

Selected Topics: Psychiatric Emergencies

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Catatonia-Like Syndrome Treated With Low-Dose Ketamine

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Introduction

Ketamine has become a staple of emergency medical care. Its short half-life, lack of clinically significant respiratory depression, and safety have made it a commonly used medication throughout the world for an ever-expanding range of uses (1-3). While its application in psychiatry has also expanded, it appears never to have been previously used to diagnose and treat the diagnostically difficult condition of catatonia-like syndrome that occasionally presents to emergency departments (EDs).

In contrast to the most common treatment for acute catatonia, lorazepam, intravenous ketamine has an almost immediate onset, with its effects effectively gone within 1 h. Used diagnostically for suspected catatonia, it provides the clinician with a rapid confirmation of the diagnosis or a reason to move quickly to a more thorough workup of other diseases.

Case Report

A 23-year-old man was brought to the ED by a friend who said that he found the patient mute and unresponsive at home about 2 h before arrival. On arrival, while his Glasgow coma scale score was 8, his vital signs were normal (blood pressure 110/70 mm Hg, pulse 81 beats/min, respiratory rate 12 breaths/min, temperature of 37.1°C, oxygen saturation of 99% on room air, and glucose 91 mg/dL). His estimated weight was 75 kg.

According to the friend, the patient had been at his girlfriend's home when he suddenly became mute. No other history was available. On physical examination, the patient remained immobile despite stimulation, was verbally unresponsive, and refused to open his eyes. A complete physical examination revealed no abnormalities, no meningeal signs, and his pupils were equal at 3 mm and bilaterally reactive. When his arm was placed above his head, it slowly fell to his side, appearing to demonstrate waxy flexibility. There was no evidence of clonus or lead-pipe rigidity.

There is no consensus on the number of clinical signs needed to diagnose catatonia, although the presence of ≥ 3 signs suggests a diagnostic sensitivity and specificity of 99% (4). Our patient had 3 common signs—immobility and stupor (extreme hypoactivity, complete immobility, and minimal response to stimuli); mutism (minimal or absent verbal response); and waxy flexibility (maintenance of a mundane or bizarre posture for long periods of time when positioned by the examiner) (5).

All laboratory work (a complete blood cell count, comprehensive metabolic panel, urinalysis, and electrocardiogram) was normal. While a catatonic state was strongly suspected, it was imperative to either confirm that diagnosis or move on to evaluate the patient for potentially life-threatening nonpsychiatric illnesses.

Neither amobarbital, an intermediate-acting barbiturate that 1 of the authors had used successfully with similar cases, nor lorazepam, the most commonly used drug for catatonia, was available in our resource-limited setting. The decision was made to try to reverse the catatonic state using low-dose ketamine, a drug that has a good safety record, was available, and with which we were familiar (6).

Ketamine 25 mg (1 mL) was diluted in 9 mL normal saline, resulting in a solution of ketamine 2.5 mg/mL, or about 0.03 mg/Kg/mL. Following successful protocols for ED treatment of conversion reactions, 1 mL of the diluted ketamine solution was given intravenously while we talked to the patient (6). Although his respirations quickly increased, he did not respond verbally and kept his eyes closed. After 3 min, another 1 mL of ketamine solution was administered. At that point, after receiving 5 mg ketamine total, he began to open his eyes, but still would not speak. Three minutes later, after another 1 mL of ketamine solution, he started to mumble a few words. Eventually, a total of 12.5 mg ketamine (0.17 mg/Kg, the low end of analgesic dosing) was administered (7). At that point he was fully conscious and provided limited psychiatric history.

Shortly after he emerged from his catatonic-like state, the patient's mother arrived and stated that his girlfriend had just broken up with him. She also related that he had experienced a similar incident a year before when he had gotten upset, although he remained alert at that time. At that ED visit, he had an extensive evaluation, including a computed tomography scan, without a definitive diagnosis. She stated that while he used marijuana occasionally, he was on no prescribed or over-the-counter medications.

Throughout his ED stay, the patient's vital signs remained normal. The psychiatric consultant confirmed the diagnosis of resolved catatonia and discharged him from the ED with a 2-day follow-up appointment. Psychiatry reported that he had had no recurrent episodes when seen in their clinic repeatedly over the following 3 weeks.

