



## Overview on Drug of Abuse: Ketamine

Ankita Dudhal, Shrenik Dugarwal, Vinod Thakare

Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune, India.

Received: 2024-10-05

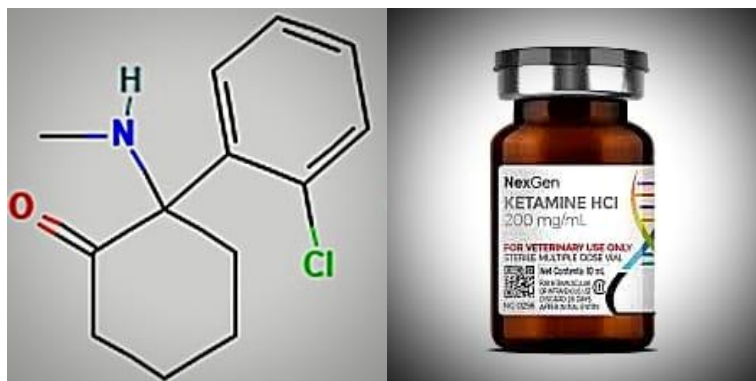
Revised: 2024-10-15

Accepted: 2024-10-20

### ABSTRACT

Ketamine is known for its dissociative anaesthetic properties and hallucinogenic effects. It can distort perceptions of sight and sound, leading to feelings of disconnection from one's surroundings. Commonly administered as an injectable, ketamine is a short-acting anaesthetic used for inducing sedation, immobility, pain relief, and amnesia in both humans and animals. However, it is often misused for its dissociative and hallucinogenic effects, and has unfortunately been used in instances of sexual assault. The term "dissociative anaesthetic" describes its ability to create a sense of detachment from pain and the environment. Ketamine, a less toxic alternative to phencyclidine, was developed decades ago. It is now approved by the FDA for treatment-resistant depression in adults. Esketamine, a derivative of ketamine, is also available as a liquid or off-white powder, known as Special K, K, super K, or Vitamin K. In this review paper we are mainly going to review origin, chemical and physical properties, mechanism of action, side effects of Ketamine. Also we are going to review 'Drug Abuse'.

**KEYWORDS:** Ketamine abuse, NMDA Receptor Antagonist, History, Mechanism of action, Legal Status.



Ketamine (chemical structure and marketed preparation) Fig. no. (1)

### INTRODUCTION:

Ketamine is a Schedule III non-narcotic medication used by doctors to induce loss of consciousness. It is approved by the FDA for general anaesthesia but can also be prescribed for "off-label" uses like depression. Some people use ketamine for its hallucinogenic properties, which can cause sedate, incapacitate, and short-term memory loss, making it a date-rape drug.<sup>(1)</sup> While ketamine is safe for controlled medical use, it becomes hazardous for recreational use due to potential life-threatening adverse effects. It is important to understand its uses, side effects, risks, and interactions with alcohol and other drugs.<sup>(2)</sup>

Ketamine, a cyclohexanone, is a compound with a 2-chlorophenyl and methylamino group substituting hydrogens at position 2. It serves as an anaesthetic, NMDA receptor antagonist, analgesic, neurotoxin, environmental contaminant, and xenobiotic. It is a secondary amino compound and a member of monochlorobenzenes.<sup>(3)</sup>

### HISTORY OF KETAMINE AND ITS COMMON NAMES:

Medical professionals have been researching post-surgery pain treatment methods for over 50 years. Ketamine, once used as an anesthetic, has been found to treat various mental health conditions. Recent scientific breakthroughs have led to the discovery of new treatment options, highlighting the potential of ketamine in various medical and psychological applications.<sup>(4)</sup> In 1962,

ketamine, a structural analog of PCP, was synthesized and tested on volunteer prisoners in 1964. Results showed similar anesthetic and analgesic properties to PCP but fewer adverse side effects. Ketamine was characterized as a dissociative anesthetic, with participants experiencing feelings of floating in outer space and dying.<sup>(5)</sup>

