

Treatment of Behavior Disturbances with Ketamine in a Patient Diagnosed with Major Neurocognitive Disorder

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A 77-year-old woman who had been previously diagnosed with a major neurocognitive disorder became highly agitated and aggressive in a long-term care facility. She did not respond to intramuscular (IM) haloperidol plus lorazepam and had to be transported to the local emergency department (ED). In the ambulance, she remained highly agitated and was given 200 mg IM ketamine. Within minutes of receiving this, she de-escalated dramatically with no apparent adverse effects and remained stable for several days. Although ketamine has been used recently in pre-hospital settings and EDs to reduce agitated behavior, there has been little if any investigation of its potential for reducing behavior disturbances in patients who suffer from major neurocognitive disorders. Ketamine could potentially be a promising treatment option for this population, but more research is needed. (Am J Geriatr Psychiatry 2018; 26:711-714)

Key Words: Neurocognitive, dementia, ketamine, behavior, agitation, elderly, geriatric

Highlights

- Shortly after receiving ketamine, a patient with major neurocognitive disorder experienced a rapid and vigorous reduction in agitation with no adverse effects.
- There is a growing body of evidence supporting the use of ketamine in reducing excited delirium and agitation in pre-hospital and emergency department settings.

- Apart from a few studies involving late-life depression, little has been published about the psychiatric use of ketamine in the elderly.
- Questions remain regarding the potential neurocognitive, respiratory, and hemodynamic effects of ketamine on older adults who are cognitively impaired.

Ketamine is an anesthetic agent that is an *N*-methyl-D-aspartate receptor antagonist. It can be administered by many routes including oral, sublingual, transmucosal, intranasal, intravenous, subcutaneous, as well as intramuscular (IM).¹ Ketamine has shown promise as an option for treatment-resistant major depression. The therapeutic effect when treating depression can be rapid, and reduction of suicidal ideation has been observed immediately following administration of the drug.² There are limited data available with respect to psychiatric treatment with ketamine in the elderly population, although some reports have described benefits in treating late-life major depression.³⁻⁵ Recently, several published studies have reported ketamine to be useful in treating excited delirium and aggression in prehospital settings⁶⁻⁸ and emergency departments (EDs).⁹⁻¹¹

There are limited options available for treatment of disruptive or dangerous behavior in cognitively impaired patients, and none of them are U.S. Food and Drug Administration–approved. Some authors have reported antidepressants to be beneficial for this indication.^{12,13} IM antipsychotics are sometimes the option of choice in situations where agitation is catastrophic, but there are many risks associated with antipsychotic use in neurocognitive disorders, including increased mortality rate. The purpose of this case report is to explore the possibility that ketamine could be a viable alternative to existing treatment options currently used to reduce severe behavior disturbances in older cognitively impaired patients.

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CASE REPORT

A 77-year-old white woman had been medically hospitalized after being involved in a motor vehicle accident that resulted from her confusion. In the hospital, her computed tomography scan was unremarkable (apart from atrophy) and she was diagnosed with a urinary tract infection. The patient was eventually transferred to an inpatient psychiatric unit where a neuropsychological assessment determined that she had deficits in multiple domains, consistent with a major neurocognitive disorder. The inpatient team felt that she did not have decision-making capacity and could not live independently. She was treated in the hospital with sertraline 25 mg/day, temazepam 15 mg/day, memantine, and donepezil.

She was discharged to a residential care facility, but it soon became apparent that she was too impaired to live at that level of care, and she was then transferred to a memory care unit. Throughout her stay at these facilities, she experienced abrupt changes in mood with sudden outbursts of anger and tearfulness. Her family told the staff that she had a long history of tantrums when she did not get her way. The treating psychiatrist diagnosed her with both a neurocognitive disorder and an unspecified depressive disorder after she expressed vague suicidal thoughts. At one point she began to throw her medications in the toilet and refused to eat. She complained of insomnia and was switched from temazepam to trazodone, gradually increased to 50 mg/day. Her sertraline dose was gradually increased to 75 mg/day. A lifelong smoker, she was not allowed to smoke while confined on the memory care unit, and this was a source of unhappiness for her. Obsessive behavior was evident as she often insisted on watching the same classic musical from the 1960s several times a day.

