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Clinical applications of ketamine: a literature review

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Abstract

Ketamine, initially recognized for its anesthetic capabilities, has emerged as a multifaceted pharmacological intervention with applications extending beyond the surgical setting. This literature review explores the diverse clinical applications of ketamine, delving into its well-established role in anesthesiology and its burgeoning potential in the psychiatric domain. The review discusses ketamine's mechanism of action, emphasizing its unique profile as an NMDA receptor antagonist. Its rapid-acting antidepressant and anti-suicidal effects are highlighted, along with its efficacy in treating conditions like treatment-resistant depression and post-traumatic stress disorder. Additionally, the review examines ketamine's utility in pain management, particularly for acute and chronic pain syndromes. This comprehensive assessment underscores ketamine's evolving role as a valuable tool in both anesthesiology and psychiatry.

Materials and methods

A comprehensive review of the scientific literature was conducted by thoroughly searching the PubMed database to closely examine the most recent findings on the various clinical applications of ketamine. The search was carefully restricted to only include articles published within the last 10 years, with a focus on those that were indexed in PubMed, written

in English, and categorized as high-quality meta-analyses, original research studies, clinical trials, or comprehensive review articles. In order to ensure the most relevant and reliable information was gathered, case reports and non-English language articles were excluded from consideration. The key terms used for searching the database encompassed the broad range of ketamine's clinical uses, including "ketamine," "anesthesia," "critical care," "psychiatry," "depression," and "pain."

Keywords:ketamine, anesthesia, critical care, psychiatry, depression, pain

Introduction

Ketamine is a dissociative anesthetic agent that has been used for over 50 years in clinical practice. Its activity spectrum is unlike any other anesthetic agent because it combines hypnotic, analgesic amnesic effects. [1]In recent years, growing evidence has emerged regarding the potential therapeutic benefits of ketamine in the treatment of various medical and psychiatric conditions, including depression, post-traumatic stress disorder (PTSD), pain management, and critical care. This literature review aims to synthesize the current understanding of the clinical applications of ketamine, highlighting its pharmacological properties, therapeutic indications, and potential limitations.

History

Ketamine was first synthesized in 1962 and introduced for clinical use in 1970 as a safer alternative to phencyclidine (PCP) for general anesthesia. In 2020 S-ketamine was approved for the treatment of adults with treatment resistant major depressive disorder by Food and Drug Administration (FDA) in the form of a nasal spray conjointly with oral antidepressants.[2]

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[1] Gao M, Rejaei D, Liu H. Ketamine use in current clinical practice. Acta Pharmacol Sin. 2016 Jul;37(7):865-72. doi: 10.1038/aps.2016.5. Epub 2016 Mar 28. PMID: 27018176; PMCID: PMC4933765

[2] Lengvenyte, A., Strumila, R., Olié, E., & Courtet, P. (2022). Ketamine and esketamine for crisis management in patients with depression: Why, whom, and how? European Neuropsychopharmacology, 57, 88-104. https://doi.org/10.1016/j.euroneuro.2022.02.004

It is also included in the List of Essential Medicines of World Health Organization (WHO).[3] Unfortunately ketamine has also a long history of illegal use as a "party drug" (street names include: Special "K", KitKat, K) that can cause visual and auditory hallucinations, feeling of detachment from reality, anxiety.[4]

Chemical properties of ketamine

Ketamine is a phencyclidine derivative with a unique chemical structure that confers distinct pharmacological properties. It is a lipophilic compound with a half-life of approximately 2-3 hours. Ketamine exists as a racemic mixture of two enantiomers, R-ketamine and S-ketamine, which exhibit slightly different potencies and effects. [5]The R-enantiomer, R-ketamine, demonstrates a more pronounced antidepressant potential compared to the racemic mixture, while also presenting with fewer side effects commonly associated with the racemic formulation, such as hallucinations and nightmares. In contrast, the S-enantiomer, S-ketamine, is metabolized more rapidly and can produce more intense analgesia, while also leading to fewer instances of delirium during the emergence phase.[5]

Pharmacology of ketamine

Ketamine undergoes hepatic metabolism primarily through multiple cytochrome P450 enzymes, leading to the formation of norketamine, a metabolite with 1/3 to 1/5 the potency of the parent compound. Norketamine is primarily cleared renally. The relatively short elimination half-life of ketamine, ranging from 2-3 hours, contributes to the rapid dissipation of its pharmacodynamic effects, allowing for efficient clearance and reduced risk of prolonged or accumulating side effects[6] However, repeated administration of ketamine can lead to the development of tolerance.[7]

