Kaohsiung Journal of Medical Sciences (2013) 29, 484–487

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: http://www.kjms-online.com

ORIGINAL ARTICLE

A comparison between succinylcholine and rocuronium on the recovery profile of the laryngeal muscles during intraoperative neuromonitoring of the recurrent laryngeal nerve: A prospective porcine model

I-Cheng Lu [a,b], Pi-Ying Chang [c], Hung-Te Hsu [c], Kuang-Yi Tseng [c], Che-Wei Wu [b,d], Ka-Wo Lee [d,e], Kuen-Yao Ho [d,e], Feng-Yu Chiang [d,e,*]

[a] *Department of Anesthesiology, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan*
[b] *Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan*
[c] *Department of Anesthesiology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan*
[d] *Department of Otorhinolaryngology — Head and Neck Surgery, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan*
[e] *Department of Otorhinolaryngology — Head and Neck Surgery, Faculty of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan*

Received 12 April 2012; accepted 6 September 2012
Available online 6 April 2013

KEYWORDS
Intraoperative neuromonitoring;
Neuromuscular blocking agent;
Porcine model;
Recurrent laryngeal nerve;
Thyroid surgery

Abstract The use of succinylcholine and rocuronium are reportedly feasible during intraoperative neuromonitoring (IONM) of the recurrent laryngeal nerve (RLN) in thyroid surgery. This study aimed to investigate and compare the recovery profiles of succinylcholine and rocuronium on the laryngeal muscle during IONM of the RLN in a porcine model. Nine male Duroc-Landrace piglets were anesthetized with thiamylal and underwent tracheal intubation without neuromuscular blocking agents (NMBAs). Needle electrodes were inserted into the vocalis muscles through the cricothyroid ligament. The RLN was exposed and stimulated. Electromyographic (EMG) signals were obtained before and after the intravenous administration of a NMBA. The EMG amplitudes were measured before and after (at 1-minute intervals) the administration of the study drug until complete recovery. The study NMBA regimen included

* Corresponding author. Department of Otorhinolaryngology, Kaohsiung Medical University Hospital, Number 100, Tzyou 1st Road, Kaohsiung City 807, Taiwan.
E-mail address: fychiang@kmu.edu.tw (F.-Y. Chiang).

http://dx.doi.org/10.1016/j.kjms.2013.01.002

succinylcholine (1 mg/kg), low-dose rocuronium (0.3 mg/kg), and standard dose rocuronium (0.6 mg/kg). The maximal neuromuscular blockade and 80% recovery (i.e., duration) of the control responses were recorded and analyzed. The 80% recovery of the control response for succinylcholine (1 mg/kg) was 19.7 ± 1.5 minutes; low-dose rocuronium (0.3 mg/kg), 16.3 ± 2.5 minutes; and standard dose rocuronium (0.6 mg/kg), 29.3 ± 5.7 minutes. Succinylcholine (1 mg/kg) and low-dose rocuronium (0.3 mg/kg) had significantly shorter durations than standard dose rocuronium (0.6 mg/kg). The EMG signal recovery returned to baseline within 30 minutes in the succinylcholine and low-dose rocuronium groups, but it did not return to baseline until 1 hour after surgery in the rocuronium (0.6 mg/kg) group. In this study, succinylcholine (1 mg/kg) and low-dose rocuronium (0.3 mg/kg) had favorable recovery profiles on the laryngeal muscle. It is recommended that low-dose rocuronium may replace succinylcholine for the induction of general anesthesia during IONM of the RLN in thyroid surgery.

