Ketamine Infusion Clinics

Ketamine infusion clinics are becoming more available. These clinics should establish clear protocols and policy for best outcomes and patient safety.[1,12] Even when using low-dose ketamine, considerations include minimizing the potential for adverse events through premedication, individualized patient therapy, and monitoring of vital signs and general condition during the peri-infusion period. The involvement of skilled psychiatric mental health nurses in the treatment monitoring of patients receiving IV ketamine is important because of the potential for psychiatric side effects, including but not limited to dissociation, agitation, and out-of-body experiences. When developing or joining a ketamine infusion service, clinicians should participate in the establishment, or review of policies and procedures, and evaluation of the availability of necessary routine and emergency supplies and equipment, as well as appropriately licensed and credentialed staff.

The $PHULFDQ $VVRFLDWLRQ RI 1XUVH $QHVWKHWLVWV has developed the *Ketamine Infusion Therapy Considerations Checklist* for CRNAs and other clinicians 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]

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.[13] 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.[14] 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.[15]

The most common side effects include psychotomimetic, dissociative psychiatric symptoms, confusion, inebriation, dizziness, euphoria, elevated blood pressure, and increased libido.[3,10,13,16,17] Ketamine can also have deleterious effects on liver and urinary tract function.[11] There may be a greater risk of ketamine-induced liver injury when infusions are prolonged or repeated over a short timeframe.[11] A clear monitoring plan should be in place to avoid or manage adverse events.[18]

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.[19] Widespread use in the outpatient setting could produce physiological and psychological dependence on ketamine.[19] 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.[4,13,20] Proper drug disposal measures are recommended to prevent the drug from being obtained illicitly.[3,21]

$PHULFDQ $VVRFLDWLRQ RI 1XUVH $QHVWKHWLVWV | 222 South Prospect Avenue | Park Ridge, Illinois 60068-4001 | AANA.com
Professional Practice Division | 847-655-8870 | practice@aana.com

Use for Psychiatric Disorders

Because major psychiatric disorders, such as MDD, are among the most disabling mental, neurologic, and substance use-related illnesses, new therapeutic approaches are being considered to treat or delay the onset of these disorders.[22]

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.[12,23] 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.[2,6,12,17,19,20,24] 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.[25]

Ketamine can effectively ameliorate symptoms of patients suffering from PTSD.[3,15] 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.[15]

Use for Chronic Pain Treatment

Chronic pain is most effectively treated using a patient-centered, interdisciplinary, multimodal approach.[26,27] 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.[3,11,16,23,26] Ketamine has also been shown to treat depression and anxiety in the context of chronic pain and other chronic illnesses.[6,28] 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.[26] 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.[26]

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.[26] For example, an opioid-ketamine combination may be effective in non-neuropathic pain or in mixed nociceptive/neuropathic pain.[26]

Clinical Competency and Continuous Quality Improvement

CRNAs are educated, licensed and may be credentialed to manage acute and chronic pain, administer ketamine, and manage any associated side effects or complications.[29] CRNAs consider the addition of new activities to their practice and practice in accordance with their personal experience and competencies, professional scope of practice, federal, state, and local law, and facility policy.[29,30] CRNAs participate with the interdisciplinary team to develop policy and required competencies for the administration and monitoring of ketamine infusion therapy. Collaborating with psychiatric clinicians involved in the care of patients receiving ketamine infusion for treatment resistant depression and acute suicidality is recommended to support the safe assessment and treatment of patients with these illnesses. The interdisciplinary team also

American Association of Nurse Anesthesiology | 222 South Prospect Ave | Park Ridge, Illinois 60068-4001 | AANA.com
Professional Practice Division I 847-655-8870 I practice@aana.com

engages in ongoing staff education, as well as review of outcomes and other metrics for 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 clinical findings and research on this topic.

