Sublingual Ketamine for Rapid Relief of Suicidal Ideation

To the Editor: Ketamine infusions can provide relief of depression with suicidal ideation within hours.[1] However, the high cost, expertise required to administer the infusions, and dissociative effects that may occur at high ketamine doses may limit patient access. Sublingual ketamine, when self-administered by the patient at home in repeated low doses, may provide the same benefit without the limitations.[2] The following cases illustrate the use of sublingual ketamine for outpatient management of acute suicidal depression.

Case 1. Mr A is a man in his 60s with a history of years of vague symptoms of depression and anxiety with no formal diagnosis. In February 2016, after a month-long crisis at work, he presented with fatigue, restlessness, and suicidal thoughts but no intent. He had slow monotone speech and slouched posture.

In addition to an upward taper of venlafaxine, Mr A was offered and accepted a prescription for ketamine syrup 16 mg/mL to be taken sublingually 16 mg every hour as needed. He reported that he felt a growing sense of calm shortly after the second dose. Two and a half hours after his first dose, he walked into the clinic with a brisk gait and upright posture. He was smiling and joking.

He was monitored by telephone contact and 4 visits during the following month. During the first few days, he took 48 to 128 mg/d in divided doses. He reported that 32 mg or less made him feel calm, but higher doses caused an unpleasant "drunk-like" sensation that lasted for about 30 minutes. After 1 week, he returned to work. After 1 month, he was back to his baseline status. By that time, he had self-discontinued ketamine because it offered no further advantage but continued venlafaxine.

Case 2. Mr B is a man in his early 20s with bipolar I disorder with psychotic features (*DSM-5*) and a history of suicide attempts, heavy alcohol use, and paranoid delusions. In November 2015, he continued to have frequent episodes of suicidal ideation that lasted several hours despite taking citalopram 40 mg/d and olanzapine 5 mg once or twice daily and receiving counseling from his psychiatric nurse practitioner.

He requested a trial of ketamine in addition to his established treatment regimen and was prescribed ketamine syrup to be taken sublingually 16 mg every 2 hours as needed. He was monitored primarily by telephone, frequently over the first 2 weeks and then occasionally. He visited the clinic at 2 and 6 months and also saw his psychiatric nurse practitioner during that period. He reported that after his first dose of sublingual ketamine, his mood improved and he fell asleep. The following morning, after awakening with a low mood, he took a series of 2 doses of ketamine 2 hours apart. He soon felt less depressed and more energetic. He had some mild agitation, however, which he addressed by engaging in a vigorous physical workout.

The dose was reduced to 8 mg twice daily with an additional 8- to 16-mg rescue dose once daily as needed. During the next 6 months, he reported using the scheduled dosing consistently and the rescue dose occasionally. He reported that his mood fluctuations were mild, suicidal thoughts were fleeting, and alcohol use was markedly decreased. After 6 months, he was able to reduce citalopram to 10 mg/d.

These cases demonstrate that low doses of sublingual ketamine repeated over a span of hours can induce rapid remission of suicidality in unipolar or bipolar depression. In contrast to the sedating effects of benzodiazepines and atypical antipsychotics commonly used for short-term relief, ketamine was an activating agent in these cases. Patients who may be suitable for this intensive outpatient treatment are those who report disturbing suicidal thoughts but firmly deny intent. Professional judgment is of course required; in theory, as with other activating antidepressants, the treatment could paradoxically increase the risk of committing a previously planned suicide.

Chronic use of oral or sublingual ketamine has been helpful in the past 4 years for many of my patients with mild depressive symptoms. For example, 9-item Patient Health Questionnaire[3] scores were lower in 11 of 15 opioid-tolerant patients surveyed after taking oral ketamine capsules for months during an open-label dose titration period following participation in a 2-week randomized controlled trial of oral ketamine for chronic pain.[4] My patients have reported more predictable results, with regard to both favorable and adverse effects (ie, the mild dissociative effect at higher doses), when taking syrup sublingually compared to swallowing capsules. For this reason, I now prescribe sublingual syrup to new patients. The starting dose in the cases presented here was equivalent to 10% of a typical dose used for infusion of ketamine for depression[1] on the basis of sublingual bioavailability of approximately 20%.[5] Within an effective dose range, dissociative symptoms were absent. The cost to these patients was approximately $50/month.

Ketamine's safety profile has been demonstrated by decades of use as an intravenous anesthetic and off-label use as an oral analgesic at low doses for chronic pain.[6] While the benefit of ketamine has extended over months to years in some of my patients, there are potential unknown adverse effects with continuous use of low doses over long periods.

Sublingual ketamine may be a practical option for managing suicidality in outpatients as an adjunct to traditional antidepressants and mood stabilizers and could shorten the hospital stay of psychiatric inpatients. Sublingual ketamine is worthy of systematic study as a treatment to provide rapid relief of suicidal ideation.

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