Journal Club Eastern Virginia Medical School
Therapy Article

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Citation: Conway, J., et al, **Ketamine Use for Tracheal Intubation in Critically Ill Children Is Associated With a Lower Occurrence of Adverse Hemodynamic Events**. *Critical Care Medicine*, 47, p.498.

I. **WHAT IS BEING STUDIED?**	
1. Study Objective	To study "whether the administration of ketamine for tracheal intubation in critically ill children with or without shock was associated with fewer adverse hemodynamic events compared with other induction agents." "We also investigated if there was a dose dependence for any association between ketamine use and adverse hemodynamic events."
2. Study Design	Retrospective analysis of prospectively collected observational data from the NEAR4KIDS and PALISI databases that included 40 PICU's in US & Canada
3. Inclusion Criteria	All tracheal intubations younger than the age of 18 from June 2013-June 2017 from participating PICU's
4. Exclusion Criteria	Tracheal tube exchange
5. Interventions Compared	Number of "adverse hemodynamic events" in ketamine vs. fentanyl and midazolam or propofol induction groups.
6. Outcomes Evaluated	Evaluated adverse events within 20 minutes of TI, defined as: 1. Dysrhythmia (brady and tachy) 2. Hypotension requiring intervention 3. Hypertension requiring intervention 4. Cardiac arrest w/ or w/o ROSC during TI

	Evaluated the first "course" of each TI encounter (any approach to secure an artificial airway) with ketamine alone or in combination Evaluated relationship between increasing the dose of Ketamine and outcomes Specifically evaluated patients with hemodynamic instability/shock Evaluated relationship between increasing dose of ketamine and doses of midazolam/fentanyl to evaluate the effect of increasing dose of ketamine may or may not potentially be explained by concomitant drug administration
II. **Are the results of the study valid**	Yes
1. Was the assignment of patients randomized?	No. This was a retrospective analysis of a prospectively collected database.
2. Was randomization concealed (blinded)?	N/A
3. Were patients analyzed in the groups to which they were randomized?	N/A
4. Were patients in the treatment and control groups similar with respect to known prognostic factors?	Probably not. Patients with sepsis and or shock disproportionally received ketamine 12.% vs. 5.7% and in cardiac disease 24.6% vs. 15.7% (p=0001) Patients with neurological insults were less likely to receive ketamine 22.8% vs. 9.5%
III. **Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1. Were patients aware of group allocation?	No.
2. Were clinicians aware of group allocation?	Yes. Clinicians selected their induction a agents of choice.

3. Were outcome assessors aware of group allocation?	Yes. There is no mention whether data analysis was performed by individuals who were blinded to study objectives.
4. Was follow-up complete?	N/A
IV. What were the results? Answer the questions posed below	Results: - 10,750 primary TI performed - 32% (3436) included ketamine - Note: ketamine was less likely to be used in patient < 12 months of age ($p < 0.01$) - 415 patients (49.7% of total patients with sepsis/shock) induced with Ketamine - 609 patients (41.4% of total patients with hemodynamic instability/shock) induced with Ketamine - Video laryngoscopy was more often used with Ketamine than without (23.5% versus 19%) - Adverse hemodynamic occurred in 5.5% of patients (total) o 3.3% hypotension o 1.4% cardiac arrest w/ or w/o ROSC (3 patients all had laryngospasm, all had ketamine and "coadministration with other agents") o 1.3% dysrhythmias Children who received ketamine had a lower odds of these events (significant) – OR 0.75(CI, 0.62–0.90), also had lower OR 0.74(95% CI,0.57–0.90) after adjusting for patient/provider characteristics, device and use of neuromuscular blockade, and clustering within a site. o OR 0.72 for children without hemodynamic instability/shock (significant) o OR 0.81 for children w/ hemodynamic instability/shock (not significant) - Higher occurrence of adverse event

	in older children (significant) o 1-7 y OR 1.42 o 8-17 y OR 1.36 - Mean dose was 1.88 mg/kg, trend for lower odds of adverse events for higher dosing in both children w/ wne w/o hemodynamic instability/shock o OR 0.64 and OR 0.79 (significant) - Laryngospasm reported in 28 TI (0.26) – 0.32% with ketamine and 0.23% without ketamine – not significant
1. How large was the treatment effect? (Difference between treatment and control group).	As above.
2. What was the estimated treatment effect at a 95% confidence interval? (Precision)	See CI's on table 3
V. **Will the results help me in caring for my patients? (Applicable?)**	Yes
1. Were the study patients similar to my patient?	Possibly. This was not an ED based study so the patient population may not be exactly representative. Also, pre-intubation interventions such as fluid boluses and other resuscitative interventions were not controlled for so hemodynamic differences could be attributable to a host of interventions.
2. Were all clinically important outcomes considered?	For the most part. No reporting on need for re-dosing or need for rescue sedation compared to other agents. Dosing of Ketamine was a useful consideration. Starting on the higher end. Stated use with caution due to the known myocardial suppressant effect. May not have had an issue as patients may not have been "catecholamine depleted" and may have had another vasodilatory induction agent.
3. Are the likely treatment benefits worth the potential harm and costs?	Unclear whether laryngospasm was present in non-ketamine group. All 3 cardiac arrests w/o ROSC had laryngospasm.

	Would have been helpful to provide more specific data on those patients. Though rare, survival in this very small group of 3 patients was 0%. Is this problematic?

Study Limitations:

- Non-ED patient population.
- Highly predisposed to selection bias which is evident in percentages of patients who were selected to receive ketamine for induction.
- The degree of pre-existing hemodynamic instability was not defined – so may have varied how unstable these patients were or if pressors were needed
- The proportion of video laryngoscopy was higher where Ketamine was used as well as resident participation was lower – could affect results
- Tracheal intubation practices may vary depending on geographic location – this was an international study
- Data was self reported – subject to reporting bias or inaccuracy

Clinical Bottom Line:

- In critically ill pediatric patients who show signs of hemodynamic instability or cardiac impairment, the use of ketamine for induction may be associated with less hemodynamic effects when compared with other induction agents. Further RCT's are warranted.