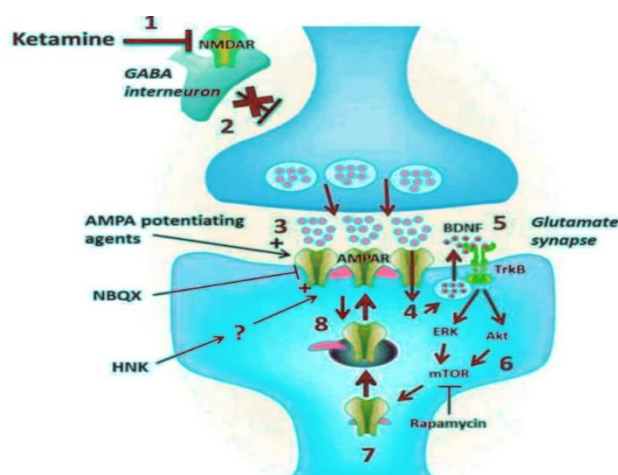
Common names: Ketalar, Ketavet and Ketamine Hydrochloride Injection, Special K, K, Kit Kat, Cat Valium, Super Acid, Special La Coke, Purple, Jet, and Vitamin K.<sup>(1)</sup>

### NEUROBIOLOGY OF KETAMINE ABUSE:

Ketamine, initially anesthetic, is now recognized for its therapeutic effects, especially in treatment-resistant depression, but also has high abuse potential leading to neurobiological changes. Here's a detailed look at the neurobiology of ketamine abuse:

Mechanism of action: Ketamine, a neurotransmitter, acts as an NMDA receptor antagonist, blocking glutamate, reducing excitatory signaling and providing anesthetic and dissociative effects, but its effects extend beyond the NMDA receptor.<sup>(6)</sup> It also influences other receptors and pathways, including:

- AMPA receptors: Ketamine's antidepressant effects are attributed to its indirect increase in activity at AMPA receptors.<sup>(7)</sup>
- Opioid receptors: The substance may interact with opioid receptors, enhancing its analgesic properties and increasing its potential for abuse.<sup>(8)</sup>
- Dopamine system: Ketamine enhances dopamine release in the brain's reward pathways, particularly in the nucleus accumbens, which is crucial for reinforcing drug-taking behavior.<sup>(9)</sup>



**Mechanism of action of Ketamine**

Fig. no. (2)

### OVERDOSE EFFECT OF KETAMINE:

Ketamine overdose can be life-threatening, causing various symptoms based on the dose, administration route, and individual's tolerance and overall health, depending on the severity. Here's an overview of the effects and clinical manifestations of a ketamine overdose:

1. Neurological and Psychological Effects: Ketamine overdose can cause extreme dissociation, known as a "K-hole," characterized by intense hallucinations and out-of-body experiences.
2. Cardiovascular Effects:
  - Ketamine can significantly elevate blood pressure, which can pose a significant risk, particularly in individuals with pre-existing cardiovascular conditions.



• Elevated heart rate is a common issue, and in severe cases, it can lead to arrhythmias, irregular heartbeats that can be life-threatening.<sup>(10)</sup>

**3. Respiratory Effects:** Ketamine, a less common sedative, can cause respiratory depression and, in severe cases, complete cessation of breathing.

**4. Death:** Ketamine overdose is rare, but can occur when combined with other depressants like alcohol, benzodiazepines, or opioids, causing respiratory and cardiovascular depression.<sup>(11)</sup>

**CLINICAL MANAGEMENT:** Treatment of ketamine overdose primarily involves supportive care:

• **Airway Management:** The task involves maintaining an open airway and ensuring adequate breathing, potentially utilizing oxygen or mechanical ventilation if necessary.

• **Cardiovascular Support:** The process involves monitoring and stabilizing blood pressure and heart rate, potentially using medications to manage hypertension or arrhythmias.

