

KEEPING UP WITH KETAMINE

- Q:** Recently, I have heard of ketamine (Ketalar®) being used for the treatment of depression or pain. Can ketamine be used for these indications, and are there any concerns for abuse? Does Aegis offer testing for ketamine?
- A:** At this time, ketamine has not been approved by the Food and Drug Administration (FDA) for use in treatment-resistant depression or chronic pain, despite current off-label uses for both indications. Ongoing clinical trials have revealed rapid and substantial antidepressant effects following ketamine infusions. However, these effects are not sustained over a long period of time. While studies have demonstrated analgesic effects of ketamine, inconsistencies in dosing regimens and therapeutic responses have led to inconclusive results. Ketamine is currently available as an add-on test in urine.

Ketamine is a noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist. It is FDA approved for the induction and maintenance of anesthesia.¹ When used for this indication, ketamine induces a “dissociative anesthesia” characterized by involuntary movement and spontaneous breathing.² At lower doses, ketamine provides pain relief without producing anesthesia.¹ Ketamine is commercially available as an injectable solution, although it can be administered orally, topically, intranasally, and rectally.^{2,3}

Ketamine is a Schedule III controlled substance with a long history of abuse dating back to the 1970s and remains popular as a “club drug” today.⁴⁻⁵ In the 2015 Monitoring the Future survey, ketamine abuse was prevalent among 1.4% of 12th graders in the United States.⁶ Psychostimulant effects of ketamine are dose dependent and include hallucinations, perceptual disturbances, and dissociative states. Ketamine may be abused through snorting, smoking, injecting or ingesting orally. At high doses, users experience feelings of complete sensory detachment often referred to as “K-hole.” During these sensory distortions, users describe out of body experiences and an altered perception of time and space.⁴⁻⁵ While the psychoactive effects of ketamine last approximately an hour, modifications of the user’s senses, judgment, and coordination may persist for up to 24 hours.⁵

Clinically, antidepressant effects have been observed in multiple studies following a low dose ketamine infusion. Zarate et al reported significant improvement over placebo in depression symptoms within 110 minutes. At one day post-infusion, 71% and 29% met response and remission criteria, respectively. Response was maintained for a week in 35% of subjects.⁷ Thakurta and colleagues reported significant improvement at 80 minutes post-infusion and found 77% of subjects met response criteria at one day post-infusion with no subjects meeting remission criteria; response was maintained for a week in 13% of patients.⁸ Common side effects noted in these studies were perceptual disturbances, increased blood pressure, euphoria, confusion, headache and dizziness. While these findings are promising, one limitation is that the antidepressant effects of ketamine have not been sustained long term. In fact, participants typically returned to their baseline depressive state seven days after treatment.⁷⁻⁸ As a result, a recent study focused on extending the duration of ketamine’s effects by administering ketamine three times a week over the course of 12 days. This dosing regimen extended ketamine’s effects to a median of 18 days following the last infusion.⁹ Limitations of ketamine studies for resistant depression included small sample sizes, lack of active comparators, and the potential for abuse in an already susceptible patient population. Of interest, an intranasal formulation and enantiomer of ketamine, esketamine, is currently being investigated to evaluate its efficacy in treatment-resistant depression against placebo or in combination with other antidepressants.¹⁰

Ketamine's analgesic effects are mainly attributed to its interaction with NMDA receptors. While many studies have been published, results are complicated by the multiple types of pain evaluated, various doses utilized, side effects limiting therapy and inconsistencies in patient outcomes. An additional complicating factor is the subjective nature of pain making it impossible to determine a dose-response association when ketamine is administered for this indication.^{3,11} Consequently, the use of ketamine for the management of chronic pain is still under investigation.

Recently, ketamine clinics have gained popularity and offer treatment for off-labeled indications. The use of ketamine for the treatment of unapproved indications is met with hesitancy as clinical trials have been conflicting and lack long-term data establishing safety and efficacy. The need for additional studies has been identified.¹¹⁻¹² Despite some promise in treating depression and pain in clinical trials, ketamine is not recommended as first line therapy for these indications and requires careful monitoring for adverse effects and substance abuse. At Aegis, samples undergo liquid chromatography/tandem mass spectrometry (LC/MS/MS) analysis to confirm the presence of ketamine. Aegis laboratories will detect ketamine in samples at a threshold of 1 ng/mL, along with dehydronorketamine and norketamine at a threshold of 5 ng/mL. Providers may test for ketamine by requesting this as an add-on test on the Aegis Laboratory Request form.

We would like to thank Prisca Taylor, a recent Pharm.D. student, for authoring this tip.

Please call our clinical scientists at 1-877-552-3232 if you require additional information.

NOTICE: The information above is intended as a resource for health care providers. Providers should use their independent medical judgment based on the clinical needs of the patient when making determinations of who to test, what medications to test, testing frequency, and the type of testing to conduct.

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