Ketamine Infusion Therapy for Psychiatric Disorders and Chronic Pain Management

Practice Considerations

The following considerations are solely for general informational purposes. Certified registered nurse anesthetists (CRNAs) practice in accordance with professional ethics, scope and standards of practice, sound professional judgment, the best available evidence, the best interests of the patient, and applicable law. Consider legal and expert assistance regarding requirements for ketamine infusion therapy, including all federal, state, and local laws and regulations, specific to your practice.

Introduction

Over several decades, research has shown that ketamine has antidepressive properties.[1-3] Ketamine is approved by the U.S. Food and Drug Administration (FDA) for the induction and maintenance of anesthesia, although it is also being used for the management of psychiatric disorders and chronic pain management.[1,4,5] Ketamine has been incorporated into the treatment of psychiatric disorders, such as major depressive disorder (MDD), bipolar disorder, and post-traumatic stress disorder (PTSD), as well as post-operative and chronic pain management.[3,6] Intravenous (IV) ketamine therapy is not a first-line therapy for psychiatric disorders or chronic pain management and may be considered by the patient's interdisciplinary team after failure of standard treatment.

Interdisciplinary Patient-Centered Care

A patient-centered interdisciplinary team approach with consistent, clear communication to coordinate the management plan is necessary to optimize the patient's outcome. Continued screening, management, monitoring, and follow-up of patients with psychiatric issues or chronic pain is important throughout treatment and management.

Clinicians should engage the patient as part of the care team in shared decision making, as well as manage patient and caregiver expectations, with attention to the potential for nonresponse and treatment-emergent adverse events.[7] Through the informed consent process, the patient is made aware of the risks and benefits of proposed treatment and provided information that ketamine infusions for his or her condition is considered an off-label use of the product.[8] Alternative therapies, and their benefits and risks, should also be explained to the patient.[8]

The dose, frequency, and length of ketamine infusion treatment are individualized to each patient's condition, needs, and responsiveness to therapy with input from the interdisciplinary team. Serial infusions appear to be more effective than a single infusion for psychiatric and chronic pain conditions.[3,9,10] Ongoing patient evaluation and communication between the patient and clinicians will help direct the continued course of treatment.

Ketamine Infusion Clinics

Ketamine infusion clinics are becoming more available. These clinics should establish clear protocols and policy for best outcomes and patient safety.[1,11] Even when using low-dose ketamine, considerations include minimizing the potential for adverse events through

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premedication, individualized patient therapy, and monitoring of vital signs and general condition during the peri-infusion period.[10] When developing or joining a ketamine infusion service, clinicians should participate in the establishment of, or review, policies and procedures and check availability of routine and emergency supplies and equipment, as well as appropriately licensed and credentialed staff.

The American Association of Nurse Anesthetists (AANA) has developed a *Ketamine Infusion Therapy Considerations Checklist* for CRNAs who are interested in integrating ketamine infusion therapy into their practice. The checklist and information in this document provide an overview of practice and policy considerations for the use of ketamine infusions as an adjunct treatment for psychiatric disorders and chronic pain.

Safety Profile

Ketamine is a noncompetitive *N*-methyl-D-aspartate (NMDA) receptor antagonist. Ketamine's interaction with the NMDA receptor is important in anesthesia, because these receptors play a key role in central sensitization.[3] Ketamine has different binding sites such as opioid, monoaminergic, cholinergic, nicotinic and muscarinic receptors. The NMDA receptor, as a glutamate-dependent mechanism, is responsible for the pharmacologic properties.[6] Ketamine is eliminated through the kidneys and has an elimination half-life of 2-3 hours.[3] Following elimination, ketamine continues to have a prolonged effect.

