

The Effectiveness and Adverse Effects Profile of "Burst" Ketamine in Refractory Cancer Pain

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Reference: Jackson K, Ashby M, Howell D, Petersen J, Brumley D, Good P, Pisasale M, Wein S, Woodruff R. *Journal of Palliative Care*, 26(3), 176-83, 2010

Abstract: This multi-centre study of adjuvant "burst" ketamine in palliative care in-patients documents its effectiveness, duration of pain relief, and adverse effects (AE) profile. Patients received a three-to-five day continuous subcutaneous infusion (CSCI) of ketamine escalated from 100 to 300 to 500 mg/24 hours if required. When the effective or maximum tolerated dose was attained, the infusion was continued for three days and each patient assessed as a responder or non-responder using strict criteria. The response rate was 22/44 (50 percent), with 4 (9 percent) becoming pain-free. Pain relief lasting two or more weeks was documented in 50 percent of responders. AEs were documented daily using the National Cancer Institute (NCI) Common Toxicity Criteria 0-4 scales. There were 11 grade 3 and 4 neurological AEs. However, no responders elected to cease treatment early due to neurological AEs. We concluded that this protocol in the controlled environment of an in-patient PC unit is relatively safe and simple with reasonable effectiveness.

Strengths:

1. Stringent criteria to characterize responders versus non-responders
2. Thorough detailed data regarding types and severity of pain experienced by each participant
3. Four of the participants reported being completely free of pain at least 2 weeks after ketamine infusions ended.
4. Evidence that ketamine's action may not be restricted to neuropathic pain
5. Thorough and detailed account of the adverse events

Weaknesses:

1. Open-label, non-controlled, non-randomized study (? selection bias, ? placebo response)
2. N = 44
3. Concurrent use of benzodiazepines and neuroleptics
4. Limited follow up
5. Lost several potential participants due to sub optimal record keeping
6. 11/22 responders reported grade 3 or 4/4 NCI Common Toxicity Criteria symptoms

Relevance to Palliative Care: Refractory cancer-associated pain(i.e. pain that has not been adequately controlled with a combination of anti-inflammatory medications, opioid analgesics, and neuropathic adjuvant agents), presents a formidable challenge for palliative care health providers and their patients. Furthermore, conducting research in this population of palliative patients presents unique challenges that undermine attempts to follow rigorous scientific methodology. These challenges necessitate creative protocols and novel combinations of medications to help address refractory pain. This study provides further evidence to suggest that ketamine, a cheap, readily available and relatively safe medication, may be used to help potentiate the analgesic properties of opioid analgesics, thereby offering relief to a subgroup of palliative patients who have exhaust most other methods of pain therapy.