**Background** Ketamine is FDA approved as a parenterally administered, rapid-acting dissociative general anesthetic. However, in the past 10 years there have been numerous reports of the use of ketamine for pain control, administered via various routes. This Fast Fact reviews the use of ketamine in palliative care as an analgesic.

**Mechanism of Action** The N-methyl-D-aspartate/glutamate receptor (NMDA) is a calcium channel closely involved in the development of central (dorsal horn) sensitization. This channel has a role in opioid-resistant pain, neuropathic pain, allodynia, and hyperalgesia. Ketamine enters and blocks the open channel at a phencyclidine site, thereby inhibiting the excitatory effects of glutamate and aspartate. Ketamine also interacts with nicotinic, muscarinic, and opioid receptors.

**Pharmacology** As an anesthetic agent ketamine is given IV or IM. However, for pain, the parenteral solution of ketamine can be delivered at much lower doses by the oral, intranasal, transdermal, rectal, and subcutaneous routes. Onset of analgesia is 15-30 minutes by subcutaneous or oral routes. Duration of action is 15 minutes to 2 hours when administered by the IM or subcutaneous route, possibly longer orally. Ketamine is physically stable when mixed with morphine, low-dose dexamethasone, haloperidol, and metoclopramide. Drugs that interact with CYP34A have the potential to affect ketamine metabolism (e.g. azole antifungals, macrolide antibiotics, HIV protease inhibitors, and cyclosporin).

**Side Effects** Undesirable effects of high dose ketamine used for general anesthesia (1-2 mg/kg IV or 6.5-13 mg/kg IM) include psychotomimetic phenomena (dysphoria, blunted affect, psychomotor retardation, nightmares, hallucinations), excessive salivation, and tachycardia. Side effects at the lower doses used for pain are dose dependent, with dissociative feelings ("spaced out"), nausea, sedation, and hallucinations reported more frequently at higher doses.

**Analgesic Effectiveness** There is an absence of large controlled trials supporting ketamine as an analgesic for cancer or neuropathic pain, but there is a large body of case reports and uncontrolled trials. Two small randomized controlled trials reported decreased morphine use and reduced neuropathic pain intensity. However, a recent systematic review found insufficient evidence that ketamine improves the effectiveness of opioid treatment in cancer pain (1).

**Titration Schedule** There are no studies comparing various titration or dosing schedules, nor routes of administration. Suggested algorithms for have been proposed (see references). Depending on the clinical setting, airway monitoring and availability of resuscitation equipment may be appropriate. Note: clinicians with limited experience in using ketamine should seek expert consultation to develop an appropriate treatment and patient monitoring plan.

**Summary** Low-dose ketamine (at sub-anesthetic doses) can be considered for use in the palliative care setting for pain refractory to opioids and adjuvant analgesics.

**References**


Fast Facts and Concepts are edited by Drew A Rosielle MD, Palliative Care Center, Medical College of Wisconsin. For more information write to: drosiell@mcw.edu. More information, as well as the complete set of Fast Facts, are available at EPERC: www.eperc.mcw.edu.

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