

## The Use of Ketamine in the Intensive Care Unit

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### Abstract

Ketamine is a clinically unique anesthetic with particular characteristics that may make its use in the ICU increasingly appropriate and helpful. A case is discussed and the drug and possible ICU uses are reviewed.

**Keywords:** *Laryngospasm; Nystagmus; Bronchodilatation; Seizures; Lacrimation*

### Case Study

A 47 year-old white man, a heavy user of alcohol and injectable illegal drugs was admitted to the medical floor because of acute alcohol withdrawal. He was a large man, measuring 1.82 meters (6 feet) tall and weighed 121 kg (267 pounds). The patient grew increasingly agitated and exhibited physically violent behavior, despite treatment with parenteral haloperidol and lorazepam. He had to be physically restrained by several aides as well as by leather restraints but continued to attempt to bite, kick and punch care takers. The patient ripped out his intravenous line and would not allow it to be restarted; because of these uncontrollable behaviors, he was transferred from the medical floor to the ICU.

The patient was administered 500 mg of ketamine intramuscularly, and within a few minutes became calmer and less physically aggressive. A femoral central venous pressure line was quickly started and then the patient was further sedated with 50 mg of propofol and easily underwent endotracheal intubation. His sedation with propofol was continued for four days until he regained a more normal mental status, whereupon he was easily extubated and made an appropriate recovery.

Chemically, Ketamine is a congener of phencyclidine (synthesized in 1962), referred to as an arylcyclohexylamine [1]. Ketamine is supplied as a mixture of R+ and S- isomers, though the S- isomer is more effective with less adverse effects. Bioavailability after an intramuscular dose is approximately 93%, intranasal dose 25-50% and oral dose 20 +/- 7% [1,2] Ketamine is active within 30 seconds administered intravenously and has a large volume of distribution, protein binding of 20-50% and an elimination half-life of 2-3 hours. [1]. It was first used in medicine as a battlefield anesthetic during the Vietnam War during the 1960's and approved for human and veterinary anesthetic use in the United States in the 1970's. It is believed that the anesthetic effect of ketamine is caused by the non-competitive antagonism of the N-methyl-D-aspartate (NMDA) receptor calcium channel pore in the central nervous system and spinal cord.

Ketamine causes an unusual hypnotic state, resulting in considerable analgesia, amnesia, and unresponsiveness, but with generally stable vital signs, open eyes, extremity movements and a regular breathing pattern. This state has been called 'dissociative anesthesia' and may be useful in patients tolerant to opiate drugs [3]. The dissociative state may be further characterized by salivation, lacrimation, nystagmus, laryngospasm and increased muscle tone, but also blood pressure support in patients who may be prone to hypotension with administration of anesthetics. Ketamine may increase cerebral blood flow and increase cerebral metabolism but this does not seem to be a clinical problem in neurosurgical or trauma patients [4,5]. Increased intraocular pressure sometimes seen with ketamine may contraindicate its use in eye surgery. Emergence delirium manifested by hallucinations, paranoia and delusions is a significant complication of

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ketamine therapy and probably contraindicates Ketamine's use in patients with a history of schizophrenia. This adverse effect is lessened or eliminated by the concomitant use of low-dose benzodiazepines [6].

Relevant to its use in the ICU, Ketamine has an indirect sympathomimetic action causing increased heart rate, blood pressure, cardiac output, myocardial oxygen demand and also bronchodilation [7,8].

As an anesthetic agent which, unlike other agents used in the ICU, supports blood pressure and cardiac output, causes bronchodilation and generally does not cause clinically significant respiratory depression, the use of Ketamine is especially appealing, as many or most of our ICU patients are dehydrated, septic, hypotensive, have respiratory acidosis, bronchospasm and/or other issues. The use of Ketamine has been, therefore, studied in a number of situations:

As we have seen from the case presentation, ketamine is very useful as an effective but safe intramuscular anesthetic in the acutely agitated patient without IV or intraosseous access. It is unlikely that significant respiratory depression will occur in this situation, assuring a high level of safety and stability to the patient's condition.

Ketamine also is appealing for use as a sedative agent for endotracheal intubation (induction of anesthesia) particularly in patients who are hypotensive or bronchospastic. Because Ketamine preserves ventilatory drive, it is appropriate for 'awake' intubations, wherein chemical paralysis might be lessened or avoided because of difficult airway concerns. Increased secretions or rarely, laryngospasm, may be complicating but are usually resolved with small doses of an anticholinergic drug (such as glycopyrrolate) and benzodiazepines respectively. The usual dose for intubation is 1-2 mg/kg with a time to effect of 30-60 seconds and duration of effect of about 10-20 minutes. A large multi-center French study [9] demonstrated that Ketamine was non-inferior to etomidate as an induction agent with substantially less adrenal insufficiency.

Ketamine may also be used as a sedative infusion in critically ill patients, similar to situations in which propofol or benzodiazepines are usually used [10-12]. In addition, Ketamine has potent analgesia and opioid sparing effects [13]. It may, therefore, be particularly appropriate to consider ketamine infusions for sedation in patients with significant bronchospasm, hypotension (without cardiogenic shock or acute myocardial ischemia), or postoperative or post-trauma patients where significant pain or necessity for opioids are issues. The usual doses are in the 0.5 mg/kg/hr to 4.0 mg/kg/hr range. Occasional adverse effects requiring changing to a different sedative infusion have included agitation, tachycardia and hypertension.

Similarly, ketamine may be used in smaller infusion doses, primarily as an adjunct to opioid therapy in patients with opioid tolerance or very high doses of opioids interfering with ventilator weaning or causing increased vasopressor dosages [14].

Ketamine has been studied as an adjunct in the therapy of refractory status epilepticus, partly because of its ability to support a patient's blood pressure in contrast to other sedating or anti-epileptic drugs [15,16]. Ketamine, however, has occasionally been implicated in lowering the seizure threshold in some patients [17] and its routine use as an anticonvulsant is not presently recommended. Since patients with acute alcohol withdrawal are at risk for seizures, the patient mentioned in the case presentation did not receive a ketamine infusion, but rather treated with propofol.

### Conclusion

Ketamine is an anesthetic agent which, unlike other agents commonly used in the ICU, supports blood pressure and cardiac output, causes bronchodilation and generally does not cause clinically significant respiratory depression. The use of Ketamine in the ICU is, therefore, especially appealing, as many or most ICU patients have conditions that may be exacerbated by other anesthetic agents. Further experience and research is necessary to determine the precise indications, dosing and duration of therapy of Ketamine in the ICU.

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