Journal Club Eastern Virginia Medical School Article

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CITATION:
Jones P. et al., **The effect of atropine on rhythm and conduction disturbances during 322 critical care intubations. Pediatr Crit Care Med. 2013 Jul; 14(6) 289-97.**

I. WHAT IS BEING STUDIED?	
1. Study Objective	a. Prevalence of arrhythmia and conduction abnormalities before critical care intubation b. Atropine has no effect on the prevalence of new arrhythmias or conduction abnormalities
2. Study Design	Prospective, observational study
3. Inclusion Criteria	• Between September 2007 and 2009 • PICU and Pediatric Neonatal Intensive Care Transport Service of l'Hopital Robert Debre, Paris, France • All intubations of children who were not asystolic and were of age less than 8 years old
4. Exclusion Criteria	Patient not at sinus rhythm at baseline
5. Interventions (Observations) Compared	a. 1 minute baseline EKG prior to start of intubation b. 1 minute EKG performed 2 minutes after injection of atropine c. Continuous EKG and SpO2 from insertion of laryngoscope to positioning of ETT in trachea and connection to ventilator
6. Outcomes Evaluated	• Baseline HR and HR 2 minutes post atropine injection • Lowest R-R complex (HR) during intubation • Any arrhythmias (not including sinus brady and sinus tach)
II. ARE THE RESULTS OF THE STUDY VALID	
1. Was the assignment of patients randomized?	No. The decision to use atropine was dependent on the discretion of the intensivist and/or junior performing the intubation. This would potentially create Selection bias

2. Was randomization concealed (blinded)?	No. This was non-randomized.
3. Were patients analyzed in the groups to which they were randomized?	Yes.
4. Were patients in the treatment and control groups similar with respect to known prognostic factors?	No. Some characteristics were different a. No atropine group: differences (no CI's or p-values reported) • 48 days median age vs 17 days • More in non neonatal respiratory distress 62 vs. 35 • Received more propofol (69 vs. 40) and ketamine (15 vs.4) as induction agents • Less midazolam 15 vs. 28
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?	Technically yes, although during emergent intubation and their age, you could argue they were not truly aware whether or not they received atropine beforehand.
2. Were clinicians aware of group allocation?	Yes. They chose whether or not a patient would get atropine based on their own judgment.
3. Were outcome assessors aware of group allocation?	Yes and no. Two pediatric intensivists reviewed the EKGs independently and were not blinded to the atropine treatment. However, blinding did occur in the electrophysiologist who reviewed all potential arrhythmias. The study clinicians who chose whether to push atropine, were the same clinicians who were analyzing the EKG for arrhythmias. The 'abnormal' EKGs (excluded: "Sinus brady/tachycardias were excluded as abnormal" brady and were then reviewed by an electrophysiologist who was not aware of the group allocation. The electrophysiologist also reviewed 10% of randomly selected normal EKGs as well.
4. Was follow-up complete?	The study design did not include further follow-up post intubation.
IV. WHAT WERE THE RESULTS? Answer the questions posed below	
1. How large was the treatment effect? (Difference between treatment and control group).	• Baseline arrhythmias before start of intubation at 1.5% (5/327) • Atropine raised mean HR from baseline

	153/min to 171/min ($p<0.001$), this was similar in all age groups • 0 EKG abnormalities were detected in the minute following atropine injection. • Higher prevalence of abnormal rhythms and conduction abnormalities during intubation without atropine (45/170; 26.5%) versus with atropine (7/152; 4.5%), Absolute Risk Reduction = 22% 95% CI and $p<0.001$
2. What was the estimated treatment effect at a 95% confidence interval? (Precision) Table 3 RR = 1 means there is no difference RR > 1 means that the exposure (atropine) is associated with the outcome (arrhythmia) RR < 1 means that the exposure (atropine) is less likely with regard to the outcome (arrhythmia)	Calculation Relative Risk = a/a+b ÷ c/c+d 7/152 ÷ 45/170 = 0.17 Relative risk reduction RR of 0.17 in this study indicates that atropine was protective for development of arrhythmias in children < 8 years of age. OR for atropine (table 3) was 0.17 [95% CI, 0.07–0.39], $p< 0.001$ for all intubations
V. **WILL THE RESULTS HELP ME IN CARING FOR MY PATIENTS? (APPLICABLE?)**	
1. Were the study patients similar to my patients?	Maybe • CHKD ED, many children <8 years old, require emergent intubation. • This study also did not include many pre-term babies, but this is applicable at CHKD ED- since they are likely still in the NICU • France used MD's on ICT EMS teams. Higher proportion of neonates may be associated with home births, which would reflect a different patient population. No • How does this pertain is children >8 years old in the ED • We use different induction agents at CHKD to include paralytics (I believe?). How do results change when added with succinylcholine or rocuronium?
2. Were all clinically important outcomes considered?	No. • Although arrhythmias were documented, were these patient

	oriented and or clinically significant? • No reporting the length of time of the arrhythmia. Duration of an arrhythmia could predispose to conversion into a fatal arrhythmia? • Does the addition of atropine alter hospital LOS or LOS in ICU
3. Are the likely treatment benefits worth the potential harm and costs?	A decrease in the number of 'arrythmias' may be clinically significant though harms associated with transient arrythmia was not included in analysis. This study shows that atropine does in fact increase HR across all age groups. No evidence that atropine predisposed to additional harms though authors did not include sinus tachycardia or bradycardia in their assessment. . Per authors, it seems as if benefits highly outweigh any potential harm and cost. But then again, I would like to review the clinically important outcomes listed above.

Limitations

- **Study Design**
  - **Non randomization**
    - **Allocated groups with different patient populations**
  - **No blinding**
    - **Selection bias in determining the who gets atropine**
    - **Reporting bias on 27 patients excluded from study due to poor quality EKG**
    - **Observer bias in analyzing the rhythms. No reporting of kappa score between two 'independent' screeners**
  - **No control over sedatives used (multiple confounders)**
    - **Older children/ no atropine group tended to get more propofol, was this the cause of the decrease in HR noted?**
    - **Significant differences in use of Propofol, Ketamine and Midazolam**
  - **Rarely any paralytics used**
  - **Single hospital and pre-hospital study**

- **Clinically relevant outcomes**
  - **Are arrhythmias noted life threatening or are these similar to bradycardia noted during physiologic events such as burping, having a BM, etc.**
  - **Do arrhythmias noted lead to decrease in brain perfusion and longterm sequelae**

Clinical Bottom Line:

- **Atropine seems safe to use and prevents arrhythmias in the emergent intubation of children <8 years old.**
- **No reporting on other potential mal effects of atropine such as urinary retention.**
- **Our Peds EM attendees state that atropine is never used prior to RSi in our community**