DEM Journal Club

Article Appraisal

Article: Propofol or Ketofol for Procedural Sedation and Analgesia in the Emergency Department: the POKER Study: A Randomized, Double-Blind Clinical Trial

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Background and Study Objective(s):

Propfol and Ketamine are frequently used for procedural sedation. Despite claims that the combination of the two medications may offset some of the adverse effects seen with use of either agent in isolation, other single-center RCT's have not shown a statistically significant result to date. This study sought to determine if a 1:1 combination of ketamine and propofol (Ketofol) resulted in significantly fewer adverse respiratory events requiring physician intervention than propofol alone.

Study Design:

This was a multicenter, randomized, double-blind clinical trial. A convenience sample of 573 patients was enrolled after assessment, and patients were included if they were 18 years or older and deemed by the ED physician to require deep procedural sedation to facilitate a painful procedure. They were excluded if they were unable to provide informed consent, pregnant, allergice to ketamine, soy or eggs, had a reduced level of consciousness, known raised intracranial pressure, uncontrolled hypertension, an abdominal aortic aneurysm, symptomatic ischemic heart disease, heart failure, or recent myocardial infarction, or known to have other severe systemic disease making them ASA class IV or greater. Patients were randomized in blocks of 4 with allocation sequence concealment to receive 1:1 ketofol or propofol. Primary outcome was occurrence of a respiratory event defined as hypoxia, hypoventilation, apnea, laryngospasm, or aspiration, plus the occurrence of a respiratory event including increased oxygen flow rate, airway repositioning/opening, use of an airway adjunct, bag valve mask, or intubation. Secondary outcomes were hypotension and patient satisfaction. The study had 90% power to show a 10% absolute reduction in adverse respiratory events from the expected 20% to 10%.

Results:

There was no difference in the occurrence of airway events requiring respiratory intervention between the groups. Hypotension was more common in the propfol group (8% vs 1%). Patient satisfaction was comparable between groups (mean = 10). Exploratory outcomes showed that ketofol patients had more emergence delirium, pleasant hallucinations and decreased pain scores at 30 minutes post-procedure. Propfol patients had more mild agitation during the procedure, but shorter times to recovery post procedure (mean = 9 min).

Validity of Results:

This paper was felt to have acceptable internal validity. Patients were randomized in blocks of four which may lead to some predictability in the randomization process. Although defined as an intention-to-treat analysis within the paper, the analysis was consistent with a per-protocol analysis, as patients were excluded after randomization and not accounted for in the final statistical analyses. Although appropriate steps were taken to ensure blinding, the mixing of drugs in the department and characteristics of the study drug may have lead to unblinding of health workers and study personnel. Consideration of an assessment tool to track what drug study personnel thought they were giving may have been helpful in this regard. The study groups were sufficiently similar to allow comparison. The treatment groups had differing use of preprocedural opiates without a washout period and interprocedural prophylactic oxygen use. These may have infliuenced study results, however, also more closely reflect real-world practice. The study was insufficiently powered assess the more rare but very serious adverse events, including airway obstruction, laryngospasm, or aspiration.

Generalizability of Results:

Overall, the consensus was this study had many factors lending itself to applicability in clinical practice. The study included a wide range of patients sedated for a wide variety of procedures, and was performed across multiple centres in Australia. The external validity was acceptable for an RCT.

The Bottom Line:

This study is the largest RCT yet confirming that 1:1 ketofol does not reduce adverse respiratory events compared to propofol. Despite this, both propfol and ketofol were shown to be safe and effective options for ED procedural sedation with consistently high patient satisfaction. Despite this, choice of agent in any particular setting should be guided by independent practitioner preference and experience, and institutional practice.