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# **Ketamine Therapy Goes Mainstream: How Clinics are Meeting the Growing Demand**

*Jack Buckanavage, Randall W. Lee, MD*

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Ketamine clinics have quickly become one of the hottest trends in medicine. Industry leader Dr. Patrick Oliver, a board-certified emergency medicine physician and medical director of MindPeace Clinics, began providing ketamine infusions in 2017. “When I started in 2017, I was about the 25th [clinic] in the nation. Now, there’s somewhere around 750-1,000 clinics.”

With a quick click, one can find nearby ketamine clinics through GPS locators on the Internet. For many providers who deal with medication titrations, ketamine provides a sliver of optimism for those struggling to feel clinical improvement after multiple medication failures. Classically, psychiatric illnesses, namely depression, have been treated with medications that typically require weeks to months to achieve symptom control. Ketamine, on the other hand, can provide rapid improvement in those simply struggling to attain clinical benefits or those dealing with acute psychiatric emergencies within six to ten infusions.

Ketamine was developed in Detroit in the 1950s in the search for an anesthetic that provided simultaneous analgesia<sup>1</sup>. This new synthetic analog of phencyclidine (PCP) was more desirable than its predecessor for its favorable side effect profile while still retaining the same anesthetic and analgesic properties. Early research uncovered its short duration of action and mind-altering properties, a characteristic that led to its abuse starting in the 1970s. Further research elucidated its effect via NMDA receptor antagonism, AMPA receptors, and its tyrosine kinase activity.<sup>1,2</sup> According to Dr. Oliver, this mechanism allows for neuroplasticity, specifically

the regrowth of dendritic spines. “Ketamine is like the keys that start the car. It basically tells the nerves to grow synapses that were not present before.”

Despite its regular use as an anesthetic in the operating room, ketamine’s illicit use clouded its public perception and led to it being labeled as a DEA-controlled schedule class III substance, defined as a substance with low-moderate physical abuse potential and/or high psychological abuse. For reference, oxycodone and fentanyl are scheduled as class II substances, and benzodiazepines are class IV substances.

In the early 2000s, mental health professionals saw anecdotal evidence of ketamine providing rapid relief in treatment-resistant depression. Soon after, clinical trials repeatedly supported this benefit,<sup>3,4</sup> leading to its FDA approval for depression in 2019. Off-label, ketamine has been reported to provide benefit in a multitude of conditions such as anxiety, PTSD, and chronic pains.<sup>5</sup> This provided a foundation for the rapid expansion of ketamine clinics seen in the United States today.

According to Dr. Oliver, “a typical treatment can last anywhere from 6-10 treatments, depending on their response. And for those where symptoms return, a single booster is also available.” In doing so, ketamine provides a rapid-acting treatment for depression without the need for daily medication, a stark contrast from the arduous process of medication titration that can plague those suffering from mental illness. As of right now, major depression is typically treated with either a selective serotonin reuptake inhibitor, SSRI, or a serotonin-norepinephrine reuptake inhibitor, SNRI. However, according to Dr. Oliver, “with suicidal ideation, there is no standard of care. What we’re doing is giving SSRIs/SNRIs, which do not work, and have been shown to induce or worsen suicidal ideations in some [younger] patients”. The favorability of ketamine is exemplified by the recent research demonstrating clinical improvements and

increased patient satisfaction rates with ketamine use for depression.<sup>6</sup> As expected, these benefits have sparked a demand for ketamine infusions, prompting the explosion of clinics across the United States.

After the advent of ketamine in the treatment of depression, the application of this therapy is being trialed in other mental health diseases.<sup>5</sup> Ketamine has now been shown to be effective in treating bipolar disorder, social and general anxiety disorder, obsessive-compulsive disorder, post-traumatic stress disorder, substance use disorders, and eating disorders.<sup>5</sup>

On top of these chronic disorders, ketamine has been shown to decrease acute suicidal ideation in a matter of hours. A comprehensive systematic review showed a moderate-severe decrease in suicidal ideation within 4 hours of ketamine treatment, although the authors admit to the risk of bias in underlying studies.<sup>6</sup> In Dr. Oliver's peer-reviewed article, which includes patients suffering from treatment-resistant depression, the findings were even more staggering: a 75% decrease in suicidal ideation after ten infusions ( $p < .001$ ).<sup>7</sup> His study also showed significant symptom response and remission with increased success with 10+ infusions.

Despite its positive treatment response for mental health, intravenous ketamine remains a largely uninsured treatment option, proving a significant barrier to many lower socio-economic patients who seek help. Hopefully, as providers and insurance plans become more comfortable with ketamine's use to treat depression and related diseases, insurance companies will begin to reimburse. And if insurance companies reimburse, ketamine will become mainstream in medicine, if it's not already.

*The authors have no conflicts to report.*

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