

Safety and efficacy of intranasal ketamine for the treatment of breakthrough pain in patients with chronic pain: a randomized, double-blind, placebo-controlled, crossover study

Reference: Carr DB, Goudas LC, Denman WT, et al. Pain 2004; 108 (1-2): 17-27.

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Abstract

Few placebo-controlled trials have investigated the treatment of breakthrough pain (BTP) in patients with chronic pain. We evaluated the efficacy and safety of intranasal ketamine for BTP in a randomized, double-blind, placebo-controlled, crossover trial. Twenty patients with chronic pain and at least two spontaneous BTP episodes daily self-administered up to five doses of intranasal ketamine or placebo at the onset of a spontaneous BTP episode (pain intensity ≥ 5 on a 0-10 scale). Two BTP episodes at least 48 h apart were treated with either ketamine or placebo. Patients reported significantly lower BTP intensity following intranasal ketamine than after placebo ($P < 0.0001$) with pain relief within 10 min of dosing and lasting for up to 60 min. No patient in the ketamine group required his/her usual rescue medication to treat the BTP episode, while seven out of 20 (35%) patients in placebo group did ($P = 0.0135$). Intranasal ketamine was well tolerated with no serious adverse events. After ketamine administration, four patients reported a transient change in taste, one patient reported rhinorrhea, one patient reported nasal passage irritation, and two patients experienced transient elevation in blood pressure. A side effect questionnaire administered 60 min and 24 h after drug or placebo administration elicited no reports of auditory or visual hallucinations. These data suggest that intranasal administration of ketamine provides rapid, safe and effective relief for BTP.

Comments

Strengths: Strong design: double-blind, placebo-controlled RCT, describes appropriate protocols for randomization/blinding and reports losses to follow up (Jadad score 5). Standardized outcome measures: used accepted thresholds for meaningful reductions in numeric pain scale and previously developed score for side effect evaluation specific to dissociative anaesthetics. Appropriate time intervals (5-60 min) used to assess efficacy and adverse effects.

Weaknesses: Does not evaluate whether ketamine is better than or synergistic with opioids for initial breakthrough pain treatment. Restrictive incl criteria: excluded patients with any cardiac, hepatic, lung or psychiatric Hx (limits generalizability). Not powered for adverse events. Groups may be unbalanced at baseline due to small n: median age for ketamine/placebo vs placebo/ketamine 53.1 vs 44.0 years.

Relevance to Palliative Care: Breakthrough treatment of chronic pain is not well studied and is challenging given tolerance and toxicity of high opioid doses; establishing efficacy of non-opioid analgesic options is important. Furthermore, NMDAR antagonists may modulate chronic pain.