Introduction

Intraoperative neuromonitoring (IONM) of the recurrent laryngeal nerve (RLN) is commonly used in thyroid operations to prevent RLN injury [1–4]. However, troubleshooting IONM problems is persistently reported in the literature. The misuse of neuromuscular blocking agents (NMBAs) is a potential cause of unsuccessful IONM. To achieve muscle relaxation for tracheal intubation and operating conditions, administering a NMBA is usually mandatory. However, a NMBA can reduce the electromyographic (EMG) amplitude and make monitoring less sensitive to impending neural injury. When using a NMBA to induce general anesthesia, it is best to allow all neuromuscular blockade drugs to wear off and a full return of muscular activity as soon as possible after the intubation. The use of depolarizing NMBAs (e.g., succinylcholine) or nondepolarizing NMBAs (e.g., rocuronium) are reportedly feasible during IONM of the RLN in thyroid surgery [5–7]. However, it is impossible to obtain the continuous recovery profile of each NMBA in human subjects because of repeated nerve stimulation at 1-minute intervals. Furthermore, the dose of a NMBA and the timepoint of nerve stimulation are critical for successful IONM. Therefore, it is necessary to understand the recovery profile of different NMBAs at different doses. This study used an established porcine model with the aim of comparing the recovery profile of the laryngeal muscle to succinylcholine and rocuronium (at a low dose and the standard dose) and to find a relatively optimal NMBA for IONM.

Materials and methods

Animals and anesthesia

Duroc-Landrace male piglets (n = 9) weighing 18–20 kg were obtained through the Kaohsiung Medical University, Laboratory Animal Center (Kaohsiung, Taiwan). The piglets were allocated into one of three groups, based on the delivered NMBA regimen (each group had 3 piglets). The animal use protocol was approved by the Institutional Animal Care and Use Committee of the Kaohsiung Medical University (Kaohsiung, Taiwan) (protocol number 97146). The piglets were fasted for 8 hours, but were allowed water before the experiment. The piglets were anesthetized with 4% sevoflurane in pure oxygen at a flow rate of 4 L/min and were administered intravenous thiamylal (5 mg/kg). An endotracheal tube (size #6) was then inserted without the administration of a NMBA. General anesthesia was maintained with 1–3% sevoflurane and the piglets were controlled ventilated. They were continuously monitored through physiological monitors such as electrocardiography (EKG), oximetry, end-tidal CO_2, and airway pressure.

Equipment setting and experimental design

After surgical disinfection, a midline vertical cervical incision was created to expose the animal's neck and larynx. The RLN was identified and dissected free from the overlying soft tissue and fascia. Needle electrodes (Medtronic Xomed, Jacksonville, FL) were inserted into the vocalis muscles through the cricothyroid ligament. The channel leads from

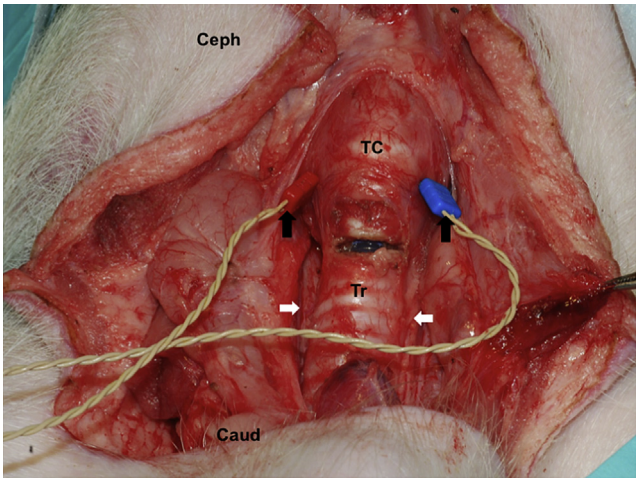

Figure 1. The neuromonitoring setup of the recurrent laryngeal nerve in a porcine model. The bilateral recurrent laryngeal nerve (white arrows) is exposed and stimulated. A pair of needle electrodes (black arrows) is inserted into the vocalis muscles. Caud = caudal; Ceph = cephalad; TC = thyroid cartilage; Tr = trachea.

