Intravenous Ketamine Relieves Pain and Depression After Traumatic Suicide Attempts
A Case Series

To the Editors:

Suicide is believed to be the second leading cause of death among Americans aged 15 to 34 years and is the 10th leading cause among Americans of all ages. For every suicide completed in the United States, there are approximately 25 failed attempts, and the estimated societal cost of suicide is more than 50 billion dollars.[1] In addition, rural areas tend to have higher suicide rates and poor access to specialized medical treatment.[2] Suicide rates have continued to increase in the last decade despite research efforts.[3] If the suicide-related injuries are severe, these individuals are likely to be initially hospitalized on medical wards, which routinely have less mental health monitoring than inpatient psychiatry units. It is noteworthy that suicide attempts can occur in the hospital setting, and approximately one quarter of them take place within the first week of hospital admission.[4] After a physically traumatic suicide attempt, pain becomes a factor that contributes to suicidal thoughts and behaviors.[5] Effective and rapid-acting pharmacologic interventions in the treatment for patients with continued suicidality and depressive symptoms after a traumatic suicide attempt are needed, and this is an area of active research.[6] The leading accepted intervention that shows evidence for quickly reducing suicidal ideation during inpatient admissions is electroconvulsive therapy (ECT).[7] Although ECT remains the criterion standard for treatment of suicidal depression, it is limited by availability and relative contradictions as well as not addressing pain after traumatic suicide attempts.

Subanesthetic doses of intravenous ketamine (usually 0.5 mg/kg over 40 minutes) have been shown in small studies to have antisuicidal properties and have been shown to work within 2 hours of administration. The time for which this effect is sustained varies in individuals and ranges from 1 to 2 weeks in different studies.[8–10] Ketamine is also a medication known for its analgesic properties and can produce a reduction of opioid requirements in acute traumatic and nontraumatic settings.[11] We present a series of cases where, after traumatic suicide attempts, we administered intravenous doses of ketamine to decrease pain and acute suicidal thoughts.

CASE REPORTS

The first case is an 81-year-old man who presented with a suicide attempt involving self-inflicted neck laceration and left wrist laceration. The patient had an extensive psychiatric history of depression, anxiety, and one suicide attempt 15 years ago. It was reported that the patient had abruptly left his wife at a church service and had crashed his car at a supermarket after severely lacerating his wrists and neck. When police arrived, he ran toward the police with a knife in an apparent attempt to be killed by police. On presentation to the hospital, the patient was unable to speak but spelled out "help me die" on the whiteboard to the medical team. He was subsequently transferred to the operating room where his transected right internal jugular vein was repaired and the free ends of his left radial artery were ligated. Because of the severity of damage to structures at the level of the patient's thoracic inlet, he was transferred to the intensive care unit. On initial psychiatric consultation, it was discovered that the patient had been holding a delusional belief that he and his wife were developing dementia. His thought patterns were rapid and disorganized. During the initial psychiatric interview, the patient was given a diagnosis of major depressive disorder (MDD), recurrent, severe, with psychotic features. After discussion with the patient, family, and surgical specialists, it was decided that the patient was not medically stable for ECT and pharmacotherapy was initiated to target symptoms of depression and psychosis using venlafaxine, mirtazapine, and aripiprazole on hospital day 3. Given the patient's severe pain from his injuries and subsequent surgical interventions, continuous infusion of ketamine was considered for the primary indication of pain management and secondarily in its ability to decrease depressive symptoms and suicidal ideation from recent studies. Intravenous ketamine infusion was started on hospital day 12 at 0.4 $mg \cdot kg^{-1} \cdot h^{-1}$ for 24 consecutive hours. Ketamine was paused for 16 hours because of ICU staff's concern for dissociative effects and restarted at 0.3 $mg \cdot kg^{-1} \cdot h^{-1}$ for 48 consecutive hours. On hospital day 14, the patient reported that his suicidal ideation had abated, writing on a whiteboard, "I don't want to kill myself, thank you for helping me." He reported that his symptoms of depression decreased after ketamine and his family reported that he had a brighter affect. After a complicated course on our combined medicine-psychiatry service, he was discharged on hospital day 53. In 3 months of follow-up, chart review since the suicide attempt has indicated that there is no recurrence of suicidal ideation. He has continued on venlafaxine and mirtazapine since discharge from the inpatient setting and is followed by one of our geriatric psychiatrists. The patient gave verbal consent to publish the case.

