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Review Article

REVIEW ARTICLE

Avoidance *vs* use of neuromuscular blocking agent for improving conditions during tracheal intubation: a Cochrane systematic review

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This article is based on a Cochrane Review published in the Cochrane Database of Systematic Reviews 2017, Issue 5, DOI: 10.1002/14651858.CD009237.pub2 (see www.thecochranelibrary.com for information). Cochrane reviews are regularly updated as new evidence emerges and in response to feedback, and the database should be consulted for the most recent version of the review.

Abstract

Cohort studies have indicated that avoiding neuromuscular blocking agents (NMBA) is a risk factor for difficult tracheal intubation (DTI). However, the impact of avoiding NMBA on tracheal intubation, possible adverse effects, and post-operative discomfort has not been evaluated in a systematic review of randomised trials. We searched several databases for trials published until January 2017. We included randomised controlled trials comparing the effect of avoiding *vs* using NMBA. Two independent authors assessed risk of bias and extracted data. The risk of random errors was assessed by trial sequential analysis (TSA). We included 34 trials (3565 participants). In the four trials judged to have low risk of bias, there was an increased risk of DTI with no use of NMBA [random-effects model, risk ratio (RR) 13.27, 95% confidence interval (CI) 8.19–21.49, $P<0.00001$, TSA-adjusted CI 1.85–95.04]. The result was confirmed when including all trials, (RR 5.00, 95% CI 3.49–7.15, $P<0.00001$, TSA-adjusted CI 1.20–20.77). There was a significant risk of upper airway discomfort or injury by avoiding NMBA (RR=1.37, 95% CI 1.09–1.74, $P=0.008$, TSA-adjusted CI 1.00–1.86). None of the trials reported mortality. Avoiding NMBA was significantly associated with difficult laryngoscopy, (RR 2.54, 95% CI 1.53–4.21, $P=0.0003$, TSA-adjusted CI 0.27–21.75). In a clinical context, one must balance arguments for using NMBA when performing tracheal intubation.

Keywords: neuromuscular blocking agent; systematic review; tracheal intubation

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Editor's key points

- This Cochrane review evaluates the effect of avoiding or using neuromuscular blocking agents on adverse events and difficulty in airway management.
- The results suggest that avoidance of neuromuscular blocking agents is associated with increased difficulty in intubation, and an increased risk of upper airway injury.
- The quality of evidence was rated as moderate to low. Large, high-quality trials are needed to examine the effect on airway injury, serious adverse events and mortality.

The use of neuromuscular blocking agents (NMBA) to facilitate tracheal intubation is a widely accepted procedure. Direct laryngoscopy stimulates the oropharynx and activates oropharyngeal reflexes. However, the use of NMBA will inhibit muscular contractions and improve conditions for tracheal intubation.[1] Due to adverse effects the use of NMBA may be undesirable. Both depolarising and non-depolarising NMBA may have side effect as anaphylaxis, cardiovascular effects related to histamine release or sympathomimetic properties, bronchospasm and prolonged paralysis. Depolarising NMBA may specifically cause muscle pain, increased serum potassium, malignant hyperthermia and increased intraocular pressure.[2] Thus, on the one hand, the use of NMBA may be associated with minor or (rare) serious adverse events (SAEs), but, on the other hand, cohort studies[3,4] have demonstrated that avoiding neuromuscular blocking drugs may be an independent risk factor for difficult and failed tracheal intubation.

Difficulties with tracheal intubation (DTI) by direct laryngoscopy can cause serious soft tissue damage[5] and DTI may be the principal causes of hypoxemic death and brain damage in relation to anaesthesia.[6] A review identified difficult airway management as the main cause of death and severe morbidity related to anaesthesia.[7] The risk of DTI may be reduced by choosing an induction strategy including, or avoiding, NMBA for facilitating tracheal intubation.