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[3] WHO Model Lists of Essential Medicines https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists [access: 7.07.2024]

[4] DEA Ketamine https://www.dea.gov/factsheets/ketamine [access 7.07.2024]

[5] Das, J. (2020). Repurposing of Drugs–The Ketamine Story. Journal of Medicinal Chemistry. doi:10.1021/acs.jmedchem.0c01193

[6] Walsh, Z., Mollaahmetoğlu, Ö M., Rootman, J M., Golsof, S., Keeler, J L., Marsh, B., Nutt, D., & Morgan, P G. (2021, December 23). Ketamine for the treatment of mental health and substance use disorders: comprehensive systematic review. Cambridge University Press, 8(1). https://doi.org/10.1192/bjo.2021.1061

[7] Kurdi, M. S., Theerth, K. A., & Deva, R. S. (2014). Ketamine: Current applications in anesthesia, pain, and critical care. *Anesthesia, Essays and Researches*, *8*(3), 283-290. https://doi.org/10.4103/0259-1162.143110

Ketamine's primary mechanism of action involves the antagonism of the N-methyl-D-aspartate (NMDA) receptor, a major excitatory neurotransmitter receptor in the central nervous system. This NMDAR antagonism triggers a cascade of downstream effects, including inhibited glutamatergic transmission, activation of synaptic proteins, and the stimulation of neuroplasticity-related signaling pathways. Those effects are responsible for its analgesic and sedative effect but are also hypothesized to contribute to its rapid antidepressant effects.[5]Additionally, ketamine interacts with opioid receptors, voltage-gated L-type calcium channels and the adrenergic receptor system. [8]Furthermore, it has a protective anti-inflammatory effect against the sepsis process by suppressing the induction of nitric oxide synthase activity and protein expression triggered by endotoxins, as well as by suppressing proinflammatory cytokines.[9]

Physiologic effects of ketamine

When administered intravenously at an induction dose of 1-2 mg/kg, ketamine demonstrates a sympathomimetic action, inducing the release of systemic catecholamines and suppressing vagal tone. This pharmacodynamic profile distinguishes ketamine from other anesthetic agents, as it elicits increases in heart rate, blood pressure, and cardiac output, thereby elevating myocardial oxygen demand.[10]Additionally, ketamine increases cerebral blood flow, particularly in the frontal gyrus and dorsolateral prefrontal cortex[11]. Its generates concerns regarding its effects on intracranial pressure (ICP) and ketamine is used cautiously in patients with brain injuries. However, it was shown in numerous publications that ketamine does not increase ICP. [12] [13]Seizure threshold is unaffected by ketamine moreover it is believed to have

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[8] Robinson, B., Gu, Q., & Kanungo, J. (2021). Antidepressant Actions of Ketamine: Potential Role of L-Type Calcium Channels. Chemical Research in Toxicology, 34(5), 1198–1207. doi:10.1021/acs.chemrestox.0c00411

[9] De Kock M, Loix S, Lavand'homme P. Ketamine and peripheral inflammation. CNS Neurosci Ther. 2013 Jun;19(6):403-10. doi: 10.1111/cns.12104. Epub 2013 Apr 10. PMID: 23574634; PMCID: PMC6493703.

[10] Goddard, K B., Sampson, C., Bedy, S., Ghadban, R., & Stilley, J A. (2021, March 31). Effect of Ketamine on Cardiovascular Function During Procedural Sedation of Adults. Cureus, Inc.. https://doi.org/10.7759/cureus.14228

[11] Gärtner, M., Weigand, A., Meiering, M. S., Weigner, D., Carstens, L., Keicher, C., Hertrampf, R., Beckmann, C., Mennes, M., Wunder, A., & Grimm, S. (2023). Region- and time- specific effects of ketamine on cerebral blood flow: A randomized controlled trial. *Neuropsychopharmacology*, *48*(12), 1735-1741. https://doi.org/10.1038/s41386-023-01605-4

[12] Zeiler FA, Teitelbaum J, West M, Gillman LM. The ketamine effect on ICP in traumatic brain injury. Neurocrit Care 2014;21:163–173.

