

Ketamine as an Adjunct for the Long-term Sedation and Analgesia of a Patient with a Left Ventricular Assist Device (LVAD) and an Open Chest

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Introduction:

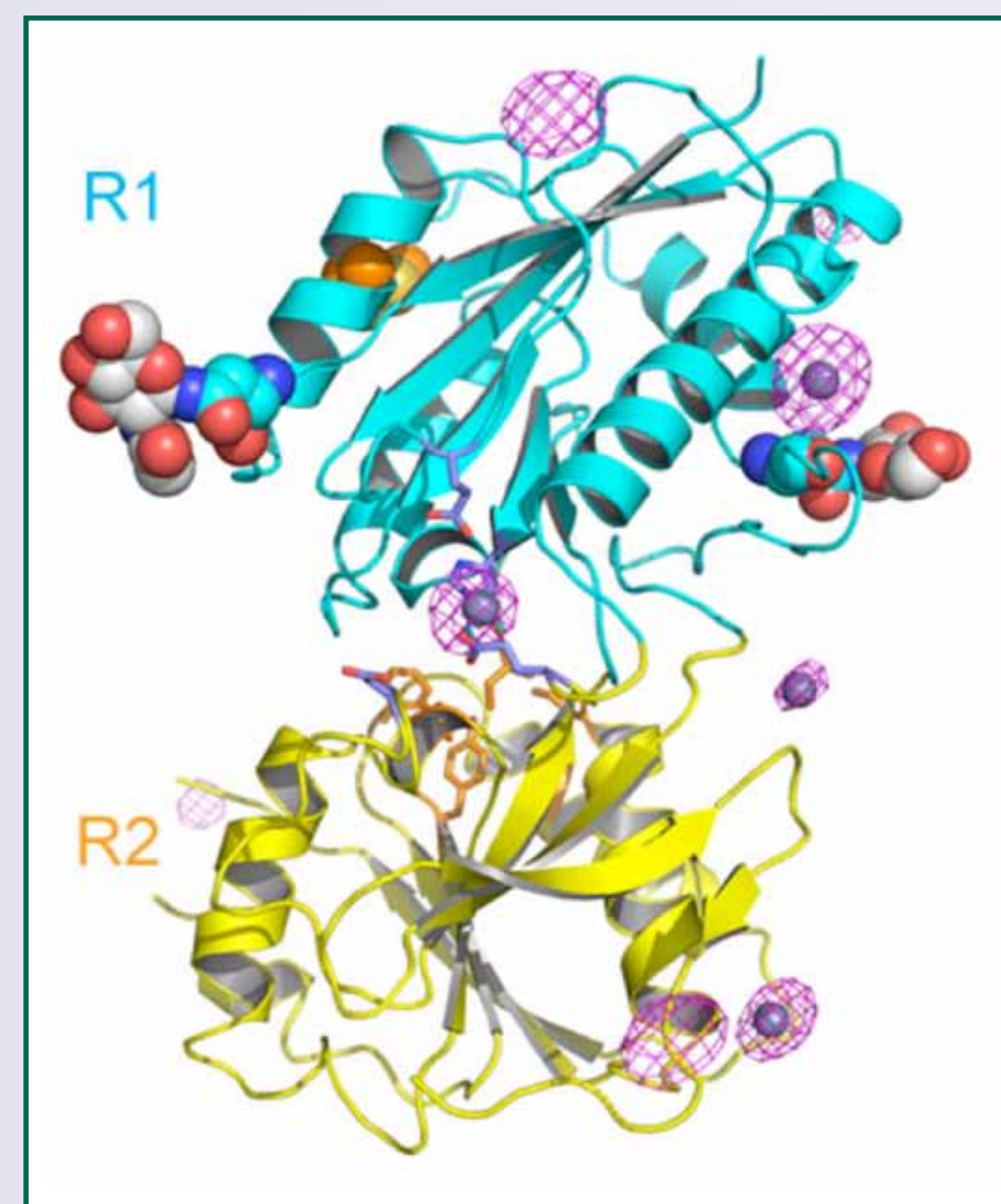
- Sedation is necessary in the Intensive Care Unit (ICU) for patient comfort and the avoidance of ventilator dyssynchrony and unplanned extubation.
- Opioid tolerant patients can be challenging to sedate despite high doses of benzodiazepines and opioids.
- Escalating opioid doses may actually exacerbate opioid tolerance, induce hyperalgesia, and cause/worsen cardiovascular and respiratory depression.^{1,7}
- Ketamine may be useful as an adjunct in a multimodal approach in order to maximize both pain control and sedation in select patients who require very high doses of opioids and benzodiazepines.⁶

Case Description:

- **Day #1:** A 5'10", 110 kg 28 year old male with no past medical history is admitted for workup of progressive shortness of breath over 2 months and worsening lower extremity edema over 2 weeks.
- **Day #2:** TEE shows pulmonary arterial pressure of 60/30, wedge pressure of 28, right atrial pressure of 22, and cardiac output of 4.5. Nonischemic cardiomyopathy is suspected.

