Case Reports

Ketamine Dependence in Anesthesia Providers

NICOLE N. MOORE, MAJ, USAF, MC
JOHN MICHAEL BOSTWICK, M.D.

Ketamine is an arylcyclohexamine compound similar to the dangerous street drug, phencyclidine (PCP). It acts as an antagonist at receptors for *N*-methyl-D-aspartic acid (NMDA), an important excitatory neurotransmitter, by nonspecifically blocking NMDA receptor calcium channels. Although it also has weak opioid properties, its anesthetic action is felt to be through NMDA antagonism.[1]

Synthesized in 1962, ketamine was first used in humans in 1970. Like its close relative PCP, it was designed specifically to be a dissociative anesthetic, but free of the violent, confused behavior patients emerging from PCP anesthesia had often demonstrated. Although PCP failed as an anesthetic agent, it quickly became a popular street drug. Although PCP abusers valued it for its psychedelic properties, the terrifying hallucinations and sensory numbing it induced often led those under its influence to display violent and erratic behavior, including superhuman strength and imperviousness to painful stimuli along with telltale ataxia and nystagmus. Those in a user's path, including emergency personnel, were at risk of serious injury if the paranoid or disoriented user attacked. Ketamine, on the other hand, comparatively gentle, was touted as safe and reliable and has filled an important niche in anesthesia because, unlike barbiturates, it increases cardiac drive and does not depress respiratory drive. These characteristics have made ketamine a useful anesthetic in pediatric, geriatric, obstetric, and trauma patients.[2]

From its first use in humans, ketamine was known to cause dissociation, a disconnection between the sensory system and the limbic/cortical system, resulting in lack of awareness of pain sensations.[3] From patient testimony, anesthesiologists soon discovered that it had many other psychotropic effects. Patients described fantastic dreams while under ketamine's influence. Some reported flashback phenomena for several days after surgery. Others experienced agitation coming out of anesthesia, requiring sedation with benzodiazapines to prevent accidental self-harm. In reality ketamine was not very different from PCP except that it had a much shorter half-life, and therefore the "emergence phenomena" were easily controlled and short lived. In addition, those requiring frequent anesthesia developed tolerance to the drug.[4–8]

Almost immediately, ketamine became a popular street drug. Recreational users valued it for dreamlike hallucinations, floating sensations, perceptions of increased efficiency and creativity, feelings of arousal and euphoria, and mystical experiences of self-transcendence. Unlike PCP-induced hallucinations, these sensations were usually peaceful. Users under ketamine's influence were generally not aggressive. Immediate noxious effects included ataxia, slurred speech, blurred vision, dizziness, confusion, cognitive impairment, hyperexcitability, unpleasant imagery, decreased sociability, anxiety, nausea, and insomnia.[9–13] Long-term adverse effects included flashbacks, attentional dysfunction, memory impairment, tolerance, and high dependency potential.[8,10,14]

In 1979, the Federal Drug Administration warned of ketamine's abuse potential and considered making it a controlled substance.[15] For unclear reasons this did not happen. In the 1980s, ketamine lost its popularity among recreational users while remaining a popular drug of abuse among anesthesia providers, as evidenced by sporadic case reports appearing during the last two decades in journals throughout the world.[14,16–19]

We report two cases of ketamine dependence among hospital personnel used ketamine for extended periods without being caught. Our goals include illustrating the dangers of ketamine abuse and the near impossibility of abuse detection if the abuser is not forthcoming.

Received July 15, 1998; revised October 27, 1998; accepted November 6, 1998. From the Mental Health Flight, 51st Medical Group, Osan AB, South Korea and the Department of Psychiatry, Mayo Clinic, Rochester, Minnesota. Address correspondence and reprint requests to Dr. Bostwick, Mayo Clinic, Department of Psychiatry, 200 First Street, Rochester, Minnesota 55905.