Discussion

Emergency physicians infrequently encounter patients presenting in catatonia-like states (6,8). This situation represents a true emergency because it is imperative to differentiate catatonia-like symptoms caused by psychiatric disease from those caused by urgent nonpsychiatric conditions, such as central nervous system infections or other disorders, unsuspected trauma, or severe toxic-metabolic derangements (9-11). Patients presenting in catatonic-like states have had intracranial infections and hemorrhage, endocrine abnormalities, liver failure, systemic lupus, late-onset Tay-Sachs disease, multiple sclerosis, arteriovenous malformations, tumors, and drug ingestions (12-20). Delaying diagnosis and therapy for patients with nonpsychiatric disorders, as well as in “acute lethal catatonic” patients, has led to deaths (21). In psychiatric-related catatonia, the inability to make a definitive diagnosis and alleviate acute symptomatology, even among neurologists, often causes difficulty and confusion in the patient's proper evaluation, disposition, and treatment (6,22).

While it initially was associated purely with schizophrenia, the DSM-5 now describes catatonia as being associated variously with another mental disorder, due to another medical condition, or unspecified (23,24). No definitive explanation exists for catatonia, although there is some evidence suggesting that it may be caused by hypoactivity of gamma-aminobutyric acid receptors in the cortical areas of the frontal lobes or hypoactivity of dopaminergic transmission in subcortical areas (25-27). Evidence exists that most cases of autoimmune catatonia are caused by *N*-methyl-D-aspartate (NMDA) receptor encephalitis (28). A possible mechanism for ketamine's action in catatonia is its antagonism of NMDA-type glutamate receptors (29).

For more than a century, clinicians have studied multiple treatments for catatonia, although none has shown clear superiority or been universally effective. During much of the 20th century, sodium amobarbital was the treatment of choice, but it is now generally unavailable for clinical use (6). Other treatments have included benzodiazepines, with oral lorazepam over several days the most widely studied. Response and remission rates vary between 0% and 100%, with Western studies generally demonstrating higher response rates than elsewhere. Electroconvulsive therapy, with response and remission ranging from 59% to 100%, has most often been used when other methods fail but is rarely (if ever) performed in the ED, since it could be used neither in a timely manner nor as a diagnostic modality. Antipsychotics have been used particularly in patients with known underlying psychotic disorders, but their use poses what has been termed the “catatonic dilemma.” As dopamine blockers, first-generation antipsychotics may cause or worsen catatonic signs. This happens less frequently with second-generation antipsychotics (30). Carbamazepine, NMDA, topiramate, amineptine, and “packing therapy” (wrapping patients in cold wet towels) have also been tried with limited success (27).

The goal in emergency medicine is to use a safe, rapidly effective, readily available intervention to diagnose and reverse catatonic states. Ketamine may serve that purpose. It can induce dissociative anesthesia at doses ranging from 1 to 2 mg/kg administered intravenously or from 4 to 11 mg/kg administered intramuscularly. Subanesthetic analgesic doses range from 0.15 to 0.25 mg/kg, when administered intravenously (31).

Subanesthetic intravenous ketamine often produces psychoactive effects even at low doses, as in the case presented, although they seem to lessen with very slow administration (32). In clinical trials, these effects most commonly include dissociation (visual, auditory, or somatosensory distortions), positive psychotomimetic effects (disorganized thoughts, hallucinations, or suspiciousness), and negative psychotomimetic effects (blunted affect, emotional withdrawal, or motor retardation) (28). Contraindications to using subanesthetic dose ketamine on at-risk individuals is largely unknown (33).

Conclusion

Patients presenting in catatonia-like states represent a difficult and potentially life-threatening diagnostic and therapeutic dilemma. Multiple interventions have been used for this condition with varying levels of success.

Subanesthetic ketamine may be superior to commonly used lorazepam because of its quick onset, short duration of action, safety record, and NMDA receptor antagonism. While additional cases or studies should verify this result, ketamine's pharmacology appears to make its use a valuable addition to our clinical armamentarium in diagnosing and treating this complex presentation.

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