• **Activated Charcoal:** Early detection of an overdose can be achieved by administering activated charcoal to restrict absorption in the gastrointestinal tract.<sup>(11)</sup>

#### **WITHDRAWAL SYMPTOMS OF KETAMINE:**

Ketamine withdrawal occurs when a person stops or significantly reduces their ketamine intake, often leading to psychological and physical withdrawal symptoms. These symptoms vary in intensity depending on the duration and frequency of use, as well as the individual's overall health and tolerance, and are not typically associated with severe physical dependence like opioids or alcohol.<sup>(12)</sup>

##### **1. Psychological Symptoms:**

• **Anxiety:** Users may experience increased anxiety, restlessness, and nervousness after stopping ketamine, which is a common withdrawal symptom.

• **Depression:** Ketamine withdrawal can cause depressive symptoms like low mood, hopelessness, and motivation, especially for those who self-medicate for depression.<sup>(12)</sup>

• **Cravings:** Individuals may experience intense cravings for ketamine, making it challenging to resist the urge to re-use the drug.

##### **2. Physical Symptoms:**

• **Fatigue:** Ketamine withdrawal can lead to significant fatigue and lethargy in many individuals.

• **Tremors:** Ketamine withdrawal can lead to significant fatigue and lethargy in many individuals.

• **Sweating:** Excessive sweating, particularly at night, may be a physical symptom of withdrawal.<sup>(13)</sup>

#### **DURATION OF WITHDRAWAL:**

Ketamine withdrawal symptoms can begin within hours to a day after the last dose, with the acute phase lasting a few days to a week. However, psychological symptoms like anxiety, depression, and cravings may persist for weeks or even months, especially if there is an underlying mental health disorder.<sup>(13)</sup>

#### **TREATMENT OF KETAMINE DRUG ABUSE:**

Ketamine abuse treatment involves a holistic approach that addresses both physical and psychological aspects, involving detoxification, behavioral therapies, and ongoing support to prevent relapse. Here's an overview of the main strategies used in the treatment of ketamine abuse:



1. **Detoxification:** Detoxification is the initial treatment for ketamine abuse, allowing the drug to be eliminated under medical supervision. This process may involve:

- **Medical Supervision:** Medical supervision during ketamine withdrawal helps manage discomfort and monitor complications, providing supportive care like hydration, nutrition, and sleep management.<sup>(14)</sup>
- **Symptom Management:** Medications can be prescribed to manage withdrawal symptoms like anxiety, insomnia, or agitation, but no specific medications are approved for ketamine withdrawal.

2. **Behavioral Therapies:** Behavioral therapies are the primary method for treating ketamine addiction, focusing on addressing the psychological and behavioral aspects of the addiction and promoting healthier coping mechanisms.

- **Cognitive-Behavioral Therapy (CBT):** CBT is a widely used treatment for addiction, assisting individuals in identifying and changing negative thought patterns, behaviors, and coping strategies to manage cravings and prevent relapse.
- **Motivational Interviewing (MI):** MI is a counseling method that motivates individuals to change their behavior by encouraging self-reflection and fostering a desire to quit ketamine and seek treatment.
- **Dialectical Behavior Therapy (DBT):** DBT, a combination of Cognitive Behavioral Therapy and mindfulness techniques, is particularly effective for individuals with co-occurring mental health disorders like borderline personality disorder or depression.<sup>(14)</sup>

3. **Holistic and Complementary Therapies:** Holistic approaches, which consider the physical, emotional, and spiritual aspects of recovery, can be beneficial for some individuals.

- **Mindfulness and Meditation:** Mindfulness meditation is a practice that aids individuals in managing stress, reducing cravings, and maintaining focus on their recovery goals.
- **Exercise and Nutrition:** Physical activity and a healthy diet can enhance overall well-being, support mental health, and decrease the likelihood of relapse.<sup>(15)</sup>

## LEGAL STATUS OF KETAMINE IN INDIA :

Ketamine is a controlled substance in India under the Narcotic Drugs and Psychotropic Substances (NDPS) Act of 1985. Here's a detailed overview of its legal status:

### 1. Classification:

- **Psychotropic Substance:** Ketamine, classified as a psychotropic substance under the NDPS Act, is subject to government regulation in its production, distribution, sale, and use.