[13] Zeiler FA, Teitelbaum J, West M, Gillman LM. The ketamine effect on intracranial pressure in nontraumatic neurological illness. J Crit Care 2014;29:1096–1106.

antiepileptic activity. [14] It is strong bronchodilatatory agent. It typically preserves spontaneous ventilation with a strong central respiratory drive, upper airway reflexes, and skeletal muscle function. However, transient apnea may occur when a large dose is administered rapidly. Furthermore, ketamine can increase salivation- it is common practice to co-administer atropine to mitigate this effect.[15]

Analgosedation

Ketamine induces a unique state of dissociation, manifested by visual hallucinations, profound pain relief, and a sense of detachment from one's surroundings. Patients may appear alert despite being deeply sedated. The onset of action is rapid and lasts approximately 30 minutes. These distinctive characteristics have established ketamine as a valuable tool in various clinical settings, such as emergency departments, intensive care units, and procedural sedation. [16]Additionally, its dissociative properties can be advantageous in patients with severe pain, such as those with burns or traumatic injuries, as it allows for procedures to be performed without the need for paralysis, which can be particularly beneficial in resource-limited settings like pre-hospital treatment or combat or casualty extraction. [17]

Ketamine is often utilized for rapid induction in hemodynamically unstable patients, including those with cardiac tamponade. Its ability to maintain cardiovascular stability and avoid the negative inotropic effects of other anesthetic agents makes it a preferred choice in such scenarios. However, due to its ability to increase heart rate, ketamine may not be the optimal induction agent for patients with severe aortic stenosis, as the increased heart rate could exacerbate the underlying condition.

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[14] Zanza, C., Piccolella, F., Racca, F., Romenskaya, T., Longhitano, Y., Franceschi, F., Savioli, G., Bertozzi, G., Simone, S D., Cipolloni, L., & Russa, R L. (2022, March 17). Ketamine in Acute Brain Injury: Current Opinion Following Cerebral Circulation and Electrical Activity. Multidisciplinary Digital Publishing Institute, 10(3), 566-566. https://doi.org/10.3390/healthcare10030566

[15] Heinz P, Geelhoed GC, Wee C, Pascoe EM. Is atropine needed with ketamine sedation? A prospective, randomised, double blind study. Emerg Med J. 2006 Mar;23(3):206-9. doi: 10.1136/emj.2005.028969. PMID: 16498158; PMCID: PMC2464444.

[16] Pruskowski, K A., Harbourt, K., Pajoumand, M., Chui, S J., & Reynolds, H N. (2017, November 29). Impact of Ketamine Use on Adjunctive Analgesic and Sedative Medications in Critically Ill Trauma Patients. Wiley-Blackwell, 37(12), 1537-1544. https://doi.org/10.1002/phar.2042

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Pain management

Ketamine's analgesic properties have made it a valuable tool in the management of acute postoperative pain. When administered intravenously in the perioperative setting, ketamine has been shown to reduce opioid consumption and improve pain control, with the added benefit of reducing the risk of opioid-related adverse effects.[18] Hublet et al. showed in their study that opioid free anasthesia using ketamine is possible even in procedures as painful as pancreatic resection.[19]

Ketamine has also demonstrated efficacy in the management of chronic pain. Chronic pain and depression frequently coexist and exacerbate each other's symptoms. Ketamine has emerged as a promising therapeutic option for both conditions, which can contribute to improved overall outcomes. As previously mentioned, ketamine can limit the dosage of opioids required by reducing opioid tolerance and hyperalgesia, factors that can lead to chronic pain. Various dosing regimens for ketamine in chronic pain have been proposed, yielding differing durations of pain relief. For instance, a rapid infusion of 0.5 mg/kg in patients with fibromyalgia resulted in pain relief lasting less than one week, while a regimen suggested by Sigtermans of three infusions with subsequently higher doses over 4 days led to 12 weeks of pain relief. [20] [21]This highlights the importance of considering the appropriate dosing strategy when using ketamine to manage chronic pain, as the duration of pain relief can vary significantly depending on the specific treatment protocol.