Although low (sub-anesthetic) doses administered once or in a series of infusions has been shown as safe, the safety profile of prolonged ketamine use has not been established.[12] One of ketamine's positive features is the minimal effect on the central respiratory drive if given slowly, although rapid IV injection may cause transient apnea.[13] Ketamine is associated with very few drug-drug interactions and no contraindications are currently known to exist when combined with antidepressants, benzodiazepines, or other psychotropic medications.[14]

The most common side effects include psychotomimetic, dissociative psychiatric symptoms, confusion, inebriation, dizziness, euphoria, elevated blood pressure, and increased libido.[3,9,12,15,16] Ketamine can also have deleterious effects on liver and urinary tract function.[10] There may be a greater risk of ketamine-induced liver injury when infusions are prolonged or repeated over a short timeframe.[10] A clear monitoring plan should be in place to avoid or manage adverse events.[17]

Abuse/Addiction Properties

Ketamine abuse and diversion is a widely recognized problem in several countries in Europe and Asia, as well as in the United States.[18] Widespread use in the outpatient setting could produce physiological and psychological dependence on ketamine.[18] Appropriate patient screening should be conducted and caution taken when administering ketamine infusions due to the risk of abuse, addiction, or complications of long-term use.[4,12,19] Proper drug disposal measures are recommended to prevent the drug from being obtained illicitly.[3,20]

Use for Psychiatric Disorders

Because major psychiatric disorders, such as MDD, are among the most disabling mental, neurological, and substance use-related illnesses, new therapeutic approaches are being considered to treat or delay the onset of these disorders.[21]

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Ketamine infusions have been used as an adjunct to psychiatric treatment and can offer substantial short-term resolution of symptoms, although long-term resolution has not been noted.[11,22] IV low-dose ketamine can induce rapid and robust, although temporary, antidepressive effects, even in treatment-resistant patients who do not respond to electroconvulsive therapy.[2,6,11,16,18,19,23] Studies have shown that ketamine infusion reduces depressive symptoms and suicidal thoughts within a 30-40 minute period in approximately 60-75 percent of patients.[24]

Ketamine can effectively ameliorate symptoms of patients suffering from PTSD.[3,14] Feder et al. demonstrated that a single dose of ketamine, compared with a psychoactive placebo control medication, was associated with a rapid reduction in core PTSD symptoms and the benefit was often maintained beyond 24 hours, with some patients continuing to see reduced symptoms at two weeks.[14]

Use for Chronic Pain Treatment

Chronic pain is most effectively treated using a patient- centered, interdisciplinary, multimodal approach.[25,26] Ketamine may be used for chronic pain management for a range of disorders, including complex regional pain syndrome (CRPS), ischemic limb pain, phantom limb pain, fibromyalgia, and other neuropathic conditions.[3,10,15,22,25] Ketamine has also been shown to treat depression and anxiety in the context of chronic pain and other chronic illnesses.[6,27] As part of a multimodal approach, ketamine is not considered as the first or second choice in treatment for neuropathic pain, irrespective of the cause.[25] Since potential long-term effects on memory and cognition in chronic pain patients require further study, ketamine should be restricted to patients with therapy-resistant neuropathic pain, such as in refractory CRPS pain.[25]

Ketamine may have a role as an opiate adjunct for cancer pain, primarily of neuropathic origin, and may be a treatment option for patients who cannot tolerate opioids or those with problems with opioid responsiveness.[3] Ketamine can reduce the incidence and severity of opioid side effects, which is an important factor in patient compliance.[25] For example, an opioid-ketamine combination may be effective in non-neuropathic pain or in mixed nociceptive/neuropathic pain.[25]

Clinical Competency and Continuous Quality Improvement

CRNAs are educated and may be credentialed to manage acute and chronic pain, administer ketamine, assess the patient, and manage any associated side effects or complications.[28] CRNAs assess the addition of new activities to their practice and practice in accordance with their professional scope of practice, federal, state, and local law, and facility policy.[28,29] CRNAs participate with their practice team to develop policy and required competencies for the administration and monitoring of ketamine infusion therapy. The interdisciplinary team also engages in ongoing staff education, as well as continuous quality improvement and research to improve processes and patient outcomes.

Conclusion

The clinical use of ketamine infusion therapy for psychiatric disorders and chronic pain management continues to evolve. Clinicians, including CRNAs, should continue to contribute and monitor the development of related science, as well as engage in publication of new research on this topic.

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