### 2. Medical Use:

- **Permitted for Medical Purposes:** Ketamine, a widely used anesthetic in human and veterinary medicine in India, is legally available for medical use but is strictly regulated and only authorized by licensed practitioners.
- **Prescription Requirement:** Ketamine is a drug that requires a valid prescription from a licensed healthcare provider and is illegal for unauthorised possession or use.<sup>(16)</sup>

### 3. Control and Regulation:

- **Licensing:** Ketamine production, distribution, and sale require government-issued licenses, ensuring its use only for legitimate medical or scientific purposes under strict conditions.
- **Record-Keeping:** Ketamine production and distribution entities are required to maintain detailed records of its use, including production, sales, and administration.<sup>(17)</sup>



#### 4. Penalties for Illegal Use:

- **Illegal Possession:** Ketamine possession without a prescription or license is a criminal offense under the NDPS Act, with penalties ranging from imprisonment to fines depending on the quantity involved.
- **Trafficking and Distribution:** Ketamine trafficking, distribution, or production leads to severe penalties like long-term imprisonment and heavy fines, with the severity increasing with the substance quantity involved.<sup>(18)</sup>

#### 5. Abuse and Recreational Use:

- **Illegal and Punishable:** The Indian government is enforcing the law against the illegal recreational use of ketamine due to its potential for abuse and addiction.
- **Law Enforcement:** India's law enforcement agencies are actively monitoring and enforcing regulations related to ketamine to curb its illicit use and distribution.<sup>(18)</sup>

#### 6. Recent Developments:

- **Stricter Regulations:** India has increased monitoring and control measures to prevent the diversion of ketamine for recreational use due to concerns about its abuse potential over the years.

#### CONCLUSION:

Ketamine abuse is a global public health concern due to its potent dissociative and hallucinogenic effects, causing physical, psychological, and social harm. Despite its medical uses, its potential for abuse and addiction is a global concern.

Ketamine abuse poses significant risks to individuals and society, necessitating robust preventive measures, effective treatment strategies, and ongoing research. Public awareness, education, and accessible treatment are crucial for addressing the challenges and helping those affected recover and lead healthier lives.

#### REFERENCES:

1. Morgan, Celia J. A., H. Valerie Curran, and the Independent Scientific Committee on Drugs (ISCD). "Ketamine Use: A Review." *Addiction* 107, no. 1 (January 2012): 27–38.
2. Sassano-Higgins, Sean, Dave Baron, Grace Juarez, Neevon Esmaili, and Mark Gold. "A REVIEW OF KETAMINE ABUSE AND DIVERSION: Review: Ketamine." *Depression and Anxiety* 33, no. 8 (August 2016): 718–27.
3. Marraffa, J.M. "Drugs of Abuse." In *Encyclopedia of Toxicology*, 248–51. Elsevier, 2014.
4. Domino, Edward F., and David S. Warner. "Taming the Ketamine Tiger." *Anesthesiology* 113, no. 3 (September 1, 2010): 678–84.
5. Chang, Lee C., Suman Rajagopalan, and Sanjay J. Mathew. "The History of Ketamine Use and Its Clinical Indications." In *Ketamine for Treatment-Resistant Depression*, edited by Sanjay J. Mathew and Carlos A. Zarate, 1–12. Cham: Springer International Publishing, 2016.
6. Aleksandrova, Lily R., Anthony G. Phillips, and Yu Tian Wang. "Antidepressant Effects of Ketamine and the Roles of AMPA Glutamate Receptors and Other Mechanisms beyond NMDA Receptor Antagonism." *Journal of Psychiatry and Neuroscience* 42, no. 4 (July 1, 2017): 222–29.
7. Abdallah, Chadi G., Gerard Sanacora, Ronald S. Duman, and John H. Krystal. "The Neurobiology of Depression, Ketamine and Rapid-Acting Antidepressants: Is It Glutamate Inhibition or Activation?" *Pharmacology & Therapeutics* 190 (October 2018): 148–58.
8. Krystal, John H., Alfred P. Kaye, Sarah Jefferson, Matthew J. Girgenti, Samuel T. Wilkinson, Gerard Sanacora, and Irina Esterlis. "Ketamine and the Neurobiology of Depression: Toward next-Generation Rapid-Acting Antidepressant Treatments." *Proceedings of the National Academy of Sciences* 120, no. 49 (December 5, 2023): e2305772120.
9. Shinohara, Ryota, George K. Aghajanian, and Chadi G. Abdallah. "Neurobiology of the Rapid-Acting Antidepressant Effects of Ketamine: Impact and Opportunities." *Biological Psychiatry* 90, no. 2 (July 2021): 85–95.
10. Chaves, Tharcila V., Bob Wilffert, and Zila M. Sanchez. "Overdoses and Deaths Related to the Use of Ketamine and Its Analogues: A Systematic Review." *The American Journal of Drug and Alcohol Abuse* 49, no. 2 (March 4, 2023): 141–50.
11. Green, Steven M, Richard Clark, Mark A Hostetler, Michael Cohen, Douglas Carlson, and Steven G Rothrock. "Inadvertent Ketamine Overdose in Children: Clinical Manifestations and Outcome." *Annals of Emergency Medicine* 34, no. 4 (October 1999): 492–97.



