The Rise of Ketamine in Clinical Practice

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This issue of Psychiatric Annals focuses on ketamine, an exciting advance in the treatment of depression that has been sitting right under our noses for 50 years. The preponderance of research and development in the past 5 decades has focused on drugs with monoaminergic targets. These drugs have saved millions of lives but, sadly, are only moderately effective, take weeks to months to take effect, and leave up to one-third of patients with unresolved symptoms despite multiple trials.1 Enter ketamine, a drug synthesized in 1962, but only recently studied and employed for off-label use in mood and anxiety disorders.2–4

Ketamine is US Food and Drug Administration-approved as an off-label medication for use in some mainstream procedures;5 however, it is not FDA-approved for psychiatric disorders such as depression and bipolar depression. Ketamine has served as a general anesthetic in humans and animals (battlefield/trauma settings as an acute analgesic, pediatric procedural anesthetic, burn unit analgesic, treatment of complex regional pain syndrome) since approval in 1970. Unlike other antidepressants, ketamine has the potential to safely reduce symptoms of depression and suicidality within hours of a single, low-dose infusion. Perhaps this is due to the diversity of its mechanism. Ketamine has glutamatergic, monoaminergic, and opioid targets, as well as anti-inflammatory and dissociative properties.6–8

The first article, “Ketamine and Its Pharmacologic Profile in Psychiatric Disorders,” by Dr. Anand Dugar and colleagues focuses on important considerations of safety in the administration of ketamine. When given slowly in low intravenous doses, in a properly supervised medical setting, by well-trained medical providers, ketamine has a favorable safety profile.

In the second article, “Ketamine Treatment for Mood Disorders,” Dr. Andrew Klise and colleagues recount ketamine’s history, early development, and its mechanism of action. The article also discusses the research and application of ketamine for unipolar and bipolar depression, as well as suicidal thinking.

The next article, “Considering Ketamine for Treatment of Comorbid Pain, Depression, and Substance Use Disorders,” by Dr. Marc F. Ettenson and colleagues explores applications in pain disorders and substance use disorders, including the potential for ketamine to assist in the current opioid crisis. Ketamine’s use in these areas predates the widespread application to mood and anxiety disorders, which often present comorbidly.

In the final article, “Beyond Depression: Ketamine and Glutamatergic Agents for PTSD, OCD, and Other Potential Applications,” Dr. John W. Dougherty III and colleagues look beyond depression to the potential applications of ketamine in other psychiatric disorders. The article also examines preliminary evidence in traumatic brain injury, autism spectrum disorders, and eating disorders.

There are many unanswered questions in the psychiatric applications of ketamine. Many are appraised, but not answered in a recent American Psychiatric Association publication.9 Ultimately, given the limitations of funding large-scale trials for a generic medication, the most effective way to measure the long-term safety and effectiveness of ketamine is through further research and clinical trials.
of ketamine will come from a patient registry. In the meantime, ketamine may serve as a beacon of hope in the face of stagnation in the development of novel, rapidly acting treatments for depression and other mental health conditions.

REFERENCES