Case Reports

Case 1. An anesthesiology provider found to be ataxic and disoriented at work was admitted to a medicine unit for a medical

work-up. He quickly reconstituted and his admission physical exam was unremarkable. Standard labs were normal and urine toxicology screen and blood alcohol were negative. When confronted by the consult team, he admitted to injecting himself with ketamine procured at work. He stated he took ketamine recreationally for its "hallucinatory effects" but denied that several ongoing life stressors motivated his drug use. In response to decreased hallucinatory effect after several months of daily use, he had had to increase both the dosage of drug and frequency of use. This provider had a history of experimental drug use in his youth. He also had a previous history of substance abuse at work, having lost his credentials several years earlier for abusing both ketamine and alcohol. After attending a 4-week inpatient rehabilitation program followed by a 6-week outpatient rehabilitation program, he had been recredentialed. Although he had not been able to resist reinitiating ketamine abuse, he had abstained from alcohol and all other recreational drugs since his rehabilitation. He denied any psychotic symptoms including flashbacks except when under the influence of ketamine. His only psychiatric symptoms were mild depression and anxiety he attributed to a pending divorce and financial setbacks including job loss resulting from the discovery of his ketamine abuse.

Case 2. The consult team was called to the emergency department to assess an anesthesia provider requesting rehabilitation for ketamine dependence. Although he had used ketamine 4 hours earlier at work, he showed no signs of drug impairment at the time of consultation. Two weeks prior to his self-referral, during a case in the operating room, his supervisor found him in an unresponsive, "trance-like" state. His vital signs showed elevated blood pressure and tachycardia. By the time he reached the emergency room 20 minutes later his mental status had cleared. His medical/neurologic work-up in the ER included an unremarkable physical exam and negative blood alcohol and urine toxicology screens. A psychiatric evaluation was ordered but canceled when the medicine consultant opined that the patient's mental status change was most likely secondary to low blood sugar. Fearing job repercussions and loss of confidentiality, the patient did not reveal to the emergency physicians his ketamine abuse. Instead, he related his concerns to an independent psychiatrist not affiliated with the institution where he worked. Having decided to follow the psychiatrist's recommendation to turn himself in, he returned to the emergency room where the consult psychiatry team saw him. He described 2 years of snorting ketamine obtained from work. He started using the drug to alleviate dysphoric feelings related to job dissatisfaction and stress. He denied either auditory or visual hallucinations with use, stating he ingested just enough to calm himself, as a small amount of alcohol might do. Since larger amounts impaired both speech and motor function, he carefully adjusted his doses so as to not affect his ability to work. He had had to increase his use to three times a day to obtain the same effect once achieved with a single daily dose. He had tried to quit without help, achieved 2-months of sobriety, but returned to ketamine use because he found its addictive powers so compelling. He denied past psychiatric history or any other substance abuse, stating that he drank alcohol only rarely. He denied psychiatric symptoms other than frequent initial insomnia and anhedonia with lost of interest in his hobbies.

Discussion

Why would a provider abuse a drug like ketamine? McAuliffe and colleagues[20] and Hughes and associates[21] in surveys on physician substance abuse define two types of doctor-users: recreational users and physicians self-medicating for depression or anxiety. Like the individual in our first case, recreational users had frequently abused drugs prior to medical training. Like the individual in our second case, self-medicators hope to dispel feelings of dissatisfaction and depression. A stressful lifestyle with minimal attention to maintaining physical health or emotional well-being promotes self-medication.[22,23] Hughes and colleagues[21] discovered that both recreational and self-medicating medical professionals abuse what is familiar and available to them in their medical practice. Professional familiarity breeds a sense of false security in anesthesia providers who believe they can manage themselves safely on these drugs. The provider in the second case felt he wasn't endangering himself or his patients because he thought he knew just the right amount of drug to use to stop him from "feeling" while allowing him to continue work "unimpaired." Clearly, as his trance-like state indicated, he was deluding himself.