the needle electrodes were connected to a NIM 2.0 monitor (Medtronic Xomed, Jacksonville, FL). A Prass monopolar probe (Medtronic Xomed, Jacksonville, FL) was placed in direct contact with the RLN for nerve stimulation (Fig. 1). The stimuli for RLN stimulation were generated from the NIM 2.0 monitor. The stimulation level was set at 2.0 mA. The NIM 2.0 monitor was set to run with a 50 millisecond time window and an amplitude scale at 0.2 mV/division. Event capture was activated with the threshold at 100 μV. Peak-to-peak amplitudes of evoked EMG activity were directly read on the monitor screen. Once stable baseline EMG amplitudes were established, a bolus of a study drug—succinylcholine (1 mg/kg), low-dose rocuronium (0.3 mg/kg), or standard dose rocuronium (0.6 mg/kg)—was delivered intravenously within 5 seconds. Each piglet received only one regimen to avoid a residual drug effect. The EMG amplitude was immediately measured on completing the study drug administration and repeated at 1-minute intervals thereafter until neuromuscular transmission attained at least 80% recovery. The duration of each NMBA dose was defined as the return to stability between 80% and 120% of the control response (i.e., the baseline EMG amplitude). The nonparametric data (e.g., EMG amplitude and duration) were assessed by one-way ANOVA test. Data were presented as the mean ± the standard deviation (SD). A value of $p < 0.05$ was considered statistically significant.

Results

Baseline EMG amplitudes recorded directly from vocalis muscle before the administration of succinylcholine (1 mg/kg), low-dose rocuronium (0.3 mg/kg), and standard dose rocuronium (0.6 mg/kg) were 2457 ± 1994 μV, 2431 ± 2571 μV, and 1277 ± 513 μV, respectively. Succinylcholine (1 mg/kg) and standard dose rocuronium (0.6 mg/kg) achieved complete neuromuscular block (>95% block). However, the maximal extent of the neuromuscular block was only 87% with low-dose rocuronium (0.3 mg/kg).

The 80% recovery of the control responses for succinylcholine (1 mg/kg), low-dose rocuronium (0.3 mg/kg), and standard dose rocuronium (0.6 mg/kg) were 19.7 ± 1.5 minutes, 16.3 ± 2.5 minutes, and 29.3 ± 5.7 minutes, respectively. Succinylcholine (1 mg/kg) and low-dose rocuronium (0.3 mg/kg) had a significantly shorter duration than standard dose rocuronium (0.6 mg/kg) (for both, $p < 0.05$). Fig. 2 presents the recovery profile of the neuromuscular transmission of the laryngeal muscle after each NMBA regimen. The EMG signal recovery returned to baseline within 30 minutes in the succinylcholine and low-dose rocuronium groups. However, it did not return to baseline until an hour after the standard dose of rocuronium (0.6 mg/kg).

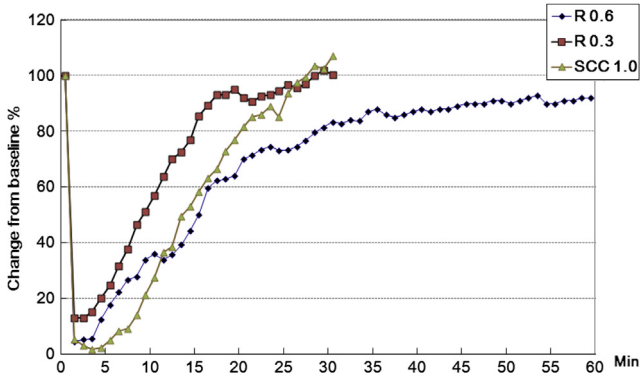

Figure 2. The recovery profile of the EMG signal of the recurrent laryngeal nerve after a bolus of succinylcholine (1 mg/kg), low-dose rocuronium (0.3 mg/kg), and standard dose rocuronium (0.6 mg/kg). R0.3 = rocuronium (0.3 mg/kg); R0.6 = rocuronium (0.6 mg/kg); SCC1.0 = succinylcholine 1.0 mg/kg.

