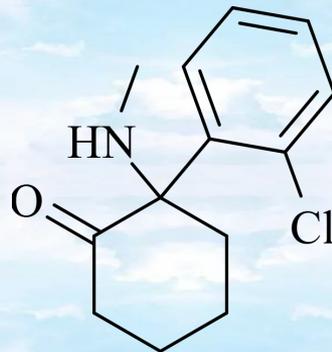
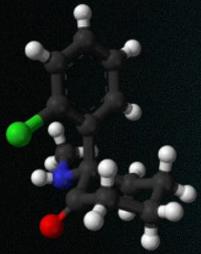


KETAMINE

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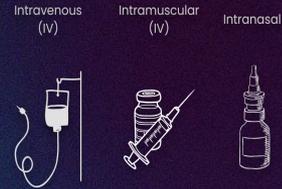
Overview



What is Ketamine?



Mechanism of Action



Indications and Administration of Ketamine



Contraindications and Adverse Effects of Ketamine

What is Ketamine



❖ Early History

- Began as veterinary anaesthetic (1966)
- FDA approved for humans (1970)
 - Field anaesthetic for soldiers during the Vietnam War
- Peaked as psychedelic party drug (1980's-90's)
 - "Special K" big in Hong Kong
- Federally Controlled Substance in USA (1999)



❖ Modern Use in Psychiatry

- Esketamine (K-derivative) FDA approved (2019) for treatment-refractory depression
 - Spravato nasal spray
- Ketamine currently used off-label
 - Depression, Anxiety, PTSD, Chronic Pain, Palliative Care



Mechanism of Action

- ❖ Ketamine interacts with N-methyl-D-aspartate (NMDA) receptors. It disrupts the brain's normal excitatory signals; although, it is not fully understood.
 - Dissociative Anesthesia
 - Profound Pain Relief
 - *Somatosensory blockade*
 - Rapid-Acting General Anesthesia
 - *Thalamo-cortical system and reticular-activating system tuned down*
 - Rapid-Acting Antidepressant
 - Bliss
 - *Increased serotonin neuron firing*
 - *Potentiates glutamate*
 - *Strengthens connections in limbic system*
 - Neuroplasticity
 - *Increased AMPA Receptor activation*
 - *mTOR & BDNF*

Note- Antidepressant properties produced at much lower drug concentration (x10) than anesthetic properties



Indications for Ketamine

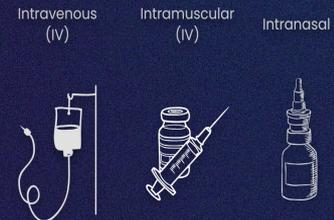
- ❖ FDA approved for the induction and maintenance of anesthesia
- ❖ Off-label Use for Management of Psychiatric Disorders
 - Only considered after failure of standard treatment:
 - No sustained change following at least two antidepressant trials
 - No sustained change in response to adjunctive group CBT or individual therapy
 - Evaluation of the contraindications to ketamine (to be described)
- ★ Major depressive disorder (MDD)
- ★ Bipolar disorder
- ★ Post-traumatic stress disorder (PTSD)
- ★ Severe Anxiety
- ★ Acute Suicidality
- ★ Obsessive Compulsive Disorder (OCD)
- ★ Post-operative and chronic pain management.

Note- Requires careful assessment of risks to benefits. Consider severity of depression and/or suicidality, duration of current episode, previous treatment history and urgency



Administration of Ketamine (Providers vary)

- ❖ Intravenously (IV) is most common route, patients absorb $\approx 99\%$
 - IV Infusion at steady rate over approx. 40 minutes
 - Six infusions over 2-3 weeks. Spaced a few weeks apart thereafter
 - If needed, maintenance infusions @ reduced frequency
 - Every 4-6 weeks with intent to taper
- ❖ Intramuscularly, $\approx 93\%$ absorption
 - Treatments are quick, but may require multiple injections in a single session
 - Six sessions over the first 2-3 weeks
 - One injection every few weeks as needed
- ❖ Intranasally, $\approx 20-30\%$ absorption
 - Ketamine & Esketamine (Spravato) offered intranasally
 - More frequent treatments to achieve full efficacy



Contraindications and Adverse Effects of Ketamine

❖ Contraindications

- Active substance abuse
- History of psychosis
- History of increased intracranial pressure
- Current Pregnancy
- Uncontrolled hypertension
- Acute or unstable cardiovascular disease
- Previous negative response to ketamine

❖ Short Term Adverse Effects May Include:

- Dissociation
- Transient psychosis
- Hallucinations
- Sedation
- Nausea
- Increased blood pressure, heart rate, breathing or body temperature

❖ Long term use raises concern of dependency

- Rare @ psychiatric doses

Note- Using ketamine with alcohol or other central nervous system depressants may result in profound respiratory depression and death



Summary

Ketamine is a drug with a storied history of use and abuse. It demonstrates speed and efficacy as both an anesthetic and as treatment for psychiatric illness. Its derivative, esketamine, is FDA approved for cases of treatment resistant depression (TRD). Meanwhile, ketamine is a controlled substance with a variety of off-label applications. From TRD to PTSD to suicidal crises, ketamine is available in multiple forms with IV being the most common route.

Considering the potential for misuse, ketamine is to be administered in a controlled setting on a case-by-case basis with adequate understanding of its drug profile. The long term effects of ketamine continue to be studied as its range of use is investigated. So expands psychiatry's horizon on the frontiers of neuroplasticity and wellness.



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