CONTROVERSIES

You need tube, me give one amp of etomidate and SUX

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SEE ALSO PAGE 347.

It is axiomatic that resuscitation begins with airway stabilization. Recognition of the need to intubate may seem straightforward compared with the task of selecting which agent(s) to give, and at what dose, at a time when seconds count. Each sedative agent has its strengths and weaknesses, and a distinct dose–response curve. The choice of agents is made more difficult by the complexity of resuscitation hemodynamics and the disjointed and fragmented information available at the moment of intubation. It would be much less stressful if there were a simple algorithmic answer. Is etomidate that answer? In a Controversies piece appearing in this issue (see page 347), Zed and colleagues review some of the recent literature regarding one aspect of a long-standing controversy surrounding this medication.[1] Unfortunately, one is left with an even broader controversy: Do we need this drug at all? This question is particularly relevant in Canada, where etomidate is not approved for general use. It must be obtained by application to the Special Access Program, which is intended for non-approved drugs on a compassionate or emergency basis when conventional therapies have failed, are unsuitable, or are unavailable.

In theory, a number of patient factors should influence selection of a sedative agent. However, local custom appears to be the most important.[2,3] Observations from the National Emergency Airway Registry confirm that in some US academic emergency departments, etomidate is used in over 80% of paralytic-assisted intubations.[2] Many emergency physicians believe that etomidate is the only agent to give with succinylcholine (SUX). Although the reasons given may vary, I suspect the most important reason is that, unlike thiopental, propofol or even midazolam, one can give the same dose to any adult and not expect the blood pressure to fall 3 minutes later. As a result, diagnostic uncertainties such as head injury with increased intracranial pressure, hemorrhagic shock, bronchospasm, systolic heart failure with acute ischemia, and cardiogenic shock are moot while the airway is being secured. It is also possible that historical barriers encouraged emergency physicians in some centres to select a drug that was no longer being used by anesthetists. These barriers are easy to forget in an era of procedural sedation by emergency physicians increasingly familiar with titrated propofol and ketamine.

Yet is etomidate the best agent for all (except perhaps the septic patient), or is it merely the agent that requires the least consideration? Many believe that the only purpose of the induction agent is to avoid paralyzing an awake patient. In fact, the sedative agent plays a key role in facilitating first-pass endotracheal intubation. Even in "paralyzed" patients, a potent centrally-acting sedative complements the peripheral action of the neuromuscular blocker to optimize intubating conditions and increase the likelihood of rapid intubation.[2,4] This effect has been demonstrated in emergency patients, and in simulated rapid sequence intubation in the operating room.[4–7]

When compared with thiopental or propofol, etomidate would appear to be a less potent sedative, and can even cause seizure-like myoclonus at doses currently used.[8–11] This is corroborated from the experience reported in patients who are given etomidate alone for emergency intu-

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bation and for procedural sedation.[12–16] In patients given a paralytic, our work with the National Emergency Airway Registry has shown 3-fold lower odds of the clinically important outcome of successful first-pass intubation when etomidate is used when compared with more potent agents, after adjustment for operator experience and other factors.[2]

What about the almost universal belief that etomidate ensures better hemodynamics? The apocryphal story of thiopental having killed more sailors at Pearl Harbor than did enemy bombs reminds us that "one drug, one dose" is especially dangerous in critically ill or injured patients.[17] Indeed, failing to consider the underlying pathophysiology in any resuscitation is likely to do more harm than good. In advanced hemorrhagic shock, for example, one can conceptualize the central circulating compartment as being severely reduced, with cardiac output travelling preferentially to the brain. Accordingly, it has been suggested that a 5- to 10-fold reduction in propofol dosing is appropriate for the same central effect.[18] Prospective cohort studies support the relatively benign effects of 0.3 mg/kg etomidate on post-intubation blood pressure, but it is important to appreciate that systolic blood pressure is only a marker of end-organ perfusion. The 25% drop seen with generous doses of thiopental are typically brief and respond to fluids, time, perhaps a touch of phenylephrine, and adjustment of the ventilator settings.[4] It may actually be seen as beneficial, signalling marginal hemodynamic reserve (cryptic shock) well before a central line can be inserted, intensifying and focusing further resuscitative efforts. Changes in systolic blood pressure 5 minutes after intubation is a surrogate outcome of unclear clinical significance, just like a blunted cosyntropin stimulation test 24 hours later.

So what about adrenocortical suppression? As reviewed by Zed and colleagues, there are more answers than questions.[1] We are beginning to appreciate that the physiologic response to stress may be both harmful and helpful, depending on degree and timing. We are attempting to mimic in high-risk patients certain responses associated with eventual survival. Unfortunately, we are far from knowing which patients might benefit from having their cortisol response iatrogenically shut down in the face of severe stress, including septic shock. The hypothesis that etomidate, followed by a fixed complementary steroid replacement dose, could be neutral or even beneficial is just that: a hypothesis for which equipoise might exist in the minds of some.[19] For others, it stretches our willingness to "first do no harm." Even Annane's data[20] originally cited as a personal communication[19] are hardly reassuring, representing an unplanned subgroup comparison between 17/31 deaths in the steroid group and 28/37 deaths in the placebo group (unadjusted $p = 0.08$, Fisher's exact). The uncertain interpretation of cosyntropin stimulation tests in critically ill patients, the largely unknown dose–response effects of corticosteroids at various phases of any severe disease process including sepsis, and the extremely high mortality rates following etomidate both historically and more recently[20,21] further limit the merits of even testing this hypothesis.

Perhaps the most serious flaw in the etomidate philosophy is that it can only be given as a one-time dose. Ten minutes post intubation the blood pressure has remained stable, the endotracheal tube is now confirmed to be in situ and has been secured, and the portable chest x-ray ordered. The sux is wearing off, as is the sedative effects of etomidate. Time to order an etomidate infusion? No, that has long been associated with acute adrenal insufficiency and high mortality rates, and was the basis for the moratorium on etomidate use.[22,23] Instead, the solution is often careful boluses of propofol, perhaps mixed with some ketamine, followed by an infusion. In short, the use of etomidate has not averted the use of these agents, and we are left with a patient whose adrenals may not work properly for a day or so, with an unknown clinical impact.[21,24–26] Indeed, whether this effect lasts 4, 12 or 24 hours, it far exceeds the duration of any other effect, beneficial or harmful, of the alternative agents.

Our sickest patients deserve our most careful attention with individualized resuscitation adapted to the available and dynamically changing information streams and patient response. Blending art and experience with incomplete science into rapid but nuanced decision is what we are expected to do and what defines our specialty. The concept of a single ideal drug for all intubations is as contrary to this philosophy as the notion that ACLS protocols are sufficient for the practice of emergency medicine. Some will argue that having etomidate available for occasional use broadens our therapeutic armamentarium and is therefore a good thing. For my part, I have seen the slide toward etomidate for all, and have difficulty asking Health Canada for access to this drug based on the "unsuitability" of available therapy.

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