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Independent Dosing of Propofol and Ketamine May Improve Procedural Sedation Compared With the Combination “Ketofol”

To the Editor:

In their recent article on ketofol, Andolfatto et al¹ demonstrate that this combination medication appears no safer than propofol alone. However, more consideration is merited for the strategy of using propofol and ketamine together for the initial sedation administration, followed by propofol monotherapy for subsequent boluses. The pharmacodynamics of ketamine requires 30 to 120 minutes of monitoring after administration compared with a maximum of 10 to 15 minutes for propofol.²⁻⁴ Because of this substantially longer duration of effect, it is illogical to redose the ketamine component of ketofol near the end of a lengthy procedure when propofol alone would suffice. Furthermore, ketamine appears to dissociate patients in a dichotomous manner, meaning that providing small additional boluses of the drug to already dissociated patients may provide zero clinical benefit.² These concerns about the coadministration of the 2 agents have been suggested before, yet most emergency medicine investigations of ketofol nevertheless have studied the combined formulation.^{5,6}

We believe that independent dosing of the 2 drugs is superior to the combined dosing, but it may also be superior to propofol alone. As the data suggest from this most recent article by Andolfatto et al,¹ ketamine may provide patients with an increased sedation consistency versus providers' having to rely solely on intermittent doses of propofol. We hope that further studies may demonstrate that separating the administration of these 2 agents can provide the sedation consistency of ketamine with the rapid recovery time inherent with propofol boluses.

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In reply:

I wish to thank Drs. Shy, Howland, and Strayer for their insightful comments about ketofol sedation. The issue of 1 syringe or 2 is an interesting one because the differing pharmacokinetics of ketamine and propofol does lead to the logical conclusion that they are best titrated separately for the reasons the authors mention. Separate-syringe titration has been used successfully in previous sedation studies,^{1,2} as well as in our emergency department (unpublished data).

However, there exists a substantial body of prospective data³⁻⁵ demonstrating the effectiveness of the single-syringe combination. As shown in our recent randomized trial,⁵ the recovery time with the single-syringe combination (8 minutes; interquartile range [IQR] 7 to 10 minutes) is longer than that with propofol alone (6 minutes; IQR 2 to 8 minutes), as one would surmise, but only by a median of 2 minutes. This longer duration of effect can be used to great advantage for those painful procedures that take a few extra minutes to perform—for example, incision and drainage of abscesses or fracture reduction with cast molding—while still maintaining a recovery time similar to that with propofol alone, and with a consistency of sedation depth that lessens the need for repeated dosing of sedative in response to patient agitation.

Ketamine displays a dissociative threshold that is reliably apparent at approximately 1.5 mg/kg intravenously,⁶ and further ketamine dosing to already dissociated patients may indeed have little value because higher doses mandate more prolonged recovery monitoring. However, when single-syringe ketofol is titrated, prolonged monitoring is usually unnecessary because most patients are maintained in deep sedation with ketamine dosages beneath this dissociative threshold (median dose of ketamine required was 0.7 mg/kg; IQR 0.6 to 0.9 mg/kg).⁵

Whether 2 syringes are superior (or not) to 1 syringe is not known, and where this purported superiority may exist is

unclear. Will separate syringe titration of these agents shorten the 2-minute difference in recovery time to a clinically appreciable degree? Would shortening this interval be a potential disadvantage in those cases in which a longer sedation time is preferable without the more erratic sedation levels observed with propofol? Would separate-syringe titration result in fewer adverse events than same-syringe titration, or to propofol alone? Will the sedation consistency observed with single-syringe ketofol be apparent with 2-syringe titration?

These are excellent questions and I look forward to further research aimed at answering them.

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DIAGNOSIS:

Adult intussusception caused by a perforated appendix. During surgical management of the intussusception, the cecum and proximal appendix were found to be necrotic, with focal perforation and an appendicolith. Partial cecectomy was performed and the patient was discharged with a percutaneous pigtail catheter in the pelvic cavity to drain fluid from an abscess formed in the cul-de-sac.

The cause of most adult intussusceptions appears to be idiopathic, with the second leading cause of adult intussusceptions being tumor (benign or malignant).¹ Intussusception from appendicitis is exceedingly rare, with an estimated 0.01% incidence rate and scarce reports of its occurrence in both children and adults.²⁻⁴ Contrast-enhanced abdominal CT is a diagnostic method of choice to reveal the underlying cause of adult intussusception.⁵ Management of intussusception with appendicitis is surgical; either appendectomy with cecectomy or right hemicolectomy is commonly undertaken, depending on the seriousness of the case.²

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