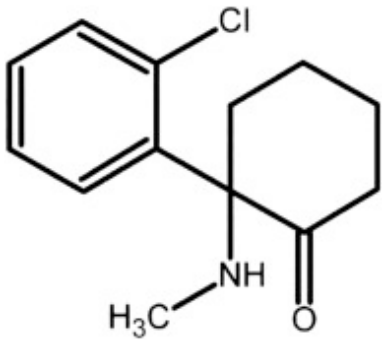
KETAMINE

A phencyclidine derivative

Mechanism of Action[1]

1. With repeated C fiber input, NMDA receptors increase C fiber activity and receptor field, which can contribute to phenomena like wind-up and sensitization
2. Ketamine's non-competitive antagonism of NMDA type glutamate receptors in the brain and spinal cord prevents calcium influx which leads to decreased downstream nociceptive signaling



On WHO list of essential medicines **since 1985[2]** due to its versatility and low cost

Dosing & indications[4]

- Induction: 1-2mg/kg IV, 2-4 mg/kg IM
- Analgesia/prevention of opioid induced hyperalgesia: 3-5 mcg/kg/min[10]
- Chronic pain: 0.35mg/kg bolus, or 8.33-33mcg/kg/min infusion (grade C)[4]
- Analgesia (oral dosing): 0.5 - 1mg/kg daily to TID (under investigation)[11]

Pharmacokinetics[1]

- Low oral bioavailability due to flow dependent hepatic clearance
- Lipophilic with rapid distribution, large Vd and low protein binding
- Half-life 2-4 hours with short context sensitive half time
- Excretion: hepatic oxidation to norketamine and other minor metabolites, glucuronidation and excretion in bile > urine

Emergence reactions & side effects

- Emergence reactions less common with intraop dosing
- Not dose dependent[4]
- Retrospective studies estimate 16% incidence[7] but wide variability between studies, and concern for observer bias in non-blinded studies[8]
- Indirect sympathomimetic and direct negative inotrope can increase myocardial work in at-risk patients[4]
- Potent bronchodilator, preserved spontaneous respiration & airway reflexes, but increased secretions[4]
- Potentially neurotoxic intrathecally[9]
- Use caution with hepatic dysfunction and elevated ICP or IOP[4]

Reduces average pain scores[5] and postop opioid use, especially in opioid tolerant patients[6]

Potency and onset time as anti-depressant equal or superior to classical pharmacological treatments or ECT[3]

37%	Reduction in 48h morphine use
26%	Reduction in pain intensity at 48h and 6 week follow up
71%	Reduction in opioid use at 6 weeks

In a double blinded prospective RCT (n>300) of chronic opioid using lumbar spine surgery patients.[6]

References:

1. Peltoniemi, Hagelberg, Olkkola, & Saari, 2016
2. WHO model list of essential medicines, 2017
3. Papadimitropoulou, Vossen, Karabis, Donatti, & Kubitz, 2017
4. Cohen, et al., 2018
5. Barreveld, et al., 2013
6. Abram, 2011
7. Schwenk, et al., 2016
8. Lemoel, et al., 2017
9. Deer, et al., 2017
10. Choi, et al., 2015
11. Buvanendran, et al., 2017