Are intubation conditions using rocuronium equivalent to those using succinylcholine?

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Authors' objectives
To investigate whether rocuronium creates equivalent intubation conditions to succinylcholine during rapid-sequence induction (RSI).

Searching
MEDLINE (from 1966 to February 2000), EMBASE (from 1988 to 2000) and the Cochrane Controlled Trials Register were searched. Details of the search strategy were presented. Studies published in any language were eligible. The reference lists of identified studies were also searched.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and controlled clinical trials were eligible for inclusion.

Specific interventions included in the review
Studies that compared rocuronium with succinylcholine RSI, if the dose of rocuronium was at least 0.6 mg/kg and the dose of succinylcholine was at least 1 mg/kg, were eligible for inclusion. Studies using thiopental, propofol, benzodiazepines or etomidate for sedation were included. Studies with and without opioids and studies using pre-treatment sedatives were eligible.

Participants included in the review
Studies of male and female patients of any age who were undergoing RSI or modified RSI during elective or emergency intubation were eligible for inclusion. True RSI was defined as the administration of a neuromuscular blocking agent immediately after the sedative and conditions evaluated at 60 seconds. Modified RSI was defined as the use of a sedative plus a muscle relaxant, followed by intubation with either a delay between the two drugs and/or a delay of more than 60 seconds between the muscle relaxant and intubation. The included studies were of adults and children. Where stated, the patients ranged from ASA (American Society of Anaesthesiologists) grade 1 to IV.

Outcomes assessed in the review
Studies that reported scores for condition at intubation were eligible for inclusion. The primary outcome assessed in the review was the proportion of excellent intubation conditions achieved, as defined by the Goldberg scale. This scale scores ease of intubation, vocal cord movement and patient response to intubation. Excellent intubation conditions must have good conditions reported by the operator, open immobile vocal cords and no response from the patient to intubation. Where studies did not use the Goldberg scale, the outcomes were converted to this scale where sufficient data were presented. The secondary outcomes assessed were clinically acceptable intubation conditions and failed or inadequate intubations.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies and resolved any disagreements through consensus or through discussion with a third author. Inter-rater agreement was measured using the kappa statistic.

Assessment of study quality
Validity was assessed and scored using the 5-point Jadad scale which considers randomisation, blinding and withdrawals. Two reviewers independently assessed validity and resolved any disagreements through discussion.

Data extraction
Two reviewers independently extracted data onto standardised forms. The data extracted were study design, type of
induction, the number of patients, characteristics of the participants, and details of the interventions.

**Methods of synthesis**

How were the studies combined?

Pooled risk differences (RDs) and relative risks (RRs), both with 95% confidence intervals (CIs), were calculated using a random-effects model. Equivalence between succinylcholine and rocuronium was assessed by comparing the number included in the meta-analyses with the minimum sample size required to have an 0.8 probability of detecting a 0.1 difference with an alpha-value of 0.05. The minimum sample size for equivalence was 468 patients for excellent intubation conditions, 112 for clinically acceptable conditions and 298 for failed intubations. The number-needed-to-harm (NNH) was estimated for excellent, acceptable and failed intubations.

How were differences between studies investigated?

Statistical heterogeneity was assessed using the chi-squared statistic (P<0.05 taken to indicate significant heterogeneity) and by examining a graphical display of the results and 95% CIs. A sensitivity analysis was conducted by comparing the results from high-quality (Jadad score 3 or more) and low-quality (Jadad score less than 3) studies. Subgroup analyses were performed to explore the influence of the following factors on the results: true RSI versus modified RSI; sedatives; opioid use versus no use; emergency versus elective intubation; rocuronium dose; and the patients’ age (adult versus paediatric).

**Results of the review**

Twenty-six RCTs (1,606 patients) were included.

There was complete agreement on study selection (kappa = 1.0) and poor agreement on the assessment of study quality (kappa = 0.17). Study quality did not have a clinically important influence on results. The RR was 0.84 (95% CI: 0.74, 0.95) for high-quality RCTs and 0.89 (95% CI: 0.80, 0.99) for lower quality RCTs.

