MUSCLE RELAXATION AND ENDOTRACHEAL INTUBATION: TEXTBOOK OR EVIDENCE BASED? A PILOT STUDY (RELAXED STUDY)

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Abstract

Background*:* Anesthetists empirically perform endotracheal intubation (ETI) when the laryngeal muscles are supposed to be fully paralysed; however, patients' sensitivity to neuromuscular blocking agents (NMBAs) is variable and adequate muscle relaxation does not always ensue after a routine induction dose. This study aimed to determine the time needed after a standard dose of NMBAs to reach an optimal muscle paralysis for intubation.

Methods*:* Adult patients who received non-depolarising NMBAs to facilitate their ETIs during induction were recruited. A digital peripheral nerve stimulator was applied at the adductor pollicis just before anesthesia. Initial train-of-four (TOF) stimulation was activated at the time of tracheal intubation, followed by auto-TOF every 30 seconds, and finished upon the disappearance of TOF count (TOFC).

Results*:* Data from 62 patients (47 Rocuronium and 15 Atracurium) were analysed. The results indicated that Rocuronium's dosage was 0.74mg/kg ideal body weight (95% confidence interval (CI) 0.69 to 0.80) and time to perform ETI was 130 seconds (95% CI 120 to 150). However, 81% of ETIs were performed with suboptimal muscle relaxation, with an average TOF ratio (TOFR) at ETI being 40% (95%CI 27% to 53%).

Atracurium's dosage and time to ETI were 0.53mg/kg actual body weight (95% CI 0.50 to 0.56) and 179 seconds (95% CI 156 to 198) respectively, but none of the ETIs was performed at optimal condition with the average TOFR at ETI being 76% (95%CI 60% to 92%).

Conclusions: In conclusion, the time needed for both Rocuronium and Atracurium to produce optimal intubation condition after a standard induction dose was much longer than thought. Suboptimal ETIs were prevalent in routine anesthetic practice.

Ethics approval: Eastern Health Human Research Ethics Committee: approval obtained (LR85-2016).

Keywords: Neuromuscular blocking agents, neuromuscular monitoring, peripheral nerve stimulator, quantitative, train-of-four count, intubation conditions, suboptimal, airway injury.

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Introduction

Non-depolarising neuromuscular blocking agents (NMBAs) are used in anesthetic practice to paralyse the laryngeal muscles to aid mask ventilation, optimise conditions for endotracheal intubation (ETI) and reduce the risk of upper airway injury.[1-3] In clinical practice, anesthetists routinely perform ETI when these muscles are supposed to be fully paralysed, with guidance from the NMBAs' pharmacokinetic characteristics found in medical literature and textbooks. Although these characteristics are well studied, differences in baseline patient characteristics including age, cardiac output, concurrent disease states and medication interactions result in variable patient sensitivities.[4-6] The onset time for adequate muscle relaxation after a standard dose therefore also varies between patients and can deviate from 'textbook' definitions. This phenomenon creates the potential for ETI prior to maximal muscle relaxation, which may predispose to adverse events similar to those found in the ETI of an unrelaxed airway: straining, coughing, bronchospasm and injury.

Where NMBAs are administered, use of a peripheral nerve stimulator (PNS) at all stages of anesthesia are increasingly recommended as an essential part of anesthetic monitoring.[7-9] As qualitative assessments are subjective and unreliable, a quantitative device is recommended.[10,11] When monitoring is used, 'optimal' intubating conditions for laryngoscopy and ETI are indicated by the disappearance of the train-of-four count (TOFC = 0).[8] In clinical practice, the adductor pollicis is the monitoring site of choice because it is readily accessible to attach monitoring equipment and, being peripheral, has a poorer distribution and more delayed onset of block when compared to the central laryngeal muscles.[11,12] Such effect provides a larger safety margin for ETI, allowing central muscles to have relaxed to a greater degree at the time when complete paralysis is demonstrated on the PNS monitor at the adductor pollicis site.[13,14]

However, the use of PNS monitoring has not been widely adopted; a recent survey suggested only 17% of anesthesia providers in Australia and New Zealand routinely monitored neuromuscular function.[15] Guidelines for monitoring during anesthesia from the Australian and New Zealand College of Anesthetists (ANZCA) and the American Society of Anaesthesiologists (ASA) also do not specify the need for neuromuscular monitoring at the time of intubation.[16,17]

We hypothesised that a lack of routine neuromuscular monitoring and variable patient NMBA sensitivities would result in a high prevalence of suboptimal ETI attempts, with subsequent potential for harm to the upper airways. Although previous studies have examined the variable onset times of NMBAs with different dosing regiments,[18,19] and the incidence of inadequate neuromuscular blockade during general anesthesia,[20] none investigating the prevalence of inadequate neuromuscular blockade at the time of ETI in anesthetic practice were found in the literature review.

