ARTICLE:
- Citation: Tekwani KL, Watts HF, Sweis RT, Rzechula KH, Kulstad EB.
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PURPOSE:
- Research Question(s): Is the use of etomidate as an induction agent for intubation associated with a longer hospital length of stay.
- Hypothesis: Etomidate will be associated with longer hospital length of stay.

DESIGN:
- Study Design: Prospective, randomized, double-blind clinical trial.
- Dependent / outcome Variable(s):
  - Primary: Hospital Length of Stay
  - Secondary: Inhospital mortality, ICU length of stay, length of time intubated.
- Independent / research Variable: Etomoidate (0.3 mg / kg) vs. Midazolam (0.1 mg/kg).

SETTING / SUBJECTS:
- Research Setting: Large, tertiary care suburban hospital – 50 ED beds; 90,000 annual ED volume.
- Subjects:
  - Study population: All patients over 18 who were intubated in the ED and had suspected infectious cause of their illness.
    - Required 2/4 SIRS criteria and confirmed infection (via cultures, radiographic findings, or strong clinical suspicion and administration of antibiotics).
    - Secondary per-protocol analysis was performed on those patients with confirmed sepsis at the time of death / discharge.
Inclusion / Exclusion criteria: Age <18, pregnancy, DNR, pre-hospital cardiopulmonary arrest.

Number (control / intervention groups): 303 would have been eligible, 122 were enrolled - 63 Etomidate, 59 Midazolam.

- Study size was based on previous studies, which indicated a 3-day difference in LOS. Study was powered for a Type I error of 5% and power of 80%.

Demographics: Study groups were statistically similar. Additionally, baseline characteristics of enrolled patients were similar to those not enrolled.

Attrition: 2 patients in the etomidate group were transferred to outside hospitals.

METHODS:
- Interventions: Choice of induction agent.
- Study Groups: Etomidate vs. Midazolam.
- Data Collection: Patient data were recorded using a spreadsheet. Patients were followed by study investigators throughout their hospitalization. Enrollment was facilitated by an available study coordinator, study investigator, or ED pharmacist. Patients who were not enrolled were identified using the computerized medication dispenser.

DATA ANALYSIS:
- Level of Data: Interval
- Statistics Used:
  - LOS was compared with Mann-Whitner U test.
  - Mortality was compared with the chi squared test.
  - Death rates were compared using Kaplan-Meier survival curves and log-rank statistics.

- What, if any, confounding variables were controlled for / adjusted for: Steroid use, SAPS II score, SOFA score, vasopressor requirement, transfusion in the ED, MAP, puse rate, Lactate, baseline cortisol.

RESULTS:
- Brief answers to research questions:
  - Primary: There was a nonsignificant trend towards DECREASED hospital LOS in the etomidate group (etomidate 7.3 days vs. midazolam 9.5 days, P.17).
  - Secondary: There was no significant difference in ICU LOS, ventilator days, or inhospital mortality between the two groups.
There was a nonsignificant trend toward increased mortality in the etomidate group (43% vs. 36%, 95% CI -10-24%).

- There was no significant difference in the results in the intention-to-treat population vs. the per-protocol population.

- **Additional findings:**
  - There was no significant difference in steroid use between the population or association between steroid use and mortality.

- **Other possible explanation for findings:**
  - It is possible that early deaths in one of the groups could have led to the appearance of shorter hospital LOS. However, the authors adjusted for this and still found no difference.

- **Limitations?:** Low sample size and not powered for detection in mortality differences. No strict protocol on patient management following intubation.

**IMPLICATIONS FOR PRACTICE:**
- **Applicable to this clinical practice:** Absolutely.
- **Feasibility (cost, resources, etc):** Easy.
- **Clinically Relevant:** Very much.

**LEVEL OF EVIDENCE / DECISION FOR USE:**
- **Level of Evidence:**
  - Ia Evidence obtained from meta-analysis of randomized controlled trials
  - Ib Evidence obtained from at least one RCT
  - IIA Evidence obtained from at least one well-designed controlled study without randomization
  - IIB Evidence obtained from at least one other type of well-designed quasi-experimental study
  - III Well-designed non-experimental studies
  - IV Expert committee reports, opinions of experts