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## **A systematic review and meta-analysis of ketamine for the prevention of persistent post-surgical pain.**

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### **Abstract**

While post-operative pain routinely resolves, persistent post-surgical pain (PPSP) is common in certain surgeries; it causes disability, lowers quality of life and has economic consequences. The objectives of this systematic review and meta-analysis were to evaluate the effectiveness of ketamine in reducing the prevalence and severity of PPSP and to assess safety associated with its use. We searched the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE through December 2012 for articles in any language. We included randomized, controlled trials in adults in which ketamine was administered perioperatively via any route. Seventeen studies, the majority of which administered ketamine intravenously, met all inclusion criteria. The overall risk of developing PPSP was not significantly reduced at any time point in the ketamine group vs. placebo, nor did comparisons of pain severity scores reach statistical significance. Sensitivity analysis of exclusively intravenous ketamine studies included in this meta-analysis demonstrated statistically significant reductions in risk of developing PPSP at 3 and 6 months ( $P = 0.01$  and  $P = 0.04$ , respectively). Adverse event rates were similar between ketamine and placebo groups. The study data from our review are heterogeneous and demonstrate efficacy of intravenously administered ketamine only in comparison with placebo. Highly variable timing and dosing of ketamine in these studies suggest that no unifying effective regimen has emerged. Future research should focus on clinically relevant outcomes, should stratify patients with pre-existing pain and possible central sensitization and should enroll sufficiently large numbers to account for loss to follow-up in long-term studies.

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