This study primarily aimed to establish the prevalence of ETIs attempted under 'suboptimal' conditions in routine anesthetic practice. The secondary aim was to establish the time required to achieve 'optimal' muscle relaxation for common NMBAs.

Methods

This prospective cross-sectional study was approved by the local institutional ethics committee (Eastern Health Human Research Ethics Committee, Victoria, Australia). All adult patients undergoing elective surgical procedures with an anesthetic management plan of ETI facilitated by use of an NMBA were included. Seventy-eight patients were enrolled in the study and informed consent was obtained from all participants. Patients' characteristics including age, weight, height, gender and smoking status were recorded.

Prior to the surgical procedure, a quantitative PNS (TOFscan, IDMED, Marseille France) was applied to the patient's ulnar nerve at the wrist for the purpose of adductor pollicis muscle stimulation. The NMBA, dose used and the time of attempted ETI after drug administration were all recorded but remained at the anesthetist's discretion. Other aspects of the patient's anesthesia plan, including preoxygenation and other medications used during the stages of anesthesia induction and maintenance were not recorded or influenced by the study investigators. At the time of

ETI, TOF stimulation was activated and auto-TOF repeated every 30 seconds. Unless the anesthetist would have elected to use neuromuscular monitoring as part of their usual practice, the TOF results were blinded to the practitioner. All time-points with TOF ratio (TOFR) and TOFC were recorded until the TOFC reached 0, at which point data collection ceased.

A Microsoft Excel spreadsheet (2016, USA) was used to collate data offline. Descriptive statistics was performed using GraphPad Prism Mac 5.0f (GraphPad Software, San Diego, California USA, www.graphpad.com). All the values were averaged with a 95% confidence interval (CI).

Results

From the 78 participants, 9 were excluded due to data collection issues (incomplete data collection, PNS device issues or further NMBA administration prior to TOFC = 0). Three cases were excluded since modified rapid sequence induction, as opposed to standard anaesthetic induction, was used. Amongst the remaining 66 patients, data from the two most commonly used NMBAs, Rocuronium (n = 47) and Atracurium (n = 15), were included and analysed. The baseline characteristics for these patients were summarised in **Table 1**. Of interest, the majority of anesthesiologists (76%) preferred Rocuronium to Atracurium in their daily practice. The primary study results were shown in **Table 2**.

Table 1
Baseline characteristics of the participants who received Rocuronium or Atracurium during a standard anesthetic induction.

	Rocuronium, n = 47	**Atracurium, n = 15**
Age, mean (range) years	57 (25-80)	54 (18-86)
BMI, mean (range) kg/cm^2	30.3 (19.4 to 55.7)	26.1 (17.7 to 36.7)
Male, n (%)	25 (53%)	6 (40%)
Smoker, n (%)	8 (17%)	1 (7%)

BMI indicates body mass index.

In the Rocuronium group, the mean dose given was 0.74mg/kg ideal body weight (95% CI 0.69 to 0.80) with a mean ETI time of 130 seconds (95% CI 120 to 150). At the time of ETI, 9 patients (19%) had TOFC = 0 and the mean TOF ratio (TOFR) was 40% (95% CI 27% to 53%). Among these patients, 5 (11%) had a cough reflex during ETI. The mean time after Rocuronium administration for TOFC = 0 was 312 seconds (95% CI 258 to 372).

The mean dose administered in the Atracurium group was 0.53mg/kg actual body weight (95% CI 0.50 to 0.56) and mean ETI time was 179 seconds (95% CI 156 to 198). Unfortunately, none of them achieved TOFC = 0 at the time of ETI attempt, with a mean TOFR of 76% (95% CI 60% to 92%). In this

Table 2
Summary of key findings and outcomes.

