Etomidate as an Induction Agent in Sepsis

Raymond J. Devlin, DNP, CRNA*, David Kalil, DNAP, CRNA

KEYWORDS

• Etomidate • Sepsis • Mortality • Adrenal insufficiency • Rapid sequence induction

KEY POINTS

- Sepsis is defined as a life-threatening response to infection that leads to organ dysfunction. Treatment may consist of securing the patients' airway to improve oxygenation.
- Etomidate has long been considered the induction agent of choice in critically ill patients requiring endotracheal intubation because of its pharmacologic profile.
- There has been much debate as to whether etomidate is safe in septic patients because of its effect on suppressing cortisol production.
- Etomidate inhibits the conversion of 11-deoxycortisol to cortisol by inhibiting 11β-hydroxylase. The steroid 11β-hydroxylase is essential for the final step in cortisol production.
- Questions remain whether etomidate is safe for use in patients with a diagnosis of sepsis; more research is still needed on its safety margin in sepsis.

INTRODUCTION

According to the 2016 Society of Critical Care Medicine/European Society of Intensive Care Medicine, sepsis is defined as a life-threatening response to infection that leads to organ dysfunction.[1] Septic shock is a form of sepsis that includes distributive shock involving cellular and metabolic abnormalities that carries a higher mortality risk than sepsis alone.[1] The clinical presentation of sepsis involves signs of an infectious source, arterial hypotension, fever, tachycardia, tachypnea, and signs of end-organ hypoperfusion.[1] Successful treatment of sepsis requires early recognition, which in many cases comes too late. When a diagnosis is confirmed and involvement of organ dysfunction identified, mortality can exceed 10% for most cases.[1] The later the diagnosis is made in the course of patient treatment, the higher the mortality rate. Treatment for severe cases of sepsis involving respiratory dysfunction consists of

Disclosure Statement: The authors do not have any relationship with a commercial company that has a direct financial interest in subject matter or materials discussed in the article or with a company making a competing product.

Nurse Anesthesia Program, Louisiana State University Health Sciences Center, School of Nursing, 1900 Gravier Street, New Orleans, LA 70112, USA
* Corresponding author.
E-mail address: rdevli@lsuhsc.edu

Crit Care Nurs Clin N Am ■ (2018) ■–■
https://doi.org/10.1016/j.cnc.2018.05.004 ccnursing.theclinics.com

securing the patients' airway to improve oxygenation and obtaining adequate intravenous access for fluid and antibiotic administration.[2] Septic patients, having tachypnea with respiratory rates increasing more than 20 breaths per minute, will become too weak to maintain adequate oxygen saturation. When this occurs, securing the patients' airway through endotracheal intubation and mechanical ventilation is essential.

In addition to providing anesthesia services for surgical procedures, anesthesia providers (Certified Registered Nurse Anesthetists and anesthesiologists) also provide anesthesia support for emergency rooms, labor and delivery suites, and intensive care units. Anesthesia providers are considered airway experts, possessing the knowledge and skills essential for intubation in critically ill patients requiring airway support. Medically unstable patients in intensive care units often require rapid sequence intubation (RSI) in times of declining respiratory function. When anesthesia providers are called for airway assistance, they often have little history available on the patient because the situation calls for rapid intervention. Airway equipment must be gathered quickly and the choice of induction agent must be made, often times within seconds. For many years, both etomidate and succinylcholine were the induction and paralytic agents of choice, respectively, in hemodynamically unstable patients requiring RSI. Etomidate is usually the first choice for induction, because it does not cause severe hypotension following administration. Critically ill patients requiring admission into the intensive care unit are very unstable, where even the slightest drop in their blood pressure could result in disastrous outcomes.

Etomidate possesses a safe pharmacologic profile by providing hemodynamic stability and has been the induction agent of choice in hypotensive patients for many years.[3] This unique drug is a short acting, nonbarbiturate, hypnotic induction agent that offers unique qualities such as cardiovascular stability, when compared with other agents such as propofol or midazolam.[4] Although etomidate has many favorable qualities, there is a major concern regarding the predictable adrenal insufficiency that follows its use. Septic patients with low cortisol levels seem to be at highest risk for prolonged adrenal insufficiency after etomidate administration. Results of early systematic reviews linked etomidate to increased mortality rates when used as an induction agent in patients with a diagnosis of sepsis or septic shock, whereas later studies found no correlation.[5,6] Controversy continues to this day as to whether etomidate should be avoided in the setting of sepsis or septic shock.

ETOMIDATE

Etomidate is an imidazole derivative that produces a sedative effect at the γ-aminobutyric acid ($GABA_A$) receptor, the major inhibitory neurotransmitter in the brain.[7] At low concentrations, etomidate modulates $GABA_A$, which allows these receptors to become activated by lower levels of circulating GABA. At higher concentrations, etomidate can directly activate $GABA_A$ receptors in the absence of GABA.[7] Etomidate is considered a nonbarbiturate hypnotic agent with no analgesic properties. When used as an induction agent, doses range from 0.1 to 0.4 mg/kg intravenous push and is supplied in a 2 mg/mL dose. Therapeutic doses have minimal effect on myocardial function, cardiac output, and peripheral or pulmonary circulation.[8] Etomidate has a rapid onset of action within 30 to 60 seconds, a peak effect in 1 minute, and 3 to 10 minute duration of action.[8]

In 1965, the first report on etomidate was published, and this unique drug was first introduced into clinical practice in 1972.[7] Interest in studies regarding etomidate have fluctuated over time with 2 significant discoveries. In 1983, etomidate interest