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Emergency Physicians Should Give Ketamine to Patients with Acute Suicidal Ideation

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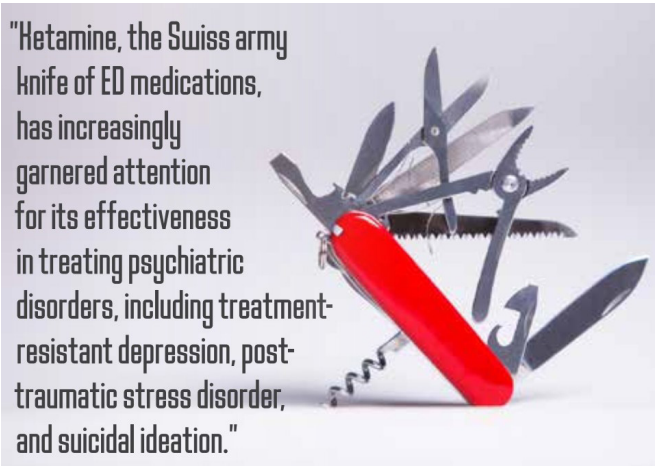
Acute suicidal ideation (SI) represents about 1% of all adult emergency department (ED) visits in the U.S. and has increased over the past few decades, especially in the wake of the COVID-19 pandemic.[1] According to the CDC, ED visits have increased for suspected suicide attempts among adolescents and young adults since 2020.[2] The ED is a frequently utilized health care resource for at risk mental health patients. Approximately 40% of patients who died by suicide had visited an ED within one year prior to death, according to retrospective studies in the UK.[3,4] Outcomes could be improved if these patients received prompt treatment. Unfortunately, many community hospitals have limited mental health resources. Patients often endure long boarding times in the ED until they are assessed by a mental health worker, admitted to inpatient psychiatry, or transferred to an appropriate facility. On average, psychiatric patients are boarded in the ED for more than 11 hours and this increases to over 15 hours if a transfer is required.[5]

While waiting for care in the ED, these patients often experience mental distress while in solitude, and are rarely provided with anything to ameliorate their symptoms. Antidepressant medications, such as SSRIs and SNRIs, are most often used to manage symptoms linked to acute SI, but are ineffective in the acute setting.[6] Antidepressants often require four to six weeks or longer to improve symptoms and many patients do not respond to the first trial of medication.[7,8] The limited options to provide immediate relief can be burdensome for many emergency physicians when managing these patients, but maybe a familiar agent could be of benefit.

Ketamine, the Swiss army knife of ED medications, has increasingly garnered attention for its effectiveness in treating psychiatric disorders, including treatment-resistant depression, post-traumatic stress disorder, and suicidal ideation. Over the past decade, randomized control trials (RCTs) have shown ketamine's efficacy in reduction of acute SI symptoms, but most of the research involving ketamine therapy for SI has been conducted in inpatient psychiatry settings. Dosing protocols ranged from 0.2 mg/kg to 0.5 mg/kg intravenously, but the most commonly utilized dose was 0.5 mg/kg in 100 mL normal saline infused over 40 minutes.[11-16] A randomized control trial from 2017 demonstrated a statistically significant reduction in SI symptoms compared to midazolam.[9] These effects were maintained for up to six weeks.[9] Meta-analyses and systematic reviews demonstrated similar conclusions for the rapid reduction of SI symptoms after ketamine infusions.[11-16] In one meta-analysis, after a single-dose ketamine infusion, a significant reduction in SI symptoms was observed for up to seven days.[11] Although most existing literature has emerged from the inpatient psychiatry setting, more recent studies suggest the evidence supports its use in the ED as well.

Over the past decade, there has been a growing body of research to investigate the efficacy of ketamine for acute SI in the ED setting. Kashani et al, a single-arm study with 49 enrolled patients

reported a significant reduction of SI symptoms at 40 minutes post-infusion.[17] However, the 0.2 mg/kg ketamine dose falls in the lower range of doses utilized in the inpatient psychiatry studies.



Burger et al, an RCT from 2016 (n=10), demonstrated a reduction of symptoms in the ketamine group at 240 minutes post-infusion that was comparable to the control group after receiving inpatient psychiatric treatment.[18] Another RCT (n=16), Domany et al, used 0.5 mg/kg ketamine and reported a statistically significant reduction in symptoms in the ketamine group compared to placebo.[19] There were two studies published in 2022. Gaither et al, a single-arm study that administered 0.5 mg/kg to patients in the ED waiting for admission to inpatient psychiatry and demonstrated significant reduction in symptoms at two hours post-infusion.[20] The other, an RCT by Domany and McCullumsmith, randomized patients (n=30) to intranasal ketamine or placebo and resulted in SI remission in 80% of the ketamine group vs 33% of the control group.[21] None of the studies reported serious adverse events. The degree of efficacy may be dose dependent, and larger RCTs with broader inclusion criteria would be beneficial to determine optimal dosing, infusion rate, and potential for ketamine to serve as a bridge to conventional therapy. Despite limited data from the ED, it largely trends with the inpatient psychiatry evidence: ketamine is an effective tool in providing rapid relief for these otherwise suffering patients.

Ketamine at a subanesthetic intravenous dose is well tolerated with minimal rates of serious adverse effects.[22] If the evidence suggests that the benefit outweighs the risk, and there are no other feasible treatment options, why are we not regularly utilizing this tool? Considering the potentially severe mental distress these patients experience while waiting in the ED, there is a strong argument for emergency physicians to offer ketamine, especially in the context that there are no other effective immediate-acting medications except for one that is ubiquitously available.

Some may critique the small sample sizes of ED-based studies, but efficacy in symptom reduction has been sufficiently demonstrated in larger inpatient studies. There may also be criticism of the short-lived symptomatic relief, but from the perspective of the common use of analgesics, it makes sense. It would be unethical to withhold pain medication for a kidney stone or severe trauma using the rationale that it is unnecessary because the relief is temporary—that is expected.

While lacking evidence for reduction of SI in the long-term, the transient symptomatic reduction is a reasonable goal in the ED, in the same way morphine provides relief for severe physiologic pain. Insufficient evidence for reduction in long-term suicidality should not prevent patients from receiving relief in the acute setting. Hesitancy to make unorthodox choices should not override evidence in medical decision making, and there is adequate evidence to suggest benefit to the patient with minimal to no reported adverse effects. Emergency physicians are skilled in managing

ketamine safely, especially at subanesthetic doses, and are in an ideal position to provide relief as the first physicians to assess these patients. I urge my colleagues to consider incorporating ketamine into the management of patients with acute SI.

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