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Illicit Cocaine Ingestion during Anesthesia

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THERE is an epidemic of cocaine use in the United States[1,2] resulting in an increasing number of patients presenting for surgery with a history of acute or chronic cocaine use. This is particularly true of patients presenting for emergency surgery. A recent study demonstrated that 57% of the violent assault victims and 22% of automobile trauma victims presenting to a Philadelphia, Pennsylvania, trauma center had urine or blood tests positive for cocaine and/or its metabolites.[3] Many of these patients require anesthesia, yet there is virtually no information regarding the impact of acute or chronic cocaine abuse on the conduct of anesthesia. We present a case demonstrating the potential impact of acute cocaine abuse during anesthesia.

Case Report

A 28-yr-old, 64-kg woman sustained an open talus fracture during a motor vehicle accident. She had no other injuries. Her medical history was unremarkable except for a history of "frequent" cocaine use. When questioned further, she admitted having used cocaine shortly before her accident. She had no surgical history. Her physical examination was remarkable only for the open ankle fracture. During her 4-h stay in the emergency room, her blood pressure (BP) ranged between 120/90 and 150/110 mmHg. Her heart rate (HR) ranged between 76 and 88 beats/min. Her hematocrit (three measurements) was stable at 40%, her blood electrolytes (Na^+, K^+ Cl^-, HCO_3^-), blood urea nitrogen, creatinine, glucose, chest x-ray, and electrocardiogram results were normal. Her arterial blood gases during room air breathing were pH 7.40, Pa_{CO_2} 41 mmHg, Pa_{O_2} 98 mmHg. She received tetanus toxoid, thiamine (100 mg), and morphine sulfate (4 mg) in the emergency room.

The patient arrived in the operating room approximately 5 h after her accident for open repair of her fracture. Her BP was 120/80 mmHg and HR was 105 beats/min. She was given 2 mg midazolam and 2.5 mg droperidol, which left her visibly sedated but able to follow commands. After approximately 500 ml of Ringer's lactate intravenously, she received a subarachnoid block (L4–L5 interspace) with 10 mg isobaric tetracaine and 0.2 mg epinephrine. Approximately 30 min later, she had a T9 block bilaterally. Over the next 120 min, she received approximately 1,200 ml of Ringer's lactate, lost approximately 50 ml of blood, and remained hemodynamically stable (BP 95/60–110/70 mmHg, HR 70–90 beats/min). During this time, she slept if undisturbed but would follow commands if roused. She received no additional sedative hypnotics.

Two hours into the procedure, she became increasingly agitated and incoherent and began rapidly moving her arms and upper body. She was unable to move her lower body because of the subarachnoid block, but two people were required to restrain her upper body. She would not follow commands or answer questions, although she vocalized unintelligibly. Over 4–6 min, she received 12 mg midazolam and 2.5 mg droperidol, but her agitation continued to escalate. She was neither hypoxic (Sa_{O_2} 100%) nor hypotensive (BP 110/70 mmHg, HR 80–90 beats/min). To gain control of the patient, general anesthesia was induced with 300 mg thiopental, muscle relaxation achieved with 100 mg succinylcholine, and laryngoscopy performed while cricoid pressure was applied. As the laryngoscope was inserted, a white foreign body was seen in the posterior pharynx. The foreign body was believed to be a tooth and was retrieved with a Magill forceps. Intubation proceeded uneventfully. Her BP increased to 165/105 mmHg during intubation, and an additional 200 mg thiopental was given.

General anesthesia was maintained with 50–60% N_2O and isoflurane (0.5–1.5%) in oxygen for the remainder of the case. While she had been hemodynamically stable before induction of general anesthesia, her BP was quite labile (BP 145/90–70/30 mmHg, HR 85–110 beats/min) for the next 40 min with no obvious surgical or anesthetic etiology for the instability. Interestingly, when her BP decreased to 70/30 mmHg approximately 30 min after induction, she was unresponsive to ephedrine (2 × 5 mg) but responded to 100 μg phenylephrine (BP returned to 100/70 mmHg). Hemodynamic stability returned approximately 1 h after induction, and the remainder of her anesthetic course and recovery were unremarkable.

Examination of the foreign body removed from her pharynx during intubation revealed that it was not a tooth. It was sent to the toxicology laboratory, where analysis determined it to be "crack" cocaine. Postoperatively, the patient was asked about this finding and admitted that she had placed six "crack rocks" in her nose and under her

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tongue when she was called to the operating room. She had done so because she feared that they would be lost or stolen while she was in surgery.

Discussion

Despite the widespread use of cocaine in the United States, there is little information regarding the effect of cocaine use on anesthetic pharmacology and physiology. This case report affords a unique opportunity to observe anesthetic physiology and pharmacology during acute cocaine intoxication.

We speculate that the "crack rocks" in this woman's mouth and nose dissolved during her anesthetic and that relatively high plasma cocaine concentrations resulted from subsequent cocaine absorption. Cocaine is readily absorbed from mucosal surfaces, producing peak plasma concentrations within 30–60 min after intranasal application of cocaine HCl solution.[4] These data suggest that our patient's cocaine concentration should have peaked about 30–60 min before she became agitated and combative. However, peak plasma concentrations may have been delayed in our patient because of the time required for the crack rocks to dissolve before absorption. Because the size and cocaine content of the crack rocks were unknown, it is impossible to estimate the cocaine dose ingested or the plasma concentration achieved.