Critical care

Beyond postoperative pain, ketamine also holds promise in the critical care setting. At subanesthetic doses, ketamine may be used for analgosedation, providing pain relief and

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[18] Brinck, E., Tiippana, E., Heesen, M., Bell, R F., Straube, S., Moore, R A., & Kontinen, V. (2018, December 20). Perioperative intravenous ketamine for acute postoperative pain in adults. Elsevier BV. https://doi.org/10.1002/14651858.cd012033.pub4

[19] Hublet, S., Galland, M., Navez, J., Loi, P., Closset, J., Forget, P., & Lafère, P. (2022). Opioid-free versus opioid-based anesthesia in pancreatic surgery. *BMC Anesthesiology*, *22*. https://doi.org/10.1186/s12871-021-01551-y

[20] Kiefer RT, Rohr P, Ploppa A, et al. Efficacy of Ketamine in Anesthetic Dosage for the Treatment of Refractory Complex Regional Pain Syndrome: An Open-Label Phase II Study. *Pain Med* 2008;9(8):1173–201

[21] Lii, T. R., & Singh, V. (2023). Ketamine for Complex Regional Pain Syndrome: A Narrative Review Highlighting Dosing Practices and Treatment Response. *Anesthesiology Clinics*, *41*(2), 357. https://doi.org/10.1016/j.anclin.2023.03.005

sedation for example in trauma patients without the respiratory depression often associated with traditional opioid-based regimens. Ketamine's unique pharmacology, including its ability to attenuate the inflammatory response to cardiac surgery, suggests potential applications in the care of critically ill cardiac patients. Ketamine has the potential to be an excellent drug for patients with ventricular assist devices, those requiring veno-arterial extracorporeal membrane oxygenation for cardiogenic shock, and other postcardiac surgery patients with poor ventricular function. The sedative and analgesic properties of ketamine may be particularly beneficial for patients with an open chest and refractory right ventricular failure or those with high opioid requirements who are being weaned from opioids.[22]

Ketamine has been investigated as a potential therapeutic option for managing acute asthma exacerbations, as it has demonstrated the ability to promote relaxation of airway smooth muscle and enhance respiratory function. Furthermore, it has been recognized as the bronchodilator of choice for rescue therapy in cases of refractory bronchospasm in the operating room and refractory status asthmaticus in the intensive care unit setting. [23]

Refractory status epilepticus

Refractory status epilepticus (RSE) is defined as a seizure episode that persists despite adequate administration of antiepileptic medications like midazolam. When anesthetic agents such as propofol are given but the seizure continues, it is referred to as super-refractory status epilepticus (SRSE).

At the molecular level, during RSE, GABA receptors within the synaptic membrane become internalized, while NMDA receptors are upregulated. Ketamine, an NMDA antagonist, can inhibit glutamatergic transmission and thus be utilized in the management of SRSE. A study by Alkhachroum et al. involving 68 patients with SRSE found that high-dose ketamine reduced seizure burden, as measured by invasive multimodality monitoring. Furthermore,

[22] Mazzeffi, M A., Johnson, K M., & Paciullo, C. (2015, January 1). Ketamine in adult cardiac surgery and the cardiac surgery Intensive Care Unit: An evidence-based clinical review. Medknow, 18(2), 202-202. https://doi.org/10.4103/0971-9784.154478

[23] Sakrikar, D G. (2018, April 14). Ketamine- The wonder drug in Status Asthmaticus. , 6(4). https://doi.org/10.18535/jmscr/v6i4.90

ketamine was associated with stable mean blood pressure, decreased vasopressor requirements, and no increase in intracranial pressure.[24]

Pediatric patients

Ketamine has been widely used in pediatric populations for its safety profile, including its preservation of airway reflexes and relatively stable hemodynamic effects. Also children under 16 experience less adverse reactions like delirium or hallucinations than adults. Rapid onset, preserved spontaneous breath and short half-life make it an excellent agent for short dissociative sedation for short painful or emotionally disturbing procedures. [7]

Due its hemodynamic stability it is especially useful in induction of children with congenital heart disease with right to left shunt. It increases systemic vascular resistance and increases pulmonary blood flow improving oxygenation. [7]

Cesarean section pain management and postpartum depression

A recent study by Han et al. in 2022 investigated the use of S-ketamine as an adjuvant in patient-controlled intravenous analgesia (PCIA) after caesarean section and its effect on the prevalence of postpartum depression (PPD). The study included 275 patients who received a transversus abdominis plane block and intravenous paracetamol, followed by spinal anesthesia for the caesarean section procedure. The PCIA regimen consisted of either sufentanil and tropisetron (control group) or sufentanil, tropisetron, and S-ketamine 0.5 mg/kg (experimental group). The results showed that the rate of postpartum depression was significantly lower in the S-ketamine group at days 3 and 14 after the procedure, but similar to the control group at one month, without an increase in adverse events.[25] Additionally, sub-anesthetic doses of ketamine during caesarean section have been demonstrated to reduce opioid consumption and postoperative pain.[2627]A recent 2024 meta-analysis further supported