12. Chen, Lian-Yu, Chih-Ken Chen, Chun-Hsin Chen, Hu-Ming Chang, Ming-Chyi Huang, and Ke Xu. "Association of Craving and Depressive Symptoms in Ketamine-Dependent Patients Undergoing Withdrawal Treatment." *The American Journal on Addictions* 29, no. 1 (January 2020): 43–50.
13. Roxas, Nichole, Chaarushi Ahuja, Jessica Isom, Samuel T. Wilkinson, and Noah Capurso. "A Potential Case of Acute Ketamine Withdrawal: Clinical Implications for the Treatment of Refractory Depression." *American Journal of Psychiatry* 178, no. 7 (July 2021): 588–91.
14. Barik, Amiya K, Rajeev Chauhan, Ashwini Reddy, and Narender Kaloria. "Concerns on the Use of Ketamine in the Treatment of Depression." *Indian Journal of Psychological Medicine* 46, no. 1 (January 2024): 94–95.
15. Jones, Jennifer L., Camilo F. Mateus, Robert J. Malcolm, Kathleen T. Brady, and Sudie E. Back. "Efficacy of Ketamine in the Treatment of Substance Use Disorders: A Systematic Review." *Frontiers in Psychiatry* 9 (July 24, 2018): 277.
16. Radvansky, Brian M., Shawn Puri, Anthony N. Sifonios, Jean D. Eloy, and Vanny Le. "Ketamine—A Narrative Review of Its Uses in Medicine." *American Journal of Therapeutics* 23, no. 6 (November 2016): e1414–26.
17. Bloomfield, Andrew, Norine Chan, Leah Fryml, Reuben Horace, and Srinivas Pyati. "Ketamine for Chronic Pain and Mental Health: Regulations, Legalities, and the Growth of Infusion Clinics." *Current Pain and Headache Reports* 27, no. 10 (October 2023): 579–85.
18. Liao, Yanhui, Yi-lang Tang, and Wei Hao. "Ketamine and International Regulations." *The American Journal of Drug and Alcohol Abuse* 43, no. 5 (September 3, 2017): 495–504.

How to cite this article:

Ankita Dudhal et al. *Ijppr.Human*, 2024; Vol. 30 (10): 23-29.

Conflict of Interest Statement: All authors have nothing else to disclose.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

	<p>Ms Ankita Dudhal Assistant professor (Pharmacology) Dr. D. Y. Patil College of Pharmacy, Akurdi</p>
	<p>Mr. Shrenik Dugarwal Final year student ( B. Pharmacy) Dr. D. Y. Patil College of Pharmacy, Akurdi</p>





Mr. Vinod Thakare

Final year student ( B. Pharmacy)  
Dr. D. Y. Patil College of Pharmacy, Akurdi