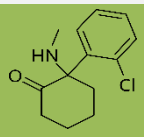
KETAMINE



2-(2-CHLOROPHENYL)-2-(METHYLAMINO)-CYCLOHEXANONE

The Signs of Life PSYCHOLOGY
Integrating science and the sacred

Ketamine is a rapid-acting general anesthetic belonging to the arylcyclohexylamine chemical class.[1] It is an important, widespread drug due to its safety, short elimination (2-4h) and unique mode of action.[2]

APPROVED INDICATIONS

- Anesthetic agent for recommended diagnostic and surgical procedures.[3]

COMMON OFF-LABEL INDICATIONS

- Pain management
- Major depressive disorder
- Suicidal Ideation
- Drug addiction*
- Post-traumatic stress disorder*

*Experimental[2,3]

MECHANISMS OF ACTION

- Non-competitive inhibitor of the N-methyl-D-aspartatereceptors (NMDARs) involved in blocking excitatory glutamatergic neurotransmission.[2]
- Direct and indirect effects at opioid, monoaminergic,muscarinic receptors.
  Unique since does not primarily act through GABAlike other anesthetic agents.[3,4]

POSITIVE EFFECTS

- DrowsinessDissociative
- Feeling happy and relaxed
- Perceptual changes for cognition and emotion
- Out-of-body experience (feeling detached from body)
- Mood enhancement[3,5]

The effects of ketamine are dose-dependent (most are self-resolving) and varies according to route of administration e.g. high doses produce deep dissociative state, amnesia, and loss of consciousness.[1,2]

POSSIBLE NEGATIVE EFFECTS

- Anxiety/Panic
- Confusion and clumsiness Dizziness,
- nausea and vomiting
- Distorted perceptions of bodyand self
- Poor coordination
- Disorientation
- Dysphoria[3,5]

NEGATIVE EFFECTS OF PROLONGED USE

- Cystitis and various lower urinary tractpathologies[1]
- Paranoid delusions, personality changesPhysical
- & psychological dependence (misuse, tolerance, and addiction) Abnormal liver or kidney function
- Withdrawal syndrome
- Flashbacks[3]

The use of ketamine for mental health symptoms falls into two broad frameworks:
pharmaceutical/biochemical & ketamine-assisted psychotherapy (KAP)

PHARMACEUTICAL/BIOCHEMICAL

Repeated administration is required to maintain symptom relief as therapeutic effects are relatively transient (days up to two weeks).[2,3]
Higher chance of dependence on ketamine since patients are offered minimal support and no talk therapy.[3]
Large, repeated doses of ketamine is associated with hepatotoxicity, bladder dysfunction, kidney toxicity and tolerance and dependence.[5,6]

ROUTES OF ADMINISTRATION

- Rectal
- Sublingual/transbuccal
- Intranasal
- Epidural
- Subcutaneous
- Oral
- Intramuscular (IM)
- Intravenous (IV) - ideal because100% bioavailable[1,3]

DOSING*

Intravenous (IV)

- 1-2 mg/kg (IV bolus) anesthesia induction (1-2min)
- 0.25-0.5 mg/kg (IV bolus) for pain management
- Rapid onset of effects - 45 seconds[2]

Intramuscular (IM)

For anxiolysis or analgesia:
- Low dose: 0.25 - 0.5 mg/kg
- Moderate dose: 0.5 - 1.0 mg/kg

To induce psychedelic effects:
- High dose: 1.0 - 2.0 mg/kg

Dose for Induction of anesthesia: 6.5 - 13.0 mg/kg
- Onset of effects 3 mins, Duration of effects 75 mins, sessions last 2-4 hours[3]

Nasal

- 25-300 mg[3]

Lozenge

- 50-300 mg for Transbuccal and/or sublingual absorption[3]

*Dosing may vary depending on clinical setting/mode of administration

KETAMINE-ASSISTED PSYCHOTHERAPY

Ketamine has been used to treat various psychiatric disorders, particularly as an intervention for treatment-resistant depression[2, 7]

- Professionals prescribe ketamine off-label
- Therapeutic practitioners deliver the KAP
  - Preparatory psychotherapy sessions conducted
  - Ketamine administration session
  - Psychotherapy support provided before and after
  - Integration sessions after each ketamine session[3]