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[24] Alkhachroum, A., Der-Nigoghossian, C. A., Mathews, E., Massad, N., Letchinger, R., Doyle, K., Chiu, T., Kromm, J., Rubinos, C., Velazquez, A., Roh, D., Agarwal, S., Park, S., Connolly, E. S., & Claassen, J. (2020). Ketamine to treat super-refractory status epilepticus. *Neurology*, *95*(16), e2286. https://doi.org/10.1212/WNL.0000000000010611

[25] Han, Y., Li, P., Miao, M., Tao, Y., Kang, X., & Zhang, J. (2022). S-ketamine as an adjuvant in patient-controlled intravenous analgesia for preventing postpartum depression: A randomized controlled trial. *BMC Anesthesiology*, *22*. https://doi.org/10.1186/s12871-022-01588-7

[26] J. Wang, Z. Xu, Z. Feng, R. Ma, X. Zhang. Impact of ketamine on pain management in cesarean section: a systematic review and meta-analysis

the finding that EPDS (Edinburgh postnatal depression scale- a questionnaire commonly used for PPD assessment) scores for postpartum depression were significantly lower in patients who received ketamine or S-ketamine, although an overall increase in adverse reactions, such as headaches and hallucinations, was observed. [28]These studies highlight the potential bridge between anesthesiology and psychiatry, demonstrating the broad spectrum of ketamine applications.

Psychiatry

Almost all currently used antidepressant drugs act by altering monoamine neurotransmitter systems. While these medications have revolutionized psychiatry, they have limitations, such as delayed onset of action and suboptimal efficacy in a significant subset of patients. Exploring new ways to treat depression is important to mitigate side effects of existing treatments, improve outcomes for those with treatment-resistant depression, and further understand the underlying molecular pathways leading to affective disorders. [5]

Ketamine has been extensively studied for its potential in treating psychiatric disorders, particularly treatment-resistant major depressive disorder and post-traumatic stress disorder. At lower doses, ketamine can rapidly and transiently modify mood and cognition, making it a promising novel intervention for refractory depression. Several Phase 2 and Phase 3 clinical trials have demonstrated the efficacy of ketamine in rapidly improving depressive symptoms, including suicidal ideation, often within hours of administration, offering a promising alternative to traditional antidepressant medications. [29] Notably, a 2020 meta-analysis found no severe psychotic episodes across the analysed studies, and the antidepressive effect of racemic ketamine was found to be more significant and with fewer side effects than S-

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Pain Physician, 23 (2) (2020), pp. 135-148

[27] Haliloglu, M., Ozdemir, M., Uzture, N., Cenksoy, P. O., & Bakan, N. (2015). Perioperative low-dose ketamine improves postoperative analgesia following Cesarean delivery with general anesthesia. The Journal of Maternal-Fetal & Neonatal Medicine, 29(6), 962–966. doi:10.3109/14767058.2015.1027190

[28] Li, S., Zhou, W., Li, P., & Lin, R. (2024). Effects of ketamine and esketamine on preventing postpartum depression after cesarean delivery: A meta-analysis. *Journal of Affective Disorders*, *351*, 720-728. https://doi.org/10.1016/j.jad.2024.01.202

[29] Schenberg, E E. (2018, July 5). Psychedelic-Assisted Psychotherapy: A Paradigm Shift in Psychiatric Research and Development. Frontiers Media, 9. https://doi.org/10.3389/fphar.2018.00733

ketamine. [30] Furthermore, a recent long-term follow-up of patients who received ketamine for treatment-resistant depression during a clinical trial at the National Institute of Mental Health found no reported symptoms of ketamine abuse after the trial, suggesting the potential for safe, long-term use.[31]

Ketamine is also a promising medication for the treatment of substance use disorders. Studies have shown that it can help promote abstinence in individuals struggling with alcohol, heroin, and cocaine dependence. The dissociative and antidepressant-like effects of ketamine may disrupt the addictive behaviours and craving associated with these substances, offering a potential new approach to addiction treatment that could significantly improve patient outcomes. [32]

