Ketamine for pain & Opioid Tolerance

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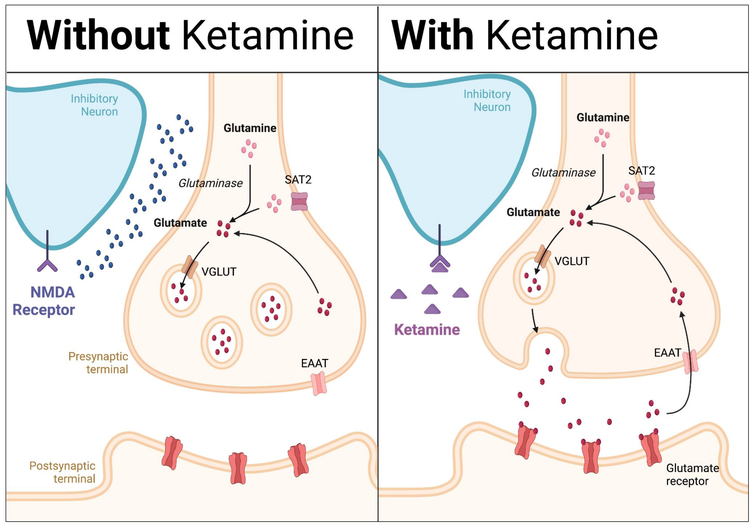
Background/Significance:

Ketamine is commonly used for anesthesia, analgesia, and agitation. A non-competitive antagonist of the N-methyl-d-aspartate (NMDA) receptor, Ketamine can be administered via intravenous, intramuscular, subcutaneous, oral, rectal, topical, intranasal, sublingual, epidural, and caudal routes. The wide variety of option for delivery facilitates multiple clinical and non-clinical environments. In light of this flexibility, our review addresses the more recent investigations into the unique ability ketamine to improve opioid tolerance

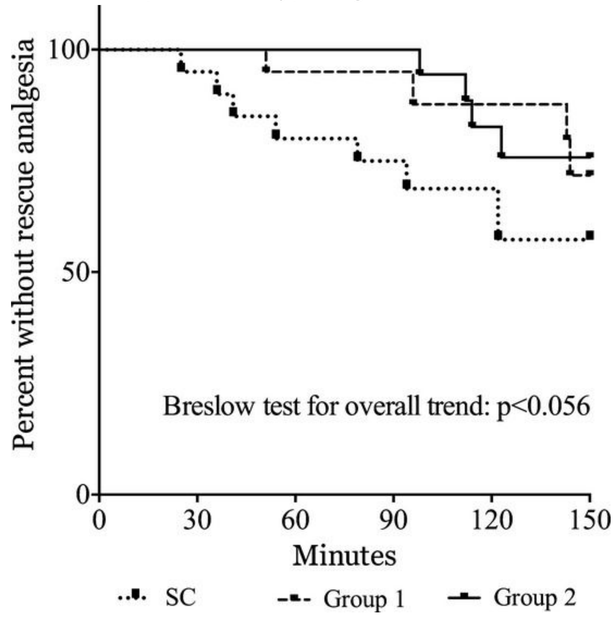


Methods:

While there are extensive reviews on the role of ketamine in anesthesia and analgesia, the publications of ketamine's roles with opioids are limited. This review is based on a comprehensive literature search and summarizes findings in recent publications related to the mechanism of ketamine and its role in improving opioid tolerance.

Discussion:

Our review incorporated randomized-trials, case studies, and retrospective studies primarily from the last 10 years. Patients with acute pain who were receiving opioids were randomized to doses of ketamine (0.1 to 4 mg/kg/hr) or placebo. Endpoints evaluated include pain level, pain control satisfaction, side effects, sedation level, and pain medication levels. In randomized trails, there was lower total opioid dose in ketamine group (9.95 mg vs 12.81 mg; P=0.02), greater pain relief for ketamine groups vs control (SPID: 4 vs 7 vs 7.8; P<0.02), and pain scores were lower in ketamine treatment groups (3.5 vs 6; P=0.018). Case studies also revealed that initiation of ketamine can reduce opioid requirements after tolerance had developed. Overall, the studies reviewed showed that minimal and low-dose ketamine are safe and effective at reducing post-operative opioid consumption and hyperalgesia.



"Global analgesic effectiveness as measured by integrated pain and morphine scores (i.e., SIA scores) are also presented in [the table above]. The lowest median scores (most pain relief with least amount of analgesia) occurred in the group 2, followed by group 1, and then the standard care group. When pairwise comparisons were performed, only group 2 and the standard care group were significantly different."

Results:

Moderate evidence supports use of subanesthetic IV ketamine bolus doses (up to 0.35 mg/kg) and infusions (up to 1 mg/kg/h) as adjuncts to opioids for perioperative analgesia.

- In multiple circumstances it was noted that single bolus ketamine intra and post operatively, decreased opioid use in post op patients
- Concomitant low dose ketamine with opioid pain management in ED suggested lower utilization of opioids.
- There is good evidence that perioperative ketamine decreases postoperative pain scores and opioid requirements, but there is a lack of consensus on dose, for both bolus and infusion

Conclusion:

Low-dose ketamine is a prospective safe and effective option to help reduce opioid requirements and resolve opioid tolerance.

References:

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Study or Subgroup	Ketamine–Morphine PCA Mean	SD	Total	Morphine PCA Mean	SD	Total	Weight	Mean Difference IV, Random, 99% CI
Dahi-taleghani 2014	7	2	70	12	3	70	18.8%	-5.00 [-6.11, -3.89]
Javery 1996	25.82	16.4	22	51.1	20.8	20	13.7%	-25.28 [-40.27, -10.29]
Michelet 2007	25.5	9	24	30	10	24	17.4%	-4.50 [-11.57, 2.57]
Reeves 2001	77	31	36	71	38	35	10.7%	6.00 [-15.23, 27.23]
kamal 2008	23.5	10.6	40	45.9	10.6	40	17.7%	-22.40 [-28.51, -16.29]
Nesher 2008	24	33.6	28	48	55.2	29	7.2%	-24.00 [-55.06, 7.06]
Kollender 2008	14.6	11.4	28	32.9	24.9	29	14.6%	-18.30 [-31.44, -5.16]
Total (98% CI)			**248**			**247**	**100.0%**	**-12.89 (-22.4, -3.35)**

Heterogeneity: $Tau^2 = 89.32$; $Chi^2 = 74.21$, df = 6 ($P < 0.00001$); $I^2 = 92\%$
Test for overall effect: Z = 3.14 (P = 0.002)

Mean Difference
IV, Random, 99% CI

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