References

1. Sisti D, Segal AG, Thase ME. Proceed with caution: off-label ketamine treatment for major depressive disorder. *Curr Psychiatry Rep.* 2014;16(12):527.
2. Williams NR, Schatzberg AF. NMDA antagonist treatment of depression. *Curr Opin Neurobiol.* 2016;36:112-117.
3. Radvansky BM, Puri S, Sifonios AN, Eloy JD, Le V. Ketamine-A Narrative Review of Its Uses in Medicine. *Am J Ther.* 2015.
4. Zhang MW, Harris KM, Ho RC. Is off-label repeat prescription of ketamine as a rapid antidepressant safe? Controversies, ethical concerns, and legal implications. *BMC Med Ethics.* 2016;17:4.
5. Ketamine Hydrochloride: Package Insert and Label Information. http://druginserts.com/lib/rx/meds/ketamine-hydrochloride-1/. Accessed July 15, 2016.
6. Parashchanka A, Schelfout S, Coppens M. Role of novel drugs in sedation outside the operating room: dexmedetomidine, ketamine and remifentanil. *Curr Opin Anaesthesiol.* 2014;27(4):442-447.
7. AANA and APNA Joint Position Statement on Ketamine Infusion Therapy for Psychiatric Disorders. Park Ridge.
8. Bobo WV, Voort JL, Croarkin PE, Leung JG, Tye SJ, Frye MA. Ketamine for Treatment-Resistant Unipolar and Bipolar Major Depression: Critical Review and Implications for Clinical Practice. *Depress Anxiety.* 2016.
9. Informed Consent for Anesthesia Care. Park Ridge, IL: American Association of Nurse Anesthetists; 2016.
10. Rasmussen KG, Lineberry TW, Galardy CW, et al. Serial infusions of low-dose ketamine for major depression. *J Psychopharmacol.* 2013;27(5):444-450.
11. O'Brien SL, Pangarkar S, Prager J. The Use of Ketamine in Neuropathic Pain. *Curr Phys Med Rehabil Rep.* 2014;2(2):128-145.
12. Howland RH. Ketamine for the treatment of depression. *J Psychosoc Nurs Ment Health Serv.* 2013;51(1):11-14.
13. Rasmussen KG. Has psychiatry tamed the "ketamine tiger?" Considerations on its use for depression and anxiety. *Prog Neuropsychopharmacol Biol Psychiatry.* 2016;64:218-224.
14. Gao M, Rejaei D, Liu H. Ketamine use in current clinical practice. *Acta Pharmacol Sin.* 2016.
15. Feder A, Parides MK, Murrough JW, et al. Efficacy of intravenous ketamine for treatment of chronic posttraumatic stress disorder: a randomized clinical trial. *JAMA Psychiatry.* 2014;71(6):681-688.
16. Schoevers RA, Chaves TV, Balukova SM, Rot MA, Kortekaas R. Oral ketamine for the treatment of pain and treatment-resistant depression. *Br J Psychiatry.* 2016;208(2):108-113.

American Association of Nurse Anesthesiology | 222 South Prospect Ave | Park Ridge, Illinois 60068-4001 |
AANA.com Professional Practice Division l 847-655-8870 l practice@aana.com

17. Singh JB, Fedgchin M, Daly EJ, et al. A Double-Blind, Randomized, Placebo-Controlled, Dose-Frequency Study of Intravenous Ketamine in Patients With Treatment-Resistant Depression. *Am J Psychiatry.* 2016.
18. Schak KM, Vande Voort JL, Johnson EK, et al. Potential Risks of Poorly Monitored Ketamine Use in Depression Treatment. *Am J Psychiatry.* 2016;173(3):215-218.
19. Newport DJ, Carpenter LL, McDonald WM, et al. Ketamine and Other NMDA Antagonists: Early Clinical Trials and Possible Mechanisms in Depression. *Am J Psychiatry.* 2015;172(10):950-966.
20. Montes JM, Lujan E, Pascual F, et al. Robust and sustained effect of ketamine infusions coadministered with conventional antidepressants in a patient with refractory major depression. *Case Rep Psychiatry.* 2015;2015:815673.
21. Addressing Substance Use Disorder for Anesthesia Professionals. Park Ridge, IL: American Association of Nurse Anesthesiology; 2016.
22. Fond G, Loundou A, Rabu C, et al. Ketamine administration in depressive disorders: a systematic review and meta-analysis. *Psychopharmacology (Berl).* 2014;231(18):3663-3676.
23. Womble AL. Effects of ketamine on major depressive disorder in a patient with posttraumatic stress disorder. *AANA J.* 2013;81(2):118-119.
24. Nguyen L, Marshalek PJ, Weaver CB, Cramer KJ, Pollard SE, Matsumoto RR. Off-label use of transmucosal ketamine as a rapid-acting antidepressant: a retrospective chart review. *Neuropsychiatr Dis Treat.* 2015;11:2667-2673.
25. Henderson TA. Practical application of the neuroregenerative properties of ketamine: real world treatment experience. *Neural Regen Res.* 2016;11(2):195-200.
26. Niesters M, Martini C, Dahan A. Ketamine for chronic pain: risks and benefits. *Br J Clin Pharmacol.* 2014;77(2):357-367.
27. Chronic Pain Management Guidelines. Park Ridge, IL: American Association of Nurse Anesthesiology; 2014.
28. Moitra VK, Patel MK, Darrah D, Moitra A, Wunsch H. Low-Dose Ketamine in Chronic Critical Illness. *J Intensive Care Med.* 2016;31(3):216-220.
29. Scope of Nurse Anesthesia Practice. Park Ridge, IL: American Association of Nurse Anesthesiology; 2013.
30. Considerations for Adding New Activities to Individual CRNA Scope of Practice. Park Ridge, IL: American Association of Nurse Anesthesiology; 2014.

Adopted by AANA Board of Directors September 2016.
Revised by AANA Board of Directors August 2019.

© Copyright 2019

American Association of Nurse Anesthesiology | 222 South Prospect Ave | Park Ridge, Illinois 60068-4001 |
AANA.com Professional Practice Division l 847-655-8870 l practice@aana.com