Discussion

A NMBA may diminish the evoked potential, delay a positive signal, and interfere with data interpretation during IONM. During neuromonitoring, a reduced dosage of rocuronium may enable adequate muscle relaxation without significantly affecting the measured evoked potentials [7]. It lacks clinical comparisons of different kinds and different dosages of NMBAs that directly and simultaneously monitor neuromuscular transmission obtained from laryngeal muscle via a neuromonitoring system. A porcine model of feasibility and safety has been established to investigate the effects of NMBAs on intraoperative neuromonitoring [8,9]. The primary results revealed that the standard dose of succinylcholine (1.0 mg/kg) and a low dose of rocuronium (0.3 mg/kg) have significantly shorter durations than the standard dose of rocuronium (0.6 mg/kg) in the recovery profile of the EMG signal of the RLN during neuromonitoring. According to our results, rocuronium has a significant dose-response effect on the recovery profile. Succinylcholine (1.0 mg/kg) and a single low dose of rocuronium (0.3 mg/kg) both obtained complete EMG signal recovery within 30 minutes. However, the EMG signal recovery did not return to baseline until 1 hour after the standard dose of rocuronium (0.6 mg/kg). Therefore, low-dose rocuronium shows a short duration and could replace succinylcholine during neuromonitoring of the RLN in thyroid surgery.

The duration of neuromuscular blockade is of great importance in IONM. The inhibition of neuromuscular transmission diminishes EMG signals and motor-evoked potentials and consequently interferes with interpreting neuromonitoring recordings [10,11]. To obtain adequate relaxation for surgery and to obtain minimal variations in EMG signals and motor-evoked potentials during neuromonitoring, it is important to administer nondepolarizing NMBAs with caution (e.g., by using a single dose or continuous infusion) [7,12]. If NMBAs are avoided to ensure the quality of the EMG signals or motor-evoked potentials, a higher dose of inhalational or intravenous anesthetics may be necessary at the expense of hemodynamic stability [12].

A shorter duration of neuromuscular blockade depicts a more favorable recovery profile for neuromonitoring. Among the three study regimens, low-dose rocuronium (0.3 mg/kg) was the optimal choice during neuromonitoring. The benefits of low-dose rocuronium are the following. The first benefit is the recovery profile. The neuromuscular blocking duration of low-dose rocuronium

was as short as 15 minutes and complete recovery was within 30 minutes. This is approximately the same effect as succinylcholine. Standard dose rocuronium (0.6 mg/kg) showed a delayed and incomplete recovery in comparison to low-dose rocuronium (0.3 mg/kg). The second benefit is pharmacological safety. However, diverse adverse effects ranging from minor (e.g., muscle pain, dysrhythmia) to lethal (e.g., malignant hyperthermia, hyperkalemia) limit its clinical application [13,14]. Succinylcholine also has a short duration; however, it is responsible for most incidents of NMBA-related anaphylaxis [15]. Rocuronium is safer to use than depolarizing NMBAs because it has fewer adverse effects than depolarizing agents. Furthermore, the hemodynamic state remains stable with rocuronium, compared to other nondepolarizing agents, because it does not induce histamine release or vagal blockade [16]. Finally, rocuronium at low dose provides acceptable tracheal intubation conditions in most subjects [7,17]. In previous reports, the further administration of a NMBA after a successful tracheal intubation could be avoided in the entire thyroid surgery [5–7]. The obvious disadvantage of low-dose rocuronium is its incomplete neuromuscular blockade, which may lead to prolonged onset time and difficulty in placing the endotracheal tube.

There are several limitations in this study. First, the sample size is small, which makes statistical analysis difficult. Second, the EMG amplitude has large variations so that extreme individual readings may be misleading. However, the main analysis was based on the percent change from the baseline and individual data depict good consistency and reliability.

In conclusion, succinylcholine (1.0 mg/kg) and low-dose rocuronium (0.3 mg/kg) showed a more favorable recovery profile than standard dose rocuronium (0.6 mg/kg) during neuromonitoring of the RLN. Titration of the rocuronium dose to replace succinylcholine for neuromonitoring during thyroid surgery is recommended. In this established porcine model, the anatomic structure and electrophysiological response of a piglet's larynx are similar to the human larynx. However, translation of these data to humans should be made cautiously.

Acknowledgments

This study was supported by grants from the Kaohsiung Municipal Hsiao-Kang Hospital Research Foundation (KMHK-100-022), the Kaohsiung Medical University Hospital (KMUH100-0R34), and the National Science Council, Taiwan (NSC101-2314-B-037-030-MY2). We also thank Hsiu-Ya Chen and Hui-Ying Yang for their contributions to this study.