We believe that this patient's uncontrolled combativeness was the result of cocaine's central nervous system (CNS)-stimulating effects. The CNS-stimulating effects of cocaine are thought to result from blockade of excitatory biogenic amine reuptake in the CNS. However, the drug's local anesthetic effects may contribute to the subjective "high" produced by cocaine.[5] Other etiologies for her agitation were considered, including hypotension, hypoxia, hypercarbia, hypoglycemia, hypothermia, drug withdrawal, and seizures. However, her BP was 110/70 mmHg, her Sa_{O_2} was 100%, there was no evidence of impaired ventilation, her blood glucose was 182 mg/dl, her skin temperature was 36.3°C, and she denied habitual use of any other drugs, including alcohol. Though cocaine can cause grand mal seizures by a variety of mechanisms,[6,7] our patient's psychomotor agitation did not resemble seizure activity.

Interestingly, 12 mg midazolam and 2.5 mg droperidol had no discernible sedative effect after she became agitated. This contrasts with the beginning of the case when only 2 mg midazolam and 2.5 mg droperidol resulted in obvious sedation. Thus, this patient effectively served as her own control for the effects of these drugs before and after acute cocaine intoxication. Therefore, it would appear that acute cocaine intoxication decreased the effective potency of midazolam. There are no data to suggest that cocaine specifically antagonizes the actions of benzodiazepines. Rather, we suspect that the intense CNS excitation produced by cocaine effectively produced a rightward shift in the benzodiazepine dose-response curve. Because benzodiazepines act by increasing inhibitory GABAergic activity in the CNS, it is not surprising that a much larger benzodiazepine dose might be required to counteract cocaine-mediated CNS stimulation.

Another interesting feature of this case was the hemodynamic instability that ensued after the onset of agitation and subsequent induction of general anesthesia. Her marked increase in BP during intubation (from 110/70 to 165/105 mmHg) was somewhat surprising given induction with 300 mg thiopental (4.7 mg/kg) preceded by 12 mg midazolam (0.19 mg/kg). As discussed above, this hemodynamic response may reflect a rightward shift in the dose-response curve for GABAergic drugs. In short, she may have been "light" despite a seemingly adequate induction dose of thiopental and midazolam. Alternatively, cocaine's ability to block reuptake of catecholamines in the peripheral sympathetic nervous system[8] may have contributed to the large BP increase by accentuating any increase in central sympathetic outflow caused by the stimulation of laryngoscopy and intubation.

More surprising was her unexplained decrease in BP (from 110/70 to 70/30 mmHg) approximately 30 min after induction of anesthesia. This decrease occurred gradually over approximately 5–10 min and was associated with a fall in HR from 110 to 85 beats/min. At that time, the isoflurane concentration was 0.5% (expired) in 58% N_2O/42% O_2. There was no blood loss, and the leg tourniquet had not been released. No surgical or anesthetic explanations could be found to explain the decrease in BP. Although cocaine typically is considered a cardiovascular stimulant, animal studies suggest that cocaine may act within the CNS to decrease central sympathetic outflow.[9] The simultaneous decrease in BP and HR are consistent with a generalized decrease in central sympathetic outflow. Another possible explanation is that cocaine depleted norepinephrine at peripheral sympathetic nerve terminals by blocking norepinephrine reuptake. Such an effect of cocaine effectively would decrease sympathetic activity. Animal studies demonstrate that subchronic cocaine

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use depletes catecholamines from the heart and peripheral autonomic nervous system.[10] Because this woman had a long history of frequent cocaine use, she may have had diminished concentrations of norepinephrine in her sympathetic nerve terminals at baseline. Her intraoperative intoxication may have acutely depleted her limited reserves of norepinephrine, resulting in the hypotension and relative bradycardia we observed. This proposed mechanism is identical to the hypotension and relative bradycardia that occur after acute depletion of norepinephrine from nerve terminals after reserpine administration to humans.[11]

To correct her hypotension, this patient received two 5-mg doses of ephedrine within 1 or 2 min of each other. Neither ephedrine bolus had a demonstrable effect on BP or HR. The reason for failure to respond to ephedrine is unclear but several possibilities exist. Ephedrine acts, in part, by causing norepinephrine to be released from sympathetic nerve terminals. Thus, if norepinephrine had been depleted from this patient's sympathetic nerve terminals, the effect of ephedrine would be diminished. This is analogous to the tachyphylaxis that occurs with repeated doses of ephedrine as available stores of norepinephrine are depleted. In addition, ephedrine must be taken up into the nerve terminal to cause epinephrine release. Therefore, cocaine-mediated blockade of ephedrine uptake would prevent norepinephrine release and diminish the cardiovascular stimulating effects of ephedrine. Finally, ephedrine's effects are mediated in part by blockade of norepinephrine reuptake.[12,13] Because the norepinephrine transporter presumably was blocked already by cocaine, ephedrine would be expected to have little additional effect *via* this mechanism. Regardless of the mechanism, this patient's lack of response to ephedrine is consistent with multiple animal studies that found that acute cocaine administration markedly reduces the hemodynamic response to ephedrine.[14,15,‡]

In summary, there is little information regarding the impact of acute or chronic cocaine use on the physiology and pharmacology of anesthetic drugs. Because cocaine has a variety of sites and mechanisms of action, it is impossible to predict how cocaine will interact with other drugs that target the CNS and cardiovascular systems. Given the widespread abuse of cocaine, such information is essential to guide the anesthetic man-

agement of these patients. This case demonstrates that acute cocaine use may have a significant impact on a patient's responses to a variety of commonly used drugs, including sedative hypnotics and indirectly acting sympathomimetics. Additional studies are indicated to better delineate cocaine's impact on anesthetic practice.

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