	Rocuronium, n = 47	**Atracurium, n = 15**
Induction dose, mean ± (95%CI) mg/kg ABW	0.56 (0.53 to 0.59)	0.53 (0.50 to 0.56)
Induction dose, mean ± (95%CI) mg/kg IBW	0.74 (0.69 to 0.80)	Not applicable
Time lapse to ETI, mean ± (95%CI) seconds	130 (120 to 150)	179 (156 to 198)
TOFR at ETI, mean ± (95%CI)	40% (27% to 53%)	72% (51% to 93%)
Time lapse to TOFC = 0, mean ± (95%CI) seconds	312 (258 to 372)	466 (330 to 498)
Suboptimal ETI, n (%)	38 (81%)	15 (100%)

ABW indicates actual body weight; IBW, ideal body weight; ETI, endotracheal intubation; TOFR, train-of-four ratio; CI, confidence interval; and TOFC, train-of-four count.

group, 2 patients (14%) coughed at the time of ETI. The mean time to achieve TOFC = 0 after Atracurium administration was 466 seconds (95% CI 330 to 498).

Discussion

A significant proportion of ETI attempts from this study occurred under suboptimal neuromuscular block following Rocuronium and Atracurium administration, 81% and 100% respectively. Previous studies have demonstrated that such 'suboptimal' intubating conditions worsen the difficulty grade of intubation and increase the incidence of airway injury and subsequent post-operative airway symptoms, *e.g.*, hoarse voice or tracheal discomfort.[1] Although such sequelae were not investigated in this study, the high prevalence of premature ETIs could suggest an unnecessarily high risk of inadvertent upper airway injury for the studied patients.

The anesthetists in this study appeared to be adherent to traditional 'textbook' definitions of dosing and ETI timings for both Rocuronium and Atracurium. For Rocuronium, the mean study dose was 0.7mg/kg (0.6mg/kg 'textbook') and the mean ETI attempt time was 130 seconds (60 to 120 seconds 'textbook'). For Atracurium, the suggested dose is 0.5mg/kg for suitable conditions for non-emergency intubation after 180 to 300 seconds, which was similar to the study mean dose of 0.5mg/kg and mean ETI attempt time of 179 seconds.[21,22] The study's results therefore have the potential to apply to other sites with anesthetic practices following similar dosing and ETI timing patterns.

The mean time to achieve 'optimal' intubating conditions (TOFC = 0) was significantly prolonged compared to the 'textbook' suggestions; 312 seconds (study) *versus* 60 to 120 ('textbook') for Rocuronium and 466 seconds (study) *versus* 180 to 300 (suggested) for Atracurium.[21,22] This discrepancy could be attributed to the choice of monitoring at the adductor pollicis, a site with relatively poorer blood supply and therefore a slower distribution and onset of NMBAs[14,23] when compared to the more central target effect site of the laryngeal muscles. Indeed, a previous study has demonstrated prolonged onset times for TOFC = 0 when monitoring the effect of Rocuronium at the adductor pollicis in comparison to other common sites (orbicularis oculi or corrugator supercilii). However, the same study found that the disappearance of TOFC at the adductor pollicis was best associated with excellent intubating conditions.[13] Furthermore, the adductor pollicis is the most commonly used muscle for neuromuscular monitoring in clinical practice.[11,12] For these reasons, the adductor pollicis was also chosen as the site for neuromuscular monitoring in this study and the study findings may also be applicable to routine clinical practice.

The small sample size, particularly for the Atracurium group, is a limiting factor to the study results. Further studies with a wider patient population and with greater variety in the NMBAs used could be conducted to investigate the reliability of this study's findings.

In conclusion, the high prevalence of ETI attempts under 'suboptimal' conditions, and significantly prolonged onset time before 'optimal' intubating conditions suggests that current 'textbook' oriented anesthetic practice unnecessarily risks upper airway harm. Such adverse events can be minimised with neuromuscular block monitoring to ensure ETI attempts occur only under 'optimal' conditions when TOFC = 0. Routine monitoring is a simple and relatively economical solution; implementing monitoring would require a one-off purchase of a PNS monitoring device and two ECG electrodes for each patient. The study findings support the increasing recommendations that neuromuscular monitoring should be used in all anesthetic cases where NMBAs are administered. The outcome data in this study suggests that a larger scale study is required to investigate a wider patient population, a greater range of NMBAs and the incidence of upper airway injury when premature ETI takes place.

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