About 3 months after her admission to the memory care unit, her family took her out of the facility and allowed her to smoke. Upon returning, the patient was very insistent for several days that she should be allowed to leave the unit without supervision and smoke. One afternoon, after her demands were gently refused, the patient then began to escalate rapidly, striking out at staff members, ripping off some of her clothing, and shouting profanities. She threatened to break windows. Her room was virtually demolished, with personal belongings scattered and framed family

pictures smashed. Broken glass and debris covered the floor. She pushed and hit anyone who came close to her. Haloperidol 2.5 mg IM plus lorazepam 0.5 mg IM was administered, but this was ineffective for the first 30 minutes after the injection. Staff called 911 and police arrived along with ambulance personnel. Despite the police officers' efforts to calmly de-escalate her, she cursed at them and threw a container of fluid on an officer. She was then placed on a gurney with four-point restraints. Ambulance personnel noted her to be highly agitated during the trip to the ED, shouting profanities, writhing, and spitting. A face cover was applied and ambulance personnel were given an order by the ED physician for ketamine 200 mg (3 mg/kg) IM, which was administered as 100 mg in each buttock. They noted that she was significantly calmer and more cooperative by the time they reached the ED. The patient remained alert and her behavior in the ED was unremarkable. A telepsychiatry clinician determined that she did not meet criteria for inpatient psychiatric care. Medical assessment found no evidence of acute physical illness. Given the magnitude of her previous behavior, she was kept overnight in the ED.

The patient's psychiatrist assessed her in the ED the following morning and found her to be completely calm, alert, and cooperative, although somewhat bland and apathetic. There was no evidence of anger or sadness at that time. She returned to the memory care unit where sertraline was increased to 100 mg/day. She remained stable for approximately 1 week, but then gradually became angry and labile again, although not as severely as before. She was started on aripiprazole 2.5 mg/day and sertraline was increased to 150 mg/day. She remained on trazodone 50 mg/day as well as memantine and donepezil. Eventually, sertraline was replaced by venlafaxine 75 mg/day because her apathy did not seem to be improving. The patient stabilized in the months that followed, spending most of her time sitting alone passively and silently watching the same 1960s musical several times a day.

DISCUSSION

Ketamine has been shown to be beneficial for some depressed patients, but it is not known whether it could be beneficial for agitated demented patients who are not depressed. In this case, it is unclear to what extent the patient may have been depressed and whether this

could account for her impressive response to ketamine. She also had a pre-existing tendency to become explosive, which may have been exacerbated by frontal lobe pathology. The patient received antipsychotic and benzodiazepine treatment prior to receiving ketamine, and this may have had some impact as well. The therapeutic effect of ketamine was rapid and dramatic in this situation, but it was short-lived and antipsychotic treatment was required after several days.

The safety of ketamine has been questioned in some populations, however. There have been concerns about hemodynamic changes, dissociative effects, nightmares, and psychosis,² all of which would obviously be problematic for elderly dementia patients. Moreover, relatively high rates of endotracheal intubation have been reported in patients receiving prehospital and ED treatment.¹⁴

Ketamine's effect on cognition has been reported variously to be positive as well as negative. Ketamine has been credited with improving postoperative cognition in some older adults.^{15,16} Healthy volunteers, however, have experienced transient cognitive impairment from ketamine.^{17,18} Schizophrenics who received ketamine deteriorated both in terms of psychotic symptoms and cognition.¹⁹ A group of patients

with Huntington disease experienced dose-dependent worsening of neuropsychiatric symptoms after using ketamine.²⁰ These findings suggest that neurocognitive side effects could be related to dose, frequency of use, diagnosis, or other variables. Finally, emergence delirium has been reported, although this may be attenuated by using benzodiazepines concomitantly.²¹

CONCLUSION

Pharmacologic treatment of dangerous behavior in cognitively impaired elderly patients is a vexing issue. The choices are limited, and new approaches that are safe and effective would be welcome. One potential benefit offered by ketamine is rapid response. The reported increase in endotracheal intubation in some settings is a serious concern. Although there may be risks associated with ketamine, the same is true of antipsychotics, which are still the treatment of choice in many cases of catastrophic behavior. Ketamine is worthy of further investigation as a treatment for behavior disturbances associated with major neurocognitive disorders, especially those with a depressive component.

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