Critical Review Form

Meta-analysis

Rocuronium versus succinylcholine for rapid sequence induction intubation. Cochrane Database Syst Rev.

Objectives: **"The objective of this study was to determine whether rocuronium creates similar intubating conditions to those of succinylcholine during RSI intubation." (p. 3)**

Methods: **A systematic review of the literature was conducted using a validated randomized controlled trial (RCT) filter (Haynes 1994). The authors searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The *Cochrane Library,* 2007 Issue 3), MEDLINE (1966 to June Week 3 2007), EMBASE (1988 to 2007 Week 26) to identify all clinical trials relating to the use of rocuronium and succinylcholine during RSI. References of included studies were searched by hand to identify additional citations.**

RCTs and controlled clinical trials were included if they 1) reported a score of intubating conditions as one of the main outcomes, 2) compared rocuronium and succinylcholine, and 3) utilized a rocuronium dose of at least 0.6 mg/kg and succinylcholine dose of at least 1 mg/kg. Two independent appraisers reviewed relevant articles for inclusion. Disagreements were settled by consensus, or by a third author when consensus could not be reached. A total of 58 studies were identified, of which 39 met inclusion criteria. Two of these were duplications resulting in 37 studies in the final analysis.

Of these 37 trials, none was conducted in emergency department patients; while four studies were conducted using patients requiring emergent intubation, these were all conducted in operating room settings. The studies were published between 1991 and 2006, and all of the included studies were randomized controlled trials. Two authors extracted data using standardized data collection forms and assessed methodological quality, rating all studies for allocation concealment. The presence of absence of blinding was not used to assess study quality: blinding of patients would not likely affect the outcomes, and blinding of physicians would not be possible given the presence of fasciculation in patients receiving succinylcholine.

Intubating conditions were assessed using the Goldberg scale (Goldberg 1989) (Table 1). When this was not directly reported, data was converted to this scale when sufficient detail was available to do so. Studies were combined using a random-effects model. The primary outcome was excellent intubation

conditions created during RSI based on the Goldberg scale (a score of 3). The secondary outcome was clinically acceptable intubation conditions (excellent or good, score 3-6).

Table 1. Intubating conditions

Score	Ease of laryngoscopy	Vocal cords	Intubation response
1 – Excellent	**Good**	**Open**	**None**
2 – Good	**Fair**	**Open**	**Diaphragmatic movement**
3 – Poor	**Difficult**	**Movement**	**Moderate coughing**
4 – Impossible	**Poor**	**Closed**	**Severe coughing or bucking**

An *a priori* subgroup analysis was performed for the following groups: simulated RSI versus modified RSI, induction agent, use versus nonuse of a narcotic, rocuronium doses (0.6, 0.9, or 1.2 mg/kg), and adult versus pediatric age groups.

Guide	Question	Comments
I	***Are the results valid?***	
1.	Did the review explicitly address a sensible question?	Yes. The question of whether rocuronium can produce similar intubating conditions to succinylcholine when used in RSI is sensible and relevant.
2.	Was the search for relevant studies detailed and exhaustive?	Yes. As with most Cochrane reviews, the search was extensive and well described. A previous review was published in 2003 (Perry 2003); the authors used the articles from the previous review and conducted an additional literature search of the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and EMBASE to identify trials published in the interim. References of included studies were searched by hand to identify additional relevant articles. Conference proceedings and abstracts were not searched, and may have yielded additional studies that were not included.
3.	Were the primary studies of high methodological quality?	Uncertain. The authors assessment of study quality involved assessing for allocation concealment, which was rated as "unclear" in many of the studies. Additional criteria such as use of an intention to treat analysis, eligibility criteria, and prognostic balance were not assessed.

<table>
<tr><td>4.</td><td>Were the assessments of the included studies reproducible?</td><td>Yes. The only criteria used to assess the quality of the studies was the presence of allocation concealment.</td></tr>
<tr><td>II.</td><td>What are the results?</td><td></td></tr>
<tr><td>1.</td><td>What are the overall results of the study?</td><td>There was a statistically significant relative risk (RR) favoring succinylcholine for the primary outcome of excellent intubating conditions: RR = 0.86 (95% CI 0.80-0.92), NNH = 8, Chi^2 = 100.43 (indicative of significant heterogeneity).

For the subgroup comparing rocuronium and succinylcholine in emergency patients, there was a significant RR favoring succinylcholine: RR = 0.79 (95% CI 0.71 to 0.88), NNH = 6.

For the secondary outcome of clinically acceptable conditions: RR = 0.96 (95% CI 0.93-0.99), NNH = 22.

