KETAMINE SHOULD BE THE PREFERRED AGENT FOR RAPID SEQUENCE INTUBATION

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Airway management in the emergency department (ED) is commonly performed using rapid sequence intubation. Rapid sequence intubation includes the administration of an induction agent to rapidly induce unconsciousness, followed by the administration of a neuromuscular blocking agent to facilitate laryngoscopy and tracheal intubation. Clinicians have several induction agents from which to choose, each with its own unique benefits and limitations. Although etomidate is commonly used, newer literature has supported the benefit of ketamine. In this Clinical Controversy article, we reviewed the literature supporting the advantages of ketamine over etomidate as a preferred agent for rapid sequence intubation.

Ketamine is an indirect, weak sympathomimetic agent that can lead to improved hemodynamic effects by limiting the reuptake of endogenous catecholamines.[1] This is particularly relevant in patients with hypotension for whom ketamine has been recommended as a preferred agent.[1] Recently, 2 large observational studies from the National Emergency Airway Registry (NEAR) reported higher rates of hypotension with ketamine versus that with etomidate.[2,3] Although referenced as a support for etomidate, these studies had significant limitations. To begin with, they were retrospective registry studies at risk of confounding. Patients in the ketamine group were more likely to have difficult intubation risk factors and disease states that may have contributed to peri-intubation hypotension. Additionally, centers participating in the NEAR may not reflect other EDs. They did not control the time to complete data, and forms were typically completed by residents relying on memory recall while likely subjected to multiple distractions in the ED. At best, the conclusions formulated from the NEAR provide a hypothesis for the generation of a randomized controlled trial; however, these data presently exist.[4] The 2009 KETASED study was a randomized controlled trial that evaluated etomidate versus ketamine for rapid sequence intubation in acutely ill patients.[4] In contrast to the observational studies identified from the NEAR, the KETASED study was a higher-quality study and was designed to ensure balance between the groups with respect to intubation conditions, hemodynamics, and acuity of illness. The KETASED study established ketamine as a viable alternative to etomidate. Given the available literature, only a larger randomized controlled trial appropriately powered to evaluate patient-centered outcomes (eg, mortality) would provide new evidence and streamline recommendations.

Ketamine possesses additional advantages. First, ketamine can cause direct bronchodilation in patients with asthma, improving oxygenation and ventilation or perfusion matching.[5] Although these benefits may also be achieved with a post-rapid sequence intubation ketamine infusion, selecting ketamine as the induction agent negates the unnecessary introduction of an additional medication (eg, etomidate) with a differing side effect profile. Next, ketamine has sedative and analgesic properties, whereas etomidate has only sedative properties. This can help bridge initial postintubation analgesia while transitioning to postintubation sedation and analgesia. Lastly, ketamine does not lead to adrenal suppression, whereas etomidate does. The 2009 KETASED study evaluated etomidate versus ketamine for rapid sequence intubation in acutely ill patients and found that etomidate increased the odds of adrenal insufficiency by 6.7-fold compared with ketamine.[4] Furthermore, the CORTICUS study, a randomized, double-blind, placebo-controlled trial evaluating hydrocortisone therapy for patients with septic shock, found that patients receiving etomidate had an increased rate of death at 28 days compared with those who did not (45.1% versus 31.5%, respectively).[6] Several limitations to the results of the CORTICUS study have been identified, including not being powered for a subgroup analysis, uncertain distribution of patient acuity, and not being a head-to-head trial for etomidate versus that for ketamine. Despite these limitations, the results are important because they clarify the misconception that etomidate-induced adrenal suppression is clinically insignificant and may be managed with corticosteroid supplementation alone. This has led the Surviving Sepsis Guidelines to provide a weak recommendation against the use of etomidate in pediatric patients with sepsis and a recommendation about the cautious use of etomidate in adults with sepsis.[7,8]

There were early concerns regarding the use of ketamine in patients with traumatic brain injury based on case reports from the 1970s suggesting that it increases intracranial pressure.[9] However, in a more recent systematic review, these concerns were found to be unjustified compared with other intravenous induction agents during rapid sequence intubation.[10] In addition, Upchurch et al[11] performed a retrospective evaluation of patients with trauma receiving etomidate or ketamine for

rapid sequence intubation. The authors found that etomidate and ketamine did not lead to differences in patient outcomes in terms of hospital mortality, ICU-free days, and ventilator-free days.

It is time to challenge the outdated practice of using etomidate in the ED for over 90% of intubations.[12] Ketamine offers unique benefits in several important patient populations while avoiding the risk of adrenal suppression. Given the information currently available, we believe that it is justified to use ketamine as the preferred first-line induction agent for rapid sequence intubation.

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