Is Single-Dose Etomidate Induction Safe in Emergency Intubation of Critically Ill Patients?

EBEM Commentators
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Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies, Number of Patients</th>
<th>Relative Effect (95% CI)</th>
<th>Heterogeneity ($I^2$), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>6 studies, 772 patients</td>
<td>OR 1.17 (0.86 to 1.6)</td>
<td>0</td>
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<tr>
<td>Duration of mechanical</td>
<td></td>
<td>Avg duration: 1.5–13 days; etomidate effect 2.14 days (-1.67 to 5.95 days)</td>
<td>86</td>
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<td>ventilation, days</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Organ dysfunction (SOFA scores)</td>
<td>1 study, 469 patients</td>
<td>Mean SOFA score: 9.6; etomidate effect 0.7 (0.01 to 1.39)</td>
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OR, Odds ratio; SOFA, Sequential Organ Failure Assessment score.

Of 1,395 potential titles screened, 8 studies were included in the review; however, only 7 were combined in a metaanalysis. Two of these 7 studies were determined to be at low risk of bias, whereas 5 were considered to be at moderate risk.

Commentary

Etomidate has been a controversial induction agent in emergency intubation for a number of years because of concerns about adrenal suppression and subsequent adverse outcomes. The concern about etomidate safety in septic patients was first raised in an observational substudy of the Corticosteroid Therapy of Septic Shock trial. The specific flaws of this study are elaborated elsewhere, revealing multiple confounding factors and reporting omissions that preclude the erroneous conclusion that etomidate increases mortality in septic patients. This mistake was perpetuated in a meta-analysis with the same conclusion, although examination of the forest plots show a clear outlier result driving the increased mortality conclusion. A recent summary of that meta-analysis discussed this outlier observational trial in the context of other randomized controlled trials that show no mortality increase. The Cochrane review by Hohl et al. rightly excluded this observational study in the overall mortality analysis and corrected the erroneous conclusion of etomidate harm from the meta-analysis by Chan et al.
A thorough systematic review by Hohl et al showed that etomidate does transiently (<24 hours) reduce adrenal function. That review was underpowered to note a difference in hospital or ICU length of stay, ventilation duration, or mortality. In this updated Cochrane review, moderate evidence (6 trials, 772 patients) confirms no increase in mortality or any other clinically important endpoint (eg, ventilation duration). A “worst-case scenario” analysis using imputation for missing patients also failed to show increased mortality (odds ratio 1.15; 95% confidence interval 0.86 to 1.53). A clinically inconsequential reduction in adrenal function was observed. No subgroup analysis focusing on specific diagnostic groups (eg, septic shock) was undertaken.

Editor's Note: This is a clinical synopsis, a regular feature of the Annals Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: Bruder EA, Ball IM, Ridi S, et al. Single induction dose of etomidate versus other induction agents for endotracheal intubation in critically ill patients. Cochrane Database Syst Rev. 2015(1): CD010225.


Michael Brown, MD, MSc, Alan Jones, MD, and David Newman, MD, serve as editors of the SRS series.