The second case is also an elderly man who presented with a suicide attempt involving self-inflicted bilateral orbit trauma. On admission, the patient had endorsed suicidal ideation and presented with symptoms consistent with a severe episode of recurrent major depression with psychotic features. Just before presenting to the hospital, the patient had a bizarre suicide attempt in which he had stabbed himself in both eyes with a medium-sized screwdriver. The patient was not a good candidate for ECT because of his cardiac irritability (frequent bigeminy) and facial traumas. The treatment team decided to start him on venlafaxine and mirtazapine with a rapid titration to doses of 225 mg and 30 mg, respectively. In efforts to provide a rather aggressive treatment regimen that may lead to a rapid antidepressant response, these antidepressants were augmented with aripiprazole at an antipsychotic dose range, accompanied by melatonin, and testosterone supplementation. Furthermore, given the lack of rapid benefit with the current medication regimen and the patient was selectively refusing pain medications (ie, he had never used his opioid patient-controlled analgesia), we recommended intravenous ketamine. After 1 week of continuous intravenous ketamine administration given at 0.3 to 0.4 $mg \cdot kg^{-1} \cdot h^{-1}$, the patient spontaneously described being in less pain and was able to also spontaneously make the following statement to his wife, "I blinded myself," coming as close as possible to acknowledging his suicide attempt. His affect and personal engagement improved significantly. Over the next weeks, the patient slowly died of complications of injuries and preexisting metastatic esophageal cancer. He was able to spend meaningful time with his wife and son before passing away shortly before noon on a Saturday, peacefully and on his birthday; he was then 77 years old. We obtained consent from the patient's immediate family at the time he died.

DISCUSSION

In this set of 2 cases, we have provided strong evidence of the utility of intravenous ketamine for treatment of comorbid pain, depression, and suicidal ideation after traumatic suicide attempts. This combines the traditional use of ketamine as an anesthetic with newly discovered antidepressant and antisuicidal properties. In these 2 cases, symptom relief was the desired outcome of treatment, and by this metric, the use of ketamine was a success in these patients in terms of management of pain, depression, and suicidality. Antidepressants and ECT are also effective in managing suicidal ideation, but given that it tends to take several weeks for the initial effects of antidepressant pharmacotherapy to be perceived in the patient and previously mentioned limitations of ECT, we consider that the use of ketamine to potentiate and hasten the antidepressant effects and reduce the risk of harm a worthwhile strategy.

Of note, both patients in this series were elderly and diagnosed as having MDD with psychotic features. These patients did not have any exacerbation of psychosis and rather appeared to lessen these symptoms, possibly by exerting treatment of their underlying depression. To our knowledge, treatment for patients with MDD with psychotic features with intravenous ketamine has very likely been attempted, but has never been formally reported on as a published case series,[12] and never with use of continuous ketamine infusions at the doses and for the duration that was administered in this report. The primary indication of ketamine infusion was for somatic pain control, and we followed our institution's protocol of 0.1 to 0.4 $mg \cdot kg^{-1} \cdot h^{-1}$ until pain control is achieved, which in these cases was on the order of days. We would like to note the difference between these cases and the methods of dosing used for anesthesia (2 mg/kg over 1 minute for 5–10 minutes of anesthesia) and primary depression (0.5 mg/kg over 40 minutes).

These treatments were given in the clinical setting, and outcomes were measured by clinicians and thus not subject to rigorous scientific scrutiny one would see in the setting of a clinical trial. Naturally, these results should not be used to justify a generalized application, rather only stimulate discussion and further study. Despite these limitations of this communication, we hope that this adds to the growing literature of the use of ketamine to treat psychiatric illness and leads to large-scale randomized, blinded, controlled clinical trials comparing ketamine to establish reasonable standards of care in suicidal patients. The applicability of intravenous administration of ketamine in postsuicide depressed patients with or without psychotic features can be a favorable alternative to standards of care, including electroconvulsive shock treatment, in select cases. Ketamine may be particularly useful after severe traumas after suicide attempts when somatic pain is present. This case series bolsters the ongoing discussion of how to best use intravenous administration of ketamine to treat psychiatric disorders, particularly when comorbid pain is present and/or ECT is unavailable.

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