Anesthesiology has a higher percentage of providers in rehabilitation than other specialties. Talbott[24] feels anesthesia providers are overrepresented because of aggressive approaches the specialty has taken to identify and rehabilitate impaired providers. After alcohol, the substance anesthesia providers most commonly abuse is fentanyl. A short-acting narcotic, fentanyl is metabolized rapidly and completely and therefore is not readily or easily detected on urine toxicology screens.[25] As a controlled drug, however, hospitals closely monitor fentanyl. Unlike ketamine, fentanyl is safeguarded in locked cabinets for which two signatures are required to gain access. Unused drug must be thrown away under the observation of two providers.

Ironically the military hospital in which these cases occurred was a leader in the effort to reduce substance abuse among anesthesia providers. In a 1985 paper, Adler and colleagues[26] outlined a system they developed that featured rigorous pharmacy monitoring of individual patterns of narcotics administration. The goal was to identify providers appropriating medication for personal rather than patient use. Their proactive program, designed in response to multiple published surveys reporting a high prevalence

of substance abuse in anesthesia providers, included an educational component dealing with occupational risks and policies for managing impaired staff. There were no incidents of provider drug abuse at Wilford Hall Medical Center in the 13 months after the program's implementation.[26] The only substances included in the surveillance effort, however, were controlled substances. Our ketamine abusers would thus not have been discovered, even if the characteristics of the drug made it more amenable to detection.

Like fentanyl, ketamine, with its short half-life and rapid clearance, is hard to detect on toxicology screens. Unlike fentanyl, however, ketamine is not a controlled drug. As a stock item in most operating rooms, it is readily obtainable off the shelf with few of the constraints of scheduled compounds. Unused drug is simply discarded (if it is not saved for personal use). Recently our hospital has instituted a policy mandating ketamine storage in a locked cabinet. This initiative, nonetheless, falls short of controlled drug guidelines.

The specifics of ketamine's pharmacokinetics include a peak effect within 20 minutes, with desired effects gone within 90 minutes. The plasma half-life is 17 minutes, and the clearance from urine is 2 hours. Only 4% of a dose is recoverable in the urine as ketamine or norketamine, most of the rest of the dose having been metabolized by the liver into unrecoverable molecules.[2,12] Standard urine toxicology screens do not include it.

Abetted by the ease of acquisition and the freedom from detection, dependence on psychotropic effects evolves quickly in ketamine abusers.[10,14,27] Subjectively positive effects of the drug are so strong that adverse effects are ignored, as they were by both our subjects, who went to work in operating rooms in obviously impaired states. The difficulty of detection and a tendency to assume a cause other than substance abuse for bizarre behavior and symptoms in medical professionals resulted in the extensive and ultimately fruitless medical work ups both our subjects received.

A survey conducted by McAuliffe and colleagues[28] showed that recreational drug abuse among physicians closely follows population patterns. After a 20-year hiatus, ketamine is beginning to reemerge as a popular street drug.[29–31] Accordingly, the state of New York made its recreational use illegal.[32] We suspect that ketamine will continue to be a drug of choice for sophisticated medical personnel seeking to abuse a drug while minimizing the chance of being caught. We believe that providers not suspected of abusing this drug will continue to endanger patients' lives. While anesthesia providers are the most obvious potential abusers, medical professionals in other specialties and disciplines with easy access to ketamine are at risk. To combat this insidious problem, we advocate that the Food and Drug Administration revisit the question abandoned in 1979 of whether to classify this useful but dangerous medication as a controlled substance.