This is a co-publication of a Cochrane Review.[8] We evaluated the effect of not using NMBA *vs* use of NMBA on difficulty of tracheal intubation by direct laryngoscopy. We addressed relevant clinical outcomes, conducted subgroup and sensitivity analyses, assessed the role of bias, and applied trial sequential analysis (TSA) to examine the level of evidence for this intervention.

Methods

This review follows the recommendations of the Cochrane Collaboration. It is based on our published Cochrane protocol[9] and Cochrane Review.[8] We included randomised controlled trials (RCTs) of participants aged ≥14 yr who underwent surgery and (attempt of) tracheal intubation by direct laryngoscopy. The participants were randomised to avoidance of NMBA (= intervention) or use of NMBA (= control) for facilitation of tracheal intubation. We defined use of NMBA as the control as it is traditionally considered standard for tracheal intubation by direct laryngoscopy, while avoidance of NMBA was defined as the experimental intervention.

We searched the Cochrane Central Register of Controlled Trials; MEDLINE; Embase; BIOSIS; International Web of Science; Latin American Caribbean Health Sciences Literature (LILACS); the Chinese Biomedical Literature Database; advanced Google and Cumulative Index to Nursing & Allied Health Literature (CINAHL) until January 11, 2017. We used a systematic and sensitive search strategy to identify relevant RCTs with no language or date restrictions. We also searched for ongoing clinical trials and unpublished studies. As an example, the MEDLINE search strategy was: (1) exp Neuromuscular Blocking Agents/or Muscle Relaxants, Central/or (suxamethonium or rapacuronium or mivacurium or atracurium or doxacurium or cisatracurium or vecuronium or rocuronium or pancuronium or tubocurarine or gallamine or pipecuronium). ti,ab; (2) Laryngoscopy/or Intubation, Intratracheal/or (difficult adj3 (intubat* or laryngoscopy or airway)).mp. or ((Intubation adj3 (score or scale)) or (Cormack or Lehane)).mp. or ((tracheal adj3 intub*) or airway or laryngoscopy).ti; (3) 1 and 2; (4) ((randomised controlled trial or controlled clinical trial).pt. or randomised.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (animals not (humans and animals)).sh; (5) 3 and 4.

In the process of selecting trials for inclusion in the review, two authors (L.H.L. and either A.N. or C.D.) independently screened the titles and abstracts to identify eligible trials. The authors (L.H.L. and one of: A.N., C.D., C.V.R., J.T.) examined the full-text reports and extracted the data on a standardised paper form. We were not blinded to author, institution, or the publication source of trials. We resolved disagreements by discussion and any residual disagreements were resolved by a third author (J.W.). If necessary, we approached all corresponding authors of the included trials for additional information on the review's outcome measures and risk of bias components.

Primary outcomes

(1) Difficult tracheal intubation. As there is no international consensus on an intubation difficulty score, the definitions of a DTI presented in the individual articles were accepted. If the authors defined a difficult laryngoscopy by the Cormack and Lehane[10] or modified Cormack and Lehane score,[11] as a difficult intubation, we included and reported the Cormack and Lehane score as the outcome measure. Difficult laryngoscopy is a surrogate outcome for a DTI. Therefore, if a trial reported both an intubation score and the Cormack and Lehane score based on the same population in the same assessment, only the intubation score was extracted for outcome assessment.
(2) Overall mortality. We used the longest follow-up data from each trial.
(3) One or more events of upper airway discomfort or injury (e.g. sore throat, hoarseness, vocal cord lesion, minor pharyngeal injury).

Secondary outcomes

(4) One or more major SAE: pulmonary aspiration, brain and heart injuries (e.g. caused by anoxia, hypotension, bradycardia, or tachycardia during tracheal intubation).
(5) Difficult laryngoscopy, defined by Cormack and Lehane score[10] or modified Cormack Lehane score.[11]

We evaluated the validity and design characteristics of each trial. To draw conclusions on the overall risk of bias for an outcome it was necessary to evaluate the trials for major sources of bias, also defined as domains. We used the risk of