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Special K with No License to Kill: Accidental Ketamine Overdose on Induction of General Anesthesia

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 65
Final Diagnosis: Ketamine overdose
Symptoms: Delayed awakening
Medication: —
Clinical Procedure: —
Specialty: Anesthesiology

Objective: Diagnostic/therapeutic accidents

Background: Ketamine is used as an induction and sedation agent in emergency departments and operating rooms throughout the country. Despite its widespread clinical use, there are few cases of significant morbidity and mortality attributed to ketamine overdose in the clinical setting.

Case Report: The anesthesia provider in the room was an oral maxillofacial surgeon who inadvertently took out a more highly concentrated bottle of ketamine that is typically used for pediatric patients. The patient received 950 mg (100 mg/ml concentration) of intravenous ketamine instead of the intended 95 mg (10 mg/ml concentration). After the ketamine was given, there were no signs to any involved provider that a mistake had occurred until the wake-up appeared to be unusually prolonged.

Conclusions: Despite this, the patient did not demonstrate any systemic effects such as hemodynamic or CNS perturbations other than prolonged awakening. This case highlights one (drug overdose) of many causes of delayed emergence from anesthesia and reminds the provider caring for the patient to be mindful of drug concentrations used when preparing to sedate a patient, as relying on effects of the parent drug is not always adequate.

MeSH Keywords: Anesthesia • Ketamine • Medication Errors

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Background

Ketamine is used as an induction and sedation agent in emergency departments and operating rooms throughout the country. It is used in all fields of anesthesiology, including pediatrics, critical care, cardiac surgery, and outpatient sedation. In the hospital setting, ketamine has recently become widely used for the management of acute and chronic pain.

Pharmacologically, ketamine is a derivative of phencyclidine. It is an NMDA receptor antagonist that facilitates dissociative anesthesia as well as analgesia, while maintaining hemodynamic stability. Its hemodynamic properties are attributable to the associated increase in circulating catecholamines, such as norepinephrine, dopamine, and serotonin. This accounts for the observed increase in heart rate, cardiac output, and blood pressure. Other secondary effects of ketamine include increased muscle tone, delirium, impaired motor function, and hyperthermia. Ketamine is primarily metabolized by N-demethylation by cytochrome P3A4, but CYP2B6 and CYP2C9 are also involved [1]. The primary metabolite, norketamine, is one-third as potent as the parent compound. In patients with hepatic or renal dysfunction, prolonged effects of the parent drug and its metabolite could potentially be observed.

Despite its wide use, there are few cases of significant morbidity and mortality attributed to ketamine overdose in the clinical setting. We present a case of ketamine overdose with minimal postoperative complications. The patient's perioperative course is described to serve as a guide for other clinicians who encounter inadvertent supratherapeutic administrations of ketamine.

Case Report

Mr. B was a 65-year-old, white male with a past medical history significant for previous supraglottic laryngectomy and neck dissection, dysphagia, dysphonia, obstructive sleep apnea, anxiety, and hypertension.

The anesthesia provider in the room was an oral maxillofacial surgeon who inadvertently took out a more highly concentrated bottle of ketamine that is typically used for pediatric patients. Oral maxillofacial surgeons are required to rotate through an anesthesiology elective and function as an anesthesiology resident because they will be delivering sedation independently. Ketamine was chosen by the anesthesia provider in the room supervising the oral maxillofacial surgical resident for pain control post-operatively as the patient had been taking oral oxycodone as an outpatient. The patient received 950 mg (100 mg/ml concentration) of intravenous ketamine instead of the intended 95 mg (10 mg/ml concentration) (Figure 1).

Figure 1. Photo of ketamine vials. Medication taken out (on the left) and the medication that was supposed to be taken out (on the right).

The procedure was a microdirect laryngoscopy where several arytenoids were removed for a vocal cord lesion and lasted approximately 90 minutes. After the ketamine was given, there were no signs to any involved provider that a mistake had occurred until the wake-up appeared to be unusually prolonged. On further examination of the medication vials, the mistake was discovered. The patient remained intubated and was brought up to the ICU for further monitoring. Shortly after arriving in the ICU, the patient was following commands with adequate respiratory effort. He was extubated uneventfully and stayed overnight in the ICU for observation. No other postoperative complications were discovered and he was discharged home the following day.

Discussion

Limited literature exists on ketamine overdose in the hospital setting, with the majority of case reports coming from forensic data [2]. Of all the ketamine overdose cases in the literature, a total of 10 children and 5 adult cases were discovered. A 3-year-old patient in the emergency department was given 450 mg instead of 45 mg, resulting in prolonged sedation but ultimately no additional complications [3]. In another emergency room study, Green et al. [4], studied 9 children who received anywhere from 5 to 100 times the intended dose of ketamine. This overdose resulted in prolonged sedation, with 2 of the children requiring ventilator support. In 5 of the 9 children, the error was not noticed until the wake-up because everything else in the case had gone smoothly, with no adverse clinical signs appreciated on discharge.

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The adult literature is even more limited since all of the overdosed cases were self-induced from recreational use and were found postmortem [5–7]. A review of ketamine-related deaths in the UK from 1993 to 2006 found that only 4 people died with ketamine as the only drug in their blood [6]. A similar study performed by the New York City Office of Chief Medical Examiner found that of the 15 non-hospital-related deaths involving ketamine, there were no instances of fatal intoxication [6]. One case report links ketamine overdose with Brugada syndrome, but this was confounded by traces of codeine, methadone, benzodiazepines, and cannabis [8].

In the Journal of Toxicology, Peyton et al. commented on the rarity of ketamine fatality and reported on 2 men in their 20's found to have ketamine as a potential cause of death, with 6.9 and 1.6 mg/L of ketamine found in their blood [5]. Interestingly, one of the deaths was also related to asthma, but many anesthesiologists use this medication for its bronchodilating effects. In the last case, there was a chronic ketamine overdose in which a woman died after her husband had poisoned her for over 1 year, with findings of cardiac muscle fibrosis and degeneration of small arteries [9].

A culture of safety is paramount to every anesthesiology practice, and medication errors are always taken very seriously. All controlled substances are dispensed via a Pyxis machine requiring a fingerprint and entry of the medication requested. There are 3 concentrations of ketamine available in this work area: 500 mg in a 5-mL vial (used for pediatric cases), 200 mg in a 20-mL (typical concentration used) vial, and 10 mg in a 1-mL (the typical concentration used is very small) vial. When typing in any medication, it is always important to check the medication and concentration prior to taking it out of the machine and also before drawing it up in the operating room. One potential way to prevent this error would be to remove pediatric-dosed medications from commonly used Pyxis machines or have an alert cueing the provider that this vial is typically used in children. A similar safety precaution exists at our institution for intrathecal morphine, where the pharmacy dispenses high concentrations in a glass vial in contrast to other more familiar containers.

Conclusions

Although our patient received other sedatives as part of his induction, he tolerated a ketamine dose of 950 mg intravenously, which was approximately 10 times higher than the induction dose based on his actual weight. Despite this, he did not demonstrate any systemic effects such as hemodynamic or CNS perturbations other than prolonged awakening. This case highlights one (drug overdose) of many causes of delayed emergence from anesthesia and reminds the provider caring for the patient to be mindful of drug concentrations used when preparing to sedate a patient, as relying on effects of the parent drug is not always adequate.

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