Low to moderate doses induces a tranceexperience that promotes openness andaccess to self.[7] **High doses** of ketamine allows a person to experience a shift ofperceptions by inducing a non-ordinary state of consciousness.[3]

Optimal Dose:
0.5 mg/kg infused intravenously over40-60 min for antidepressant effects[2]

psychological health criteria
- Dose and frequency of use determine risk profile[3]

KAP is burgeoning methodology currently under-research. It has shown high efficacy in diminishing negative symptoms of a wide variety of psychiatric diagnoses by addressing underlying psychological issues and supporting transformational healing[3,]

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KETAMINE

NON-MEDICAL USES

COMMON STREET NAMES

- Ket
- K
- Special K
- Kitkat

- Cat tranquilizer
- Vitamin K[5]

HOW IS IT USED? (and onset of effects)

- Swallowed (30 mins)
- Snorted (5-15 mins)
- Smoked with cannabis or tobacco
- Injected (1min)[5]

Effects can last approximately an hour.

PRIMARY RISKS

- Overdose (risk of death is low but higher risk for physicalharm/accidents)
- Misuse, dependence, and addiction
- Respiratory depression when mixed with alcohol, GHB, or opioids
- Pre-existing health conditions where increased blood pressure wouldbe dangerous[3,5]

DOSING

Dosing and effects are dependent on the route of administration. Ketamine can be taken in liquid or powder form.[5]

DOSAGE AND EFFECTS

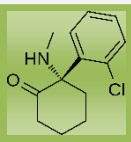
Ketamine is abused for its psychoactive qualities by recreational users. The dissociative effects involve the feelings of being drawnaway from sensory perceptions despite being conscious

High doses produces a state of deep dissociation combined by amnesia since NMDARs are crucial for excitatory neurotransmission, LTP and memory formation[2]

FACTORS AFFECTING RISK PROFILE

- History of trauma, Psychological history
- Pre-existing health conditions
- Dose, Duration and frequency of use
- Mixing ketamine with other substances (alcohol and GHB)[3]

ESKETAMINE



2-(2-CHLOROPHENYL)-2-(METHYLAMINO)-CYCLOHEXANONE

Spravata (esketamine) is a nasal spray, the S-enantiomer of racemic ketamine. Esketamine's primary antidepressant action is unique from other antidepressants since it does not directly involve monoamine, GABA, or opioid receptors[9]

COMMON EFFECTS:

dissociation, sedation, sleepiness, fainting, dizziness, spinning sensation, anxiety, or feeling disconnected from one's self, thoughts, feelings, space and time[3]

CLINICAL & THERAPEUTICS

APPROVED INDICATIONS

- Indicated for treatment-resistant depression
- For depressive symptoms in adults who have not responded sufficiently to at least 2 antidepressants[8,9]

TREATMENT DELIVERY

- Administered in conjunction with oral antidepressant (SNRI or SSRI)
- Administration and post-administration will be supervised by a healthcare professional[9]

SAFETY & TOLERABILITY

- Common adverse reactions of Spravato plus oral antidepressant: dissociation, vertigo, nausea, sedation, anxiety, hypoesthesia, increased blood pressure[3,9]
- Oral treatment was safe and well-tolerated (no early discontinuation or serious side effects) but therapeutic effects were modest.[8]

RECOMMENDED DOSING

IV infusion can lead to rapid and large symptom relief in TRD patients but it has less clinical applicability

- 0.5-1 mg/kg (IV bolus) anesthesia induction
- 0.125-0.25 mg/kg (IV bolus) for pain management
- 0.25 mg/kg (IV infusion over 40 min) for psychiatric use[2]

Nasal spray device - 28 mg dose

Recommended SPRAVATO dosing:

Week 1-4: Induction Phase

Starting Day 1 dose: **56 mg** (<65 yrs) & **28 mg** (≥65 yrs)
Subsequent doses: **28 mg** (≥ 65 years), **56 mg or 84 mg**twice weekly - (therapeutic benefit evaluated at end of this phase to determine if treatment needs to be continued)

Week 5-8: Maintenance Phase

28 mg (≥ 65 yrs), 56 mg or 84 mg once weekly

From Week 9:

28 mg (≥ 65 years), 56 mg or 84 mg every 2 weeks or onceweekly - (Re-examine if treatment needs to be continued periodically)[9]

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