There is growing interest in the use of ketamine for the treatment of post-traumatic stress disorder (PTSD).[33] The dissociative and antidepressant-like effects of ketamine may help to alleviate the intrusive thoughts, hyperarousal, and avoidance behaviours associated with PTSD.[34]

Concerns and limitations

While ketamine has shown promising therapeutic potential, there are several concerns and limitations associated with its use At higher doses, ketamine can produce psychomimetic effects, such as hallucinations and agitation, which may be problematic in certain clinical settings.[35] It is also associated with an increased risk of postoperative nausea and vomiting

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[30] Bahji, A., & Vazquez, G. H. (2020). Comparative efficacy of racemic ketamine and esketamine for depression: A systematic review and meta-analysis. Journal of Affective Disorders, 278, 542. https://doi.org/10.1016/j.jad.2020.09.071

[31] Hurst, K. T., Vogeley, A., Greenstein, D. K., Durland, L., Makel, S., Wang, P. R., Yavi, M., Zarate, C. A., & Ballard, E. D. (2024). Long-term follow-up of participants in ketamine clinical trials for mood disorders. *Journal of Affective Disorders*, *357*, 134-137. https://doi.org/10.1016/j.jad.2024.04.062

[32] Ivan Ezquerra-Romano, I., Lawn, W., Krupitsky, E., & Morgan, C. J. A. (2018). Ketamine for the treatment of addiction: Evidence and potential mechanisms. Neuropharmacology. doi:10.1016/j.neuropharm.2018.01.017

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[35] Ateş, İ., Aydın, M E., Çelik, E C., Gözeler, M S., & Ahıskalıoğlu, A. (2020, December 9). Perioperative Intravenous Low-Dose Ketamine Infusion to Minimize Pain for

(PONV).[36] Additionally, the optimal dosing regimen for ketamine in various applications remains an area of ongoing research and debate. The antidepressant effect last only about 7 days so it needs to be repeated periodically. Additionally, ketamine has a potential for abuse and dependence, which must be carefully managed, particularly in the context of its off-label use. It also has toxic effect on urinary tract causing ketamine cystitis in patients who use this drug illegally.[37] Chronic ketamine abusers were also shown to have reduction in thickness of cortex of the brain.[38] Furthermore, the long-term effects of ketamine, including its impact on cognitive function and overall health, remain largely unknown and require further investigation. It is especially important for it potential prolonged usage in managing chronic pain or depression.

Ketamine Side Effect Tool (KSET)

As illustrated in the preceding discussion, ketamine is being utilized in diverse clinical settings to address a range of distinct conditions. To ensure the safe and effective administration of ketamine by healthcare professionals, a clinical tool known as the Ketamine Side Effect Tool (KSET) has been developed. The KSET aims to capture information on adverse effects and assist in clinical decision-making. It consists of four separate forms: Screening, Baseline, Acute Treatment, and Follow-Up. Collectively, these forms are designed to facilitate the identification and evaluation of contraindications for ketamine administration, baseline symptoms, acute side effects, delayed side effects, and the presence of side effects during long-term follow-up.[39] For clinicians routinely employing ketamine in their practice, the KSET can serve as a valuable and comprehensive tool.

Conclusion

Septorhinoplasty: A Prospective, Randomized, Double-Blind Study. SAGE Publishing, 100(4), 254-259. https://doi.org/10.1177/0145561320974860

[36] Gorlin, A., Rosenfeld, D M., & Ramakrishna, H. (2016, January 1). Intravenous sub-anesthetic ketamine for perioperative analgesia. Medknow, 32(2), 160-160. https://doi.org/10.4103/0970-9185.182085

[37] Myers, F. A.; Bluth, M. H.; Cheung, W. W. Ketamine: a cause of urinary tract dysfunction. Clin. Lab. Med. 2016, 36, 721-744.

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Given the robust body of evidence on ketamine's diverse clinical applications, it is unsurprising that the compound has garnered significant interest across various medical disciplines. The growing body of research highlights the potential therapeutic benefits of ketamine in various medical and psychiatric domains, including pain management, critical care, depression, and post-traumatic stress disorder. However, further research is needed to fully elucidate the long-term effects and optimal dosing regimens of ketamine, as well as to address the concerns and limitations associated with its use.

Statement of the author's contribution

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