Etomidate use in septic patients requiring rapid sequence intubation

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Etomidate use in septic patients requiring rapid sequence intubation

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Disclosure Statement

The listed individuals have the following to disclose regarding financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation:

• Elizabeth Osmon, Pharm.D. – Nothing to disclose
• Nishika Patel, Pharm.D., BCPS, BCCCP – Nothing to disclose
Boca Raton Regional Hospital

• Not-for-profit 400 bed advanced academic tertiary medical center

• **Recognized leader in:**
  – Cardiovascular Care
  – Oncology
  – Women’s Health
  – Orthopedics
  – Emergency Medicine
  – Neurosciences

• Predominantly elderly patient population

• Highest ranked hospital in Palm Beach County

• Lynn Cancer Institute is one of the largest cancer programs in the state of Florida and accredited by the American College of Surgeons
Identify the effect etomidate has on cortisol production
During sepsis, pro-inflammatory markers stimulate the upregulation of cortisol release.

An increase in cortisol production results in metabolic, cardiovascular, and anti-inflammatory benefits in order to maintain homeostasis during stress.

A disruption in this mechanism causes primary adrenal insufficiency and a lack of adequate stress response.

Background

- Etomidate is a short-acting, sedative hypnotic that is often used as an induction agent for rapid sequence intubation (RSI)\(^1\).
- Etomidate inhibits the enzyme 11-\(\beta\) hydroxylase, which is responsible for the conversion of 11-deoxycortisol to cortisol\(^2\).
- Reduced plasma cortisol levels have been reported with a typical induction dose (0.3 mg/kg) of etomidate\(^1\).
- Although the role of etomidate in adrenal suppression has been established, the clinical consequences of this mechanism are controversial\(^2\).

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Arms</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ray, et al.¹</td>
<td>Single-center,</td>
<td>Etomidate vs. other</td>
<td>Induction agent did not affect duration ( (P = 0.54) ) or dose ( (P = 0.53) ) of vasopressor therapy</td>
</tr>
<tr>
<td>n = 159</td>
<td>retrospective</td>
<td>induction agents</td>
<td></td>
</tr>
<tr>
<td>Elliot, et al.²</td>
<td>Single-center,</td>
<td>Etomidate vs. other</td>
<td>No difference in the mean dose of vasopressor in norepinephrine</td>
</tr>
<tr>
<td>n = 50</td>
<td>retrospective</td>
<td>induction agents</td>
<td>equivalents ( (P = 0.61) )</td>
</tr>
<tr>
<td>Alday, et al.³</td>
<td>Multicenter,</td>
<td>Etomidate vs. other</td>
<td>No difference in need for</td>
</tr>
<tr>
<td>n = 411</td>
<td>retrospective</td>
<td>induction agents</td>
<td>vasopressor support with etomidate vs. non-etomidate ( (P = 0.88) )</td>
</tr>
</tbody>
</table>
To analyze if etomidate exhibits a dose dependent effect on the duration of intravenous (IV) vasopressor support and other clinical outcomes in septic patients.
Study Outcomes

Primary outcome

• Duration of IV vasopressor support between low dose (≤ 0.3 mg/kg) and high dose (> 0.3 mg/kg) etomidate

Secondary outcomes

• Number of patients requiring initiation of stress dose steroids
• Intensive care length of stay
• Duration of mechanical ventilation
• Inpatient mortality
Methods: Retrospective chart review using an electronic medical record (EMR)-generated report from October 21, 2017 to December 31, 2019

**Inclusion Criteria**
- Age $\geq$ 18 years
- Differential diagnosis of sepsis or septic shock based on provider documentation
- Received etomidate as an induction agent for RSI

**Exclusion Criteria**
- History of an adrenal disorder
- Taking medications that directly impact adrenal function prior to admission
**Statistical Analysis**

- **Primary Outcome**
  - Mann-Whitney U test

- **Secondary Outcomes**
  - Descriptive statistics
272 patients assessed

126 patients eligible

100 patients included

79 patients received low-dose

21 patients received high-dose

26 patients excluded
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low-Dose (n = 79)</th>
<th>High-Dose (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong> – years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>77</td>
<td>81</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>63 – 86.5</td>
<td>75 – 87</td>
</tr>
<tr>
<td><strong>Gender</strong> – no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>31 (39.2)</td>
<td>14 (66.7)</td>
</tr>
<tr>
<td><strong>Weight</strong> – kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>77</td>
<td>49.7</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>67.9 – 90</td>
<td>45.4 – 57</td>
</tr>
</tbody>
</table>
Primary outcome: median duration of IV vasopressor support was 32 hours vs. 50.5 hours, $P = 0.0455$
## Results

<table>
<thead>
<tr>
<th>Secondary Outcomes</th>
<th>Low-Dose (n = 79)</th>
<th>High-Dose (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated on stress dose steroids – no. (%)</td>
<td>24 (30.4)</td>
<td>6 (28.6)</td>
</tr>
<tr>
<td>Intensive care length of stay – days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>3 – 12</td>
<td>5 – 10</td>
</tr>
<tr>
<td>Duration of mechanical ventilation – days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>2 – 9.5</td>
<td>4 – 8</td>
</tr>
<tr>
<td>Inpatient mortality – no. (%)</td>
<td>27 (34.2)</td>
<td>5 (23.8)</td>
</tr>
</tbody>
</table>
Conclusion

There was a **statistically significant difference** in duration of IV vasopressor support between the low-dose and high-dose groups.

Secondary outcome results were similar between the low-dose and high-dose groups.

Despite the small sample size, the significant results of this study warrant the need for a randomized controlled trial to be conducted.
Limitations

- Inconsistent use of sepsis-3 criteria among providers
- Limited provider documentation
- Oral vasopressor support (i.e. midodrine) was not evaluated
- Small sample size
- Unequal treatment group sizes
Acknowledgment

Nishika Patel, Pharm.D., BCPS, BCCCP
Self-Assessment Question

Which of the following correctly describes the effect etomidate has on cortisol production?

A. Etomidate directly binds to cortisol, which makes it inactive.
B. Etomidate inhibits the enzyme 11-β hydroxylase, which is responsible for conversion of 11-deoxycorticisol to cortisol.
C. Etomidate regulates cortisol production through a negative feedback mechanism.
D. Etomidate does not affect cortisol production.
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