- **Days #2-21:** The patient is managed with diuretics, milrinone, nesiritide and antibiotics while demonstrating little clinical improvement.
- **Day #22:** Extracorporeal Membrane Oxygenation (ECMO) is started to compensate for the patient's decreased cardiac function in the Surgery Coronary Care Unit (SCCU).
- **Day #32:** The patient is switched to LVAD with an open chest due to inadequate intraoperative hemostasis.
- **Day #33:** The acute pain service is consulted for inadequate sedation and pain uncontrolled by conventional means. At the time of consultation, the patient is receiving 300mcg/hr of fentanyl and 18mg/hr of midazolam. RASS score is "-3 moderate sedation."
- **Day #33:** Ketamine is started at 20mg/hr with a 10mg bolus and subsequently titrated up to 60mg/hr over the next six hours.
- **Days #33-34,** 12 hours later: Fentanyl is tapered down to 100mcg/hr and midazolam to 14mg/hr.
- **Day #34:** Fentanyl is decreased to 50mcg/hr and midazolam to 4mg/hr while the ketamine infusion continues at 60mg/hr. RASS score is "-2 light sedation."

- **Days #35-48:** The patient is brought to the OR several times for washouts secondary to persistent fever and several positive bacterial cultures. His fentanyl largely hovers around the 50-100mcg/hr range and his midazolam requirements are consistently minimal (as low as 3mg/hr).
- **Day #48:** Ketamine is ultimately discontinued after the patient develops septic shock and is consequently placed on a number of vasopressors.



NMDA Receptor

Discussion:

- Ketamine may be a useful adjunct to other sedatives for improving comfort in patients who require analgesia and are already on high doses of opioids and benzodiazepines.
- Opioid tolerance is of particular concern, as benzodiazepines have been shown to accelerate this process. This is postulated to be the result of decreased activity in the descending inhibitory nervous system.³
- A multimodal regimen with ketamine offers the advantage of reducing opioid requirements as well as the risk of opioid tolerance and hyperalgesia. This may result from a reduction in central hyperexcitability due to ketamine's activity at the N-methyl-D-aspartate (NMDA) receptor.^{2,6}
- In our patient, we observed a dramatic decrease in the amount of midazolam and fentanyl required for sedation and analgesia following the administration of ketamine.
- Ketamine indirectly stimulates the sympathetic nervous system via centrally mediated mechanisms generating increases in heart rate, blood pressure, and cardiac output.⁷
- Other beneficial effects of ketamine include bronchodilation, preservation of protective airway reflexes (more so than with other IV anesthetics), and minimal respiratory depression.⁵

Conclusion:

- A multimodal sedative and analgesic regimen that incorporates ketamine offers important therapeutic advantages in select patients who require very high doses of opioids and benzodiazepines, but warrants further study.

References:

1. Bekhit, M.H. Opioid-induced hyperalgesia and tolerance. *American Journal of Therapeutics* 2010; 17: 498-510.
2. Edrich, Thomas et al. Ketamine for long-term sedation and analgesia of a burn patient. *Anesthesia and Analgesia* 2004; 99: 893-5.
3. Freye E. and L. Latsch. Development of opioid tolerance – Molecular mechanisms and clinical consequences. *Anästhesiol Intensivmed Notfallmed Schmerzther* 2003; 31: 14-26.
4. Kissin, I. et al. The effect of ketamine on opioid-induced acute tolerance: Can it explain reduction of opioid consumption with ketamine-opioid analgesic combinations? *Anesthesia and Analgesia* 2000; 91: 1483-1488.
5. Kohrs, Rainer and Marcel E. Durieux. Ketamine: Teaching an old drug new tricks. *Anesthesia and Analgesia* 1998; 87: 1186-93.
6. Lavand'homme P. et al. Intraoperative epidural analgesia combined with ketamine provides effective preventive analgesia in patients undergoing major digestive surgery. *Anesthesiology* 2005; 103: 813- 2.
7. Morgan, G.E., et al. *Clinical Anesthesiology*. New York: Lange Medical Books, 2006.