mg IV, was also administered after 10 minutes to treat a possible extrapyramidal reaction but was ineffective. The patient did not respond to propofol, 30 mg, and fentanyl, 25 μg IV. However, the spells subsided considerably after administration of midazolam, 2 mg IV. After a second dose of midazolam, 1 mg IV, the patient