EVMS Emergency Medicine Journal Club
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Citation: Barbic D et al., Rapid agitation control with ketamine in the emergency department (RACKED): a randomized controlled trial protocol.Trials. 2018 Nov 26;19(1)

Methodology (*Study design)*: This article examined whether sedation is more rapidly (safely) achieved with ketamine than the classic combination of antipsychotic plus benzodiazepine. In this RCT, the authors compared the time to onset, level of sedation, and adverse effects for ketamine vs an antipsychotic (haloperidol) plus benzodiazepine (midazolam). Patients 19 to 60 years of age with severe psychomotor agitation, according to a Richmond Agitation Sedation Scale (RASS) score ≥3 were included. The study excluded patients who were in police custody, pregnant, breastfeeding, or allergic to the study medications, and patients with several comorbidities (listed in appendix E of the article). All enrolled patients were assessed in a trauma bed and placed on a cardiac monitor, and were randomized to either the ketamine group, receiving 5 mg/kg with a maximum of 4 mL per syringe (in multiple syringes), or the haloperidol/midazolam group, receiving 5 mg haloperidol plus 5 mg midazolam (in 1 syringe). The primary outcome was the time (in minutes) after administration of the medication to adequate sedation, as measured with the RASS. The RASS was recorded every 5 minutes until a score of 1 was reached or 30 minutes had elapsed.

Strengths: Randomized control trial, blinded

Weaknesses: A limitation of the study is that outcomes after the 30 minutes of observation are not reported. This information would have been valuable, because giving ketamine to sedate acutely agitated psychiatric patients carries a risk of emergent reaction.
Unfortunately, the trial was stopped early because of COVID-19 restrictions, and the study was therefore underpowered. A total of 68% of the patients were men, and the median age was 35 years.
More men than women received ketamine, and the patients who received ketamine had slightly higher RASS scores

My Clinical Bottom Line:
The median time to sedation was 14.7 minutes for midazolam and haloperidol versus 5.8 minutes for ketamine (difference 8.8 minutes [95% confidence interval (CI) 3.0 to 14.5]). Adjusted Cox proportional model analysis favored the ketamine arm (hazard ratio 2.43, 95% CI 1.43 to 4.12). Five (12.5%) patients in the ketamine arm and 2 (5.0%) patients in the midazolam and haloperidol arm experienced serious adverse events (difference 7.5% [95% CI -4.8% to 19.8%]).
Adverse effects were rare and not serious. Of the patients who received ketamine, 5 reported adverse effects. One patient developed laryngospasm, but the condition self-resolved and did not require intubation.

This RCT comparing ketamine to haloperidol plus midazolam revealed that ketamine had a shorter time to providing adequate sedation. Given that this study was underpowered, it is difficult to make any definitive statement about safety of ketamine.

Would have liked to know whether these patients experienced emergent reactions after receiving ketamine. Would also have liked to know how many patients needed repeat dosing beyond 30 minutes in each patient population.

Good leading point for future research on ketamine in agitated patients?