Subgroup analyses for the primary outcome (rocuronium vs. succinylcholine):

<table>
<tr><th>Subgroup</th><th>RR</th><th>95% CI</th><th>NNH</th></tr>
<tr><td>Simulated RSI</td><td>0.81</td><td>0.72-0.91</td><td>7</td></tr>
<tr><td>Modified RSI</td><td>0.91</td><td>0.85-0.98</td><td>11</td></tr>
<tr><td>Rocuronium dose 0.6-0.7 mg/kg</td><td>0.81</td><td>0.73-0.9</td><td>6</td></tr>
<tr><td>Rocuronium dose 0.9-1.0 mg/kg</td><td>0.96</td><td>0.89-1.02</td><td></td></tr>
<tr><td>Rocuronium dose 1.2 mg/kg</td><td>0.93</td><td>0.75-1.15</td><td></td></tr>
<tr><td>Propofol for induction</td><td>0.88</td><td>0.80-0.97</td><td>9</td></tr>
<tr><td>Thiopental for induction</td><td>0.83</td><td>0.76-0.92</td><td>7</td></tr>
<tr><td>Narcotic used</td><td>0.85</td><td>0.78-0.92</td><td>7</td></tr>
<tr><td>Narcotic not used</td><td>0.89</td><td>0.78-1.03</td><td></td></tr>
<tr><td>Propofol w/ narcotic</td><td>0.84</td><td>0.74-0.96</td><td></td></tr>
<tr><td>Propfol w/o narcotic</td><td>0.96</td><td>0.84-1.10</td><td></td></tr>
<tr><td>Thiopental w/ narcotic</td><td>0.85</td><td>0.77-0.94</td><td></td></tr>
<tr><td>Thiopental w/o narcotic</td><td>0.82</td><td>0.65-1.04</td><td></td></tr>
</table>

The kappa statistic was 0.75 for the selected articles.</td></tr>
<tr><td>2.</td><td>How precise are the results?</td><td>See above.</td></tr>
<tr><td>3.</td><td>Were the results similar from study to study?</td><td>Yes and no. There was significant heterogeneity for the primary outcome (excellent intubating conditions), and secondary outcome (clinically acceptable conditions). There was significant heterogeneity for the primary outcome in the simulated RSI subgroup, the rocuronium 0.6-0.7 mg/kg subgroup, the propofol subgroup, the thiopental subgroup, and the subgroup in which a</td></tr>
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		narcotic was used. There was no heterogeneity for the primary outcome in the modified RSI subgroup, the 0.9-1.2 mg/kg and 1.2 mg/kg rocuronium subgroups, the pediatric subgroup, and the "emergency" intubation subgroup.
III.	***Will the results help me in caring for my patients?***	
1.	How can I best interpret the results to apply them to the care of my patients?	Overall, intubating conditions were improved when succinylcholine was used, compared with rocuronium. However, this meta-analysis did not look at the clinical significance of this (fewer intubation attempts, fewer oxygen desaturations, improved mortality of neurologic outcomes). Additionally, none of the included studies was performed on patients in the Emergency Department, making application to our patient population difficult. The four studies involving "emergency intubation" were all performed in the operating room.
2.	Were all patient important outcomes considered?	No. The primary and secondary outcomes included excellent and adequate intubating conditions based on subjective observations by the person performing the intubation. Intubation success rates, number of intubation attempts, oxygen desaturation, mortality, neurologic outcomes, length of stay, and cost were not addressed.
3.	Are the benefits worth the costs and potential risks?	Unclear. The clinical significance of the outcomes is not entirely clear as patient-important outcomes were not addressed. In addition, the articles included in the analysis were all set in the operating room, making applicability to ED patients difficult.

Limitations:

1. **None of the studies included in the meta-analysis were performed on ED patients; issues with external validity may limit applicability.**

2. **No assessment of the quality of the included studies, such as the Jadad scale, was included.**

3. **The measured outcomes were subjective. Given the inability to blind physicians to intervention, ascertainment bias may affect the measurement of these outcomes.**

4. **The primary and secondary outcomes do not necessarily represent patient-important outcomes.**

5. **Many of the included studies used lower doses of rocuronium and succinylcholine than typically used (0.6 mg/kg and 1.0 mg/kg respectively).**

Bottom Line:

This systematic review of the literature assessed intubating conditions using succinylcholine versus rocuronium in RSI. For the primary outcome and secondary outcomes there was a statistically significant difference between the groups in favor of succinylcholine. However, subgroup analysis revealed no difference in the outcomes when higher doses of rocuronium (0.9-1.0 mg/kg and 1.2 mg/kg) suggesting that when more appropriate doses are used, the two paralytics are equivalent. Unfortunately, none of the included was performed using emergency department patients, making application to this population unclear.