Excellent intubation condition (26 studies): succinylcholine significantly increased the proportion of excellent intubation conditions compared with rocuronium. The RR was 0.87 (95% CI: 0.81, 0.94). Significant heterogeneity was found. The NNH was 8.

Clinically acceptable and failed intubations: there was equivalence between rocuronium and succinylcholine for clinically acceptable intubations. The RD was -0.02 (95% CI: -0.05, 0.01). No significant heterogeneity was found. The NNH was 45. There were few failed intubations (1.7%). There was no significant difference between rocuronium and succinylcholine for failed intubations. The RD was 0.00 (95% CI: -0.01, 0.02) and the NNH was 500.

Subgroup analysis.

Propofol as induction agent (9 studies, 640 patients): there was equivalence between rocuronium and succinylcholine for excellent intubation conditions. The RR was 0.96 (95% CI: 0.87, 1.06). No significant heterogeneity was found, although visual inspection of the 95% CIs suggested one study was an outlier. There was no significant difference between rocuronium and succinylcholine for studies with and without opioids. The RR was 0.94 (95% CI: 0.81, 1.10) with opioids and 0.97 (95% CI: 0.80, 1.18) without opioids. There was no significant heterogeneity when studies with and without opioids were analysed separately. There was no significant difference between rocuronium and succinylcholine for any of three different doses of rocuronium or type of intubation (true RSI or modified RSI).

Thiopental as induction agent (966 patients): rocuronium reduced the proportion of excellent intubations compared with succinylcholine. The RR was -0.17 (95% CI: -25, -0.09). Significant heterogeneity was found (P=0.0011). Heterogeneity could not be explained by the use of opioid, age, true versus modified RSI, or the dose of opioid or sedatives.

Opioid use: studies using an opioid (1,013 patients) found that succinylcholine significantly increased excellent intubation conditions compared with rocuronium. The RR was 0.87 (95% CI: 0.80, 0.96). Studies that did not use opioids (563 patients) found that the agents were equivalent when considering the RR (0.85, 95% CI: 0.71, 1.01), but succinylcholine was better than rocuronium when considering the RD (-0.14, 95% CI: -0.28, -0.01). There was
significant heterogeneity among studies using opioids (P=0.017) and those not using opioids (P=0.004).

True RSI: in studies using true RSI (889 patients), succinylcholine increased excellent intubation conditions compared with rocuronium. The RR was 0.79 (95% CI: 0.69, 0.91). Significant heterogeneity was found (P=0.016).

Age group: there was no significant difference between rocuronium and succinylcholine for paediatric patients, but the total number of paediatric patients (3 RCTs) was 116, which was too small to determine equivalence. The RR was 0.99 (95% CI: 0.83, 1.19). No significant heterogeneity was found (P=0.30).

Authors' conclusions
Succinylcholine was more reliable in creating excellent intubation conditions than rocuronium. Rocuronium plus propofol is equivalent to succinylcholine and can be used if a second-line agent is required.

CRD commentary
The review question was clear in terms of the study design, intervention and outcomes. The inclusion criteria were broadly defined in terms of participants. Several relevant sources were searched, the search terms were stated and no language restrictions were applied. The study selection, validity assessment and data extraction processes were performed by at least two reviewers and this reduced the potential for bias and errors. Validity was assessed using validated criteria. Relevant information on the included studies was tabulated. The data were combined in a meta-analysis and statistical heterogeneity was assessed. Where significant heterogeneity was found, potential reasons were explored and the influence of study quality on the results was assessed. The distinction between no significant difference and equivalence was highlighted where appropriate. The evidence presented appears to support the authors' conclusions.

Implications of the review for practice and research
Practice: The authors state that succinylcholine should be used as the drug of choice for rapid sequence intubation.

Research: The authors did not report any implications for further research.

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