Critical Review Form

Therapy

PGY-3

Succinylcholine versus rocuronium for rapid sequence intubation in intensive care: a prospective, randomized controlled trial. *Crit Care.*

Objectives: **"to compare the incidence of hypoxemia after rocuronium or succinylcholine in critically ill patients requiring an emergent RSI." (p. 2)**

Methods: **This prospective randomized controlled single-blind trial was conducted in the medical and surgical intensive care units of the University Hospital of Basel, Switzerland, and tertiary care center between August 2006 and June 2010. All adults age ≥ 18 requiring emergent endotracheal intubation (ETI) with RSI were eligible. Exclusion criteria included:**

1) **Contraindications to succinylcholine**
2) **Allergy to rocuronium**
3) **Pregnancy**
4) **Known or anticipated difficult intubation requiring awake fiberoptic intubation**
5) **Absence of a qualified study physician to perform the intubation.**

Stratified randomization by gender was used to ensure an equal number of male and female patients. Paralytic doses used were 0.6 mg/kg of rocuronium and 1.0 mg/kg of succinylcholine. During pre-oxygenation, patients were administered 1 µg/kg of intravenous (IV) fentanyl, after which an IV induction agent was used: 0.2 mg/kg of etomidate in patients whose mean arterial pressure was < 80 mmHg and/or on catecholamine infusion, 1 mg/kg of propofol in all other patients.

The primary outcome was the incidence of oxygen desaturation defined as a drop of ≥ 5% in pulse oximetry reading at any time between the start of induction and 2 minutes following completion of intubation. A severe oxygen desaturation was defined as a drop ≥ 5% leading to an oxygen saturation level ≤ 80%. Secondary outcomes were:

1) **Duration of intubation sequence (measured by stopwatch) defined as the interval between administration of the induction agent and the first appearance of end-tidal carbon dioxide on the monitor.**
2) **Incidence of failed first intubation attempts.**
3) **Numerical and qualitative measurements of intubation conditions rated by the intubating physician (Table 1).**
4) **Hemodynamic consequence of intubation between the start of induction and 5 minutes following intubation.**

An *a priori* power analysis indicated that in order to detect a 20% difference in the primary outcome with a power of 0.9 and two-sided α of 0.05, 250 patients would be required for each group. A planned interim analysis indicated that 200 patients would be required for each group; to account for protocol violations, 210 patients were enrolled in each group.

Table 1 Scoring system for intubation conditions

	Score 3	Score 2	Score 1
Laryngoscopy • Jaw relaxation • Resistance to blade	 Relaxed None	 Acceptable relaxation Slight resistance	 Poor relaxation Active resistance
Vocal cords • Position • Movement	 Abducted None	 Intermediate Moving	 Closed Closed
Intubation Response • Limb Movement • Coughing	 None None	 Sliught Diaphragmatic	 Vigorous Severe coughing or bucking

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	Yes. Stratified randomization by gender used to ensure equal numbers of male and female patients. Allocation occurred using sealed envelopes, however the method of sequence generation was not supplied.
2.	Was randomization concealed (blinded)?	Uncertain (likely yes). While patients were randomized and allocated by sealed envelope, it is unclear if the envelopes were opaque and if the randomization sequence would prevent prior knowledge of allocation to the physician/clinician.
3.	Were patients analyzed in the groups to which they were randomized?	Yes. While 4 patients who were randomized did not receive paralytic due to decompensation (2 in each group) and 10 patients were not analyzed due to an inability to measure oxygen saturation (4 in the succinylcholine group and 6 in the rocuronium group), the primary and secondary outcomes could not be assessed in these patients.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. For succinylcholine and rocuronium, Table 3 indicates similar mean age (60 vs. 63), mean weight (73 vs. 74 kg), mean APACHE II score (21 vs. 22), number of subjects with a history of COPD (32 vs. 30), 28-day mortality rate (73 vs. 82) indications for intubation (respiratory failure: 134 vs. 130; neurology: 42 vs. 50; and shock: 24 vs. 21), and induction agent (propofol: 101 vs. 94; etomidate 99 vs. 107).
B.	**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. According to the trial registry at ClinicalTrials.gov, study subjects were blinded to group allocation.
2.	Were clinicians aware of group allocation?	Yes. This was a single-blinded study in which study subjects were blinded. Physician awareness of group allocation could lead to performance bias.
3.	Were outcome assessors aware of group allocation?	Yes. While the presence of desaturations (primary outcome), duration of the intubation sequence, and the incidence of failed first intubation attempts are fairly subjective outcomes and not as prone to bias, the scoring of intubation conditions, as assessed by the

		prone to ascertainment bias.
4.	Was follow-up complete?	Yes. All patients were followed for the duration of the study.
II.	**What are the results (answer the questions posed below)?**	
1.	How large was the treatment effect?	• Between the succinylcholine and rocuronium groups there was no significant difference in the incidence of oxygen desaturation (37% vs. 34%, p = 0.67; RR = 1.1, 95% CI 0.84-1.43) or severe desaturation (10% vs. 10%, p = 1.0; RR = 1.0, 95% CI 0.55-1.79). • There was no difference in the need for more than one intubation attempt (16% vs. 18%, p = 0.4; RR = 0.89, 95% CI 0.58-1.38). • The intubation sequence was shorter in the succinylcholine group (81 ± 38 sec) than the rocuronium group (95 ± 48 sec), p = 0.002. • The numerical scores for ease of laryngoscopy (succinylcholine 2.75 ± 0.45, rocuronium 2.75 ± 0.46; p = 0.84) and vocal cord condition (succinylcholine 2.61 ± 0.52, rocuronium 2.67 ± 0.56; p = 0.32) did not differ. • There was a statistically significant difference in the score for response to intubation (succinylcholine 2.97 ± 0.20, rocuronium 2.86 ± 0.36; p = 0.001). • There was no difference for the overall score for intubation conditions (succinylcholine 8.3 ± 0.8, rocuronium 8.2 ± 0.9; p = 0.7).
2.	How precise was the estimate of the treatment effect?	See above.
III.	**How can I apply the results to patient care (answer the questions posed below)?**	
1.	Were the study patients similar to my patient?	No. These were patients in the ICU rather than patients in the emergency department. While there are likely many similarities, these patients would at least be partially resuscitated by arrival in the ICU, were more likely to be post-operative, less likely to be acutely traumatic, and would be more likely to have known medical history and lab values (particularly serum potassium). Additionally, these were Swiss patients, and I would suspect that the average weight and/or BMI would be significantly higher in patients at our

		institution. Issues with external validity may limit applicability to our patients.
2.	Were all clinically important outcomes considered?	No. More patient-important outcomes could have been considered, neurologic status, complication rates (such as aspiration), hospital length-of-stay, and cost.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain. Succinylcholine and rocuronium appear to provide similar intubating conditions and similar rates of oxygen desaturation. The study was performed in ICU rather than ED patients, bringing external validity into question. In addition, a study with more relevant outcomes may be needed to provide additional insight.

Limitations:

1) **The study was performed in ICU patients, making external validity an issue.**

2) **While the study was randomized, physicians were not blinded to group allocation; the subjective nature of the outcomes raise concerns for ascertainment bias**

3) **The clinical significance of oxygen desaturation during intubation is questionable. More patient-important outcomes could be considered.**

Bottom Line:

This randomized, controlled, single-blinded study compared succinylcholine and rocuronium in RSI in ICU patients. No difference was seen in the primary outcome, the oxygen desaturation or severe desaturation. Issues of clinical significance, ICU setting, and bias due to lack of physician blinding make application of the results difficult.