References

[1] Lu IC, Chu KS, Tsai CJ, Wu CW, Kuo WR, Chen HY, et al. Optimal depth of NIM EMG endotracheal tube for intraoperative neuromonitoring of the recurrent laryngeal nerve during thyroidectomy. World J Surg 2008;32:1935–9.

[2] Chiang FY, Lu IC, Kuo WR, Lee KW, Chang NC, Wu CW. The mechanism of recurrent laryngeal nerve injury during thyroid surgery—the application of intraoperative neuromonitoring. Surgery 2008;143:743–9.

[3] Dralle H, Sekulla C, Lorenz K, Brauckhoff M, Machens A. German IONM Study Group. Intraoperative monitoring of the recurrent laryngeal nerve in thyroid surgery. World J Surg 2008;32:1358–66.

[4] Tsai CJ, Tseng KY, Wang FY, Lu IC, Wang HM, Wu CW, et al. Electromyographic endotracheal tube placement during thyroid surgery in neuromonitoring of recurrent laryngeal nerve. Kaohsiung J Med Sci 2011;27:96–101.

[5] Chu KS, Wu SH, Lu IC, Tsai CJ, Wu CW, Kuo WR, et al. Feasibility of intraoperative neuromonitoring during thyroid surgery after administration of nondepolarizing neuromuscular blocking agents. World J Surg 2009;33:1408–13.

[6] Chu KS, Tsai CJ, Lu IC, Tseng KY, Chau SW, Wu CW, et al. The influence of non-depolarizing muscle relaxants on intraoperative neuromonitoring during thyroid surgery. J Otolaryngol-Head Neck Surg 2010;39:397–402.

[7] Lu IC, Tsai CJ, Wu CW, Cheng KI, Wang FY, Tseng KY, et al. A comparative study between 1 and 2 effective doses of rocuronium for intraoperative neuromonitoring during thyroid surgery. Surgery 2011;149:543–8.

[8] Wu CW, Lu IC, Randolph GW, Kuo WR, Lee KW, Chen CL, et al. Investigation of optimal intensity and safety of electrical nerve stimulation during neuromonitoring of the recurrent laryngeal nerve: a prospective porcine model. Head Neck 2010;32:1295–301.

[9] Lu IC, Wang HM, Kuo YW, Shieh CF, Chiang FY, Wu CW, et al. Electromyographic study of differential sensitivity to succinylcholine of the diaphragm, laryngeal and somatic muscles: a swine model. Kaohsiung J Med Sci 2010;23:618–23.

[10] van Dongen EP, ter Beek HT, Schepens MA, Morshuis WJ, Langemeijer HJ, de Boer A, et al. Within-patient variability of myogenic motor-evoked potentials to multipulse transcranial electrical stimulation during two levels of partial neuromuscular blockade in aortic surgery. Anesth Analg 1999;88:22–7.

[11] Marusch F, Hussock J, Haring G, Hachenberg T, Gastinger I. Influence of muscle relaxation on neuromonitoring of the recurrent laryngeal nerve during thyroid surgery. Br J Aanaesth 2005;94:596–600.

[12] Pajewski TN, Arlet V, Phillips LH. Current approach on spinal cord monitoring: the point of view of the neurologist, the anesthesiologist and the spine surgeon. Eur Spine J 2007;16(Suppl. 2):S115–29.

[13] Orebaugh SL. Succinylcholine: adverse effects and alternatives in emergency medicine. Am J Emerg Med 1999;17:715–21.

[14] Miller R. Will succinylcholine ever disappear? Anesth Analg 2004;98:1674–5.

[15] Laxenaire M. Substances responsible for peranesthetic anaphylactic shock: a third French multicenter study (1992–1994). Ann Fr Anesth Reanim 1996;15:1211–8.

[16] Levy JH, Davis GK, Duggan J, Szlam F. Determination of the hemodynamics and histamine release of rocuronium (Org 9426) when administered in increased doses under N_2O/O_2-sufentanil anesthesia. Anesth Analg 1994;78:318–21.

[17] Pendeville PE, Lois F, Scholtes JL. A comparison of intubation conditions and time-course of action with rocuronium and mivacurium for day case anaesthesia. Eur J Anaesthesiol 2007;24:546–50.