References

1. Oye I, Paulsen O, Maurset A: Effects of ketamine on sensory perception: evidence for a role of *N*-methyl-D-aspartate receptors. J Pharmacol Exp Ther 1992; 260:1209–1213
2. White PF, Way WL, Trevor AJ: Ketamine: its pharmacology and therapeutic uses. Anesthesiology 1982; 56:119–136
3. Miyasaka M, Domino EF: Neuronal mechanisms of ketamine-induced anesthesia. International Journal of Neuropharmacology 1968; 7:557–573
4. Collier BB: Long term dangers of ketamine anesthesia (letter). Br J Anaesth 1981; 53:552
5. MacLennen FM: Ketamine tolerance and hallucinations in children (letter). Anaesthesia 1982; 37:1214–1225
6. Fine J, Finestone SC: Sensory disturbance following ketamine anesthesia: recurrent hallucinations. Anesth Analg 1973; 52:428–430
7. Byer DE, Gould AB: Development of tolerance to ketamine in an infant undergoing repeated anesthesia. Anesthesiology 1981; 54:225–256
8. Perel A, Davidson JT: Recurrent hallucinations following ketamine. Anaesthesia 1976; 31:1081–1083
9. Shaffer LL: Ketamine (letter). JAMA 1974; 229:763
10. Siegel RK: Phencyclidine and ketamine intoxication: a study of four populations of recreational users. NIDA Res Monogr 1978; 21:119–147
11. Malhotra AK, Pinals DA, Weingartner H, et al: NMDA receptor function and human cognition: the effects of ketamine in healthy volunteers. Neuropsychopharmacology 1996;14:301–307
12. Krystal JH, Karper LP, Seibyl JP, et al: Subanesthetic effects of the noncompetitive NMDA antagonist, ketamine, in humans. Arch Gen Psychiatry 1994; 51:199–214
13. Ghonein MM, Hinrichs JV, Mewaldt SP, et al: Ketamine: behavioral effects of subanesthetic doses. J Clin Psychopharmacol 1985;5:70–77
14. Jansen KR: Ketamine: can chronic use impair memory? Int J Addict 1990; 25:133–139
15. FDA Drug Bull 1979; 5(9):24
16. Ahmed SN, Petchkovsky L: Abuse of ketamine (letter). Br J Psychiatry 1980; 137:303
17. Kamaya H, Krishna PR: Ketamine addiction. Anesthesiology 1987; 67:861–862
18. Hurt P, Ritchie EC: A case of ketamine dependence (letter). Am J Psychiatry 1994;151:779
19. Menk, EJ, Baumgarten K, Kingsley CP, et al: Success of reentry into anesthesiology training programs by residents with a history of substance abuse. JAMA 1990; 263:3060–3062
20. McAuliffe WE, Rohman M, Santangelo S, et al: Psychoactive drug use among practicing physicians and medical students. N Engl J Med 1986; 315:805–810

21. Hughes P, Conard SE, Baldwin DC, et al: Resident physician substance use in the United States. JAMA 1991;265:2069–2073
22. McAuliffe WE, Santangelo S, Magnuson E, et al: Risk factors of drug impairment in random samples of physicians and medical students. Int J Addict 1987; 22:825–841
23. Spiegelman WG, Saunders L, Mazze RI: Addiction and anesthesiology. Anesthesiology 1984; 60:335–341
24. Talbott D, Gallegos KV, Wilson PO: The Medical Association of Georgia's Impaired Physician Program. Review of the first 1000 physicians: analysis of specialty. JAMA 1987; 257:2927–2930
25. Gallegos KV, Browne CH, Veit WV, et al: Addiction in anesthesiologists: drug access and patterns of substance abuse. Quality Review Bulletin 1988; Apr:116–122
26. Adler GR, Potts FE, Kirby RR, et al: Narcotics control in anesthesia training. JAMA 1985; 253:3133–3136
27. Lilly JC: The Scientist: A Novel Autobiography. Philadelphia, Lippincott, 1978, pp. 30–95.
28. McAuliffe WE, Rohman M, Fishman P, et al: Psychoactive drug use by young and future physicians. J Health Soc Behav 1984; 25:34–54
29. Jansen KLR: Non-medical use of ketamine. BMJ 1993; 306:601–602
30. Dotson J, Ackerman A, West L: Ketamine abuse. The Journal of Drug Issues 1995; 25:751–757
31. Dalgarno P, Shewan D: Illicit use of ketamine in Scotland. Journal of Psychoactive Drugs 1996; 28:191–199
32. Dao J: The New York Times 26 Sep1997; Sec B, page 4, column 1