

Citation: Cohen, L., et al. The Effect of Ketamine on Intracranial and Cerebral Perfusion Pressure and Health Outcomes: A Systematic Review. *Annals of Emergency Medicine*. 2014.

Clinical Question: Does ketamine have clinically significant effects upon intracranial pressure or worsen neurologic outcomes in undifferentiated patients compared to other sedative agents?

Introduction: This systematic review and meta-analysis was performed to evaluate the existing literature's evidence on the effect ketamine has upon intracranial pressure and cerebral perfusion of the undifferentiated patient requiring intubation with secondary outcomes of neurologic function, ICU LOS, and mortality. Historically, ketamine has been considered contraindicated in patients with head injuries for fear of increased ICP/neurologic outcome. Few alternative sedative agents have the favorable hemodynamic effects of ketamine, so evidence supporting its safety would be favorable for clinical practice.

Methods: The authors created a systematic search strategy and included randomized and nonrandomized prospective studies that compared the effect of ketamine with another intravenous medications in intubated patients. The primary outcome measures for this study were intracranial cerebral perfusion pressures while secondary outcome measures were neurologic outcomes, ICU length of stay, and mortality. Two authors independently performed title, abstract, and full-text reviews, and abstracted data from all studies, using standardized forms. Data from randomized controlled trials and prospective studies were synthesized in a qualitative manner because the study designs, patient populations, reported outcomes, and follow-up periods were heterogeneous. We used the Jadad score and Cochrane Risk of Bias tool to assess study quality.

Results: The authors screened 4,896 titles, but only 10 studies met their inclusion criteria, which encompassed 953 patients. These 10 studies essentially reported mixed findings on ICP, with either no change or small changes (two studies reported a small increase, whereas two other studies reported small decreases in ICP- all four of these studies' effects were deemed clinically insignificant). The studies further found no evidence to support worsened neurologic outcomes, lengthier ICU LOS, or mortality increases in patients treated with ketamine.

Discussion: I think the authors of this study have broached a useful topic for discussion on the use of ketamine. They present evidence that show no clinically significant changes in ICP with the use of ketamine and also include some patient-oriented outcome measures that show no ill effects from the use of ketamine. The study is limited somewhat, as only one of their included studies had a "low risk" for publication bias as none of the other studies reported optimal methods to randomize patients, conceal treatment allocation, or ensure blinding of study participants, treating personnel, and outcomes assessors. Furthermore, none of the included studies offered sample size calculations for the above outcomes, making these studies underpowered. I agree with the author's conclusion that the "available data suggest that ketamine does not adversely affect intracranial or cerebral perfusion pressures, neurologic outcomes, or mortality compared with other intravenous induction agents commonly used to intubate adult patients in the ED." I think this study opens the door for further investigation of the routine use of ketamine in undifferentiated patients with attention paid to patient-oriented outcomes to overcome the dogmatic avoidance of this medication that is predicated upon outdated, poor-quality evidence.

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