Etomidate for RSI in the Critically Ill

Key Article:

- *Kotani Y, Piersanti G, Maiucci G, et al. Etomidate as an induction agent for endotracheal intubation in critically ill patients: A meta-analysis of randomized trials. Journal of Critical Care 2023; Volume 77.*

Background

- Etomidate is commonly used as an induction agent for endotracheal intubation.
- Favorable for its rapid onset and hemodynamically neutral profile
- There has been conflicting evidence and ongoing controversy around etomidate's potential adverse effects including adrenal suppression, increased risk of multiorgan dysfunction and increased mortality in critically ill patients.
- Recent literature
    - Multiple meta-analysis with conflicting results
    - Etomidate vs ketamine for emergency endotracheal intubation. Intensive Care Med 2022
        - 801 critically ill patients randomized to etomidate or ketamine
        - 7d survival lower with etomidate
        - 28d survival no difference

Objective

- To compare etomidate to other anesthetic agents in terms of mortality in critically ill patients.

Methods

- Systematic review and meta-analysis of randomized controlled trials published up until September 20, 2022.
- Patients
    - Included: critically ill adults undergoing endotracheal intubation in varying settings (prehospital, ED, ICU settings)
    - Excluded: non- RCT studies (systematic reviews, editorials, lit reviews), pediatric patients < 15 yo, infusions excluded
- Trial procedures
    - Two independent investigators extracted RCTs on PubMed, EMBASE, and Cochrane Library using a standard data collection form
    - If studies lacked data, investigators would reach out to authors for further information
    - Assessed bias risk via Cochrane risk-of-bias tool
- Primary outcome
    - Mortality at time point defined by study
- Secondary outcomes
    - Development of adrenal insufficiency

Results

- 4398 records identified in total
- 11 RCTs included (2704 critically ill adults)
    - Country: USA (8), UK (1), France (1), Netherlands (1)
    - Comparison induction agent: ketamine (4), midazolam (4), thiopental (1), ketamine + midazolam (1), ketamine + propofol (1),
- Etomidate dose 0.2-0.3 mg/kg in most studies
- Primary Outcomes
    - Mortality defined by authors (measured in 11 studies)
        - Etomidate group: 23%
        - Comparison group: 20%
        - RR 1.16; 95% CI 1.01-1.33; p 0.03
        - NNH = 31
        - NO statistically significant difference with outcome mortality at longest follow up
- Secondary Outcomes
    - Risk of adrenal insufficiency (measured in 6 studies)
        - Etomidate group: 21%
        - Comparison: 10%
        - RR 2.01; 95% CI 1.59 – 2.56; $p < 0.001$
- Sensitivity analysis for 1' and 2' outcomes
    - Comparing specifically etomidate vs ketamine
    - Still increased mortality and adrenal insufficiency in etomidate group

Limitations Identified by Authors

- Heterogeneity in studies included especially with timing of mortality measurements and diagnosing adrenal insufficiency
- Addition of other induction/sedation medications due to inadequate sedation within the studies
- Etomidate vs multiple different induction agents as comparator

Take Home Points

- Study suggests etomidate confers an increased risk of mortality and adrenal insufficiency
- Authors conclude etomidate is causing harm and strongly advocate for removal of etomidate as induction agent for current international guidelines
- Still mixed evidence around safety of etomidate as an induction agent, but this is largest meta-analysis to date