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CLINICAL REPORT

Use of rocuronium–sugammadex, an alternative to succinylcholine, as a muscle relaxant during electroconvulsive therapy

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Abstract We compared the recovery time from neuromuscular blockade induced by rocuronium combined with sugammadex versus succinylcholine during electroconvulsive therapy (ECT). Anesthesia was induced using propofol, followed by succinylcholine (1 mg/kg) or rocuronium (0.6 mg/kg). Immediately after the seizure stopped, 16 mg/kg sugammadex was infused. Neuromuscular monitoring was performed and continued until recovery of the train-of-four ratio to 0.9. We compared the recovery time of T1 to 10 and 90% between groups. Patients were also assessed for clinical signs, such as time to first spontaneous breath from the administration of muscle relaxant and eye opening to verbal commands. Although recovery time of T1 to 10 and 90% in the rocuronium–sugammadex group was shorter than in the succinylcholine group, the difference was not statistically significant. Further, the seizure duration with succinylcholine (33 ± 8 s) was shorter than that with rocuronium–sugammadex (39 ± 4 s). In conclusion, this study demonstrates the potential benefit of use of rocuronium–sugammadex as an alternative to succinylcholine for muscle relaxation during ECT.

Keywords Electroconvulsive therapy · Muscle relaxant · Rocuronium · Sugammadex · Succinylcholine

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Introduction

Succinylcholine is commonly used as a muscle relaxant during electroconvulsive therapy (ECT) because of its rapid onset and short duration of action [1]. However, succinylcholine has many side effects, such as myalgia, a small increase in plasma potassium and increase in intragastric and intra-ocular pressures [1].

Sugammadex has recently been introduced as a fast-acting, selective relaxant-binding agent that was specifically designed to rapidly reverse rocuronium-induced neuromuscular blockade. Lee et al. [2] reported that reversal of profound, high-dose rocuronium-induced neuromuscular block with 16 mg/kg sugammadex was significantly faster than spontaneous recovery from succinylcholine.

We compared recovery from neuromuscular blockade induced by rocuronium–sugammadex versus that induced by succinylcholine in five patients presenting for ECT.

Case description

Informed consent was obtained from patients or their families. All protocols were approved by the local institutional clinical study committee and the institutional review board. Five patients who were scheduled to undergo ECT were studied. None of the patients had a history of cardiovascular disease.

Anesthetic management

The patients underwent at least 10 sessions of ECT (three times per week at 1- or 2-day intervals). To avoid induction of the parasympathetic reflex, the patients received

atropine sulfate (0.01 mg/kg IM) 30 min prior to the ECT procedure.

Measured parameters during the procedure included blood pressure (BP), heart rate, oxygen saturation (SpO_2; measured by pulse oximetry on the left index finger), end-expiratory partial pressure of carbon dioxide (end-tidal CO_2) at the nostrils (Capnomac UltimaTM; Datex Co, Ltd., Helsinki, Finland) and electrocardiogram (ECG; lead II). Measurements were initiated prior to ECT and were terminated at the end of the procedure.

Anesthesia was induced using propofol (1.0 mg/kg intravenously over 5 s), followed by either succinylcholine (SCC) (1 mg/kg intravenously) or rocuronium (0.6 mg/kg intravenously) over 5 s, followed by a 10-ml saline bolus. Assisted mask ventilation was initiated with 100% oxygen. After T1 was assessed as being zero by neuromuscular monitoring, an electroshock stimulus was applied bilaterally for 5 s.

End-tidal CO_2 was maintained at 30–35 mmHg and the SpO_2 value was maintained above 98% by manual mask assistance throughout the therapy. For patients who were given rocuronium, 16 mg/kg sugammadex was infused with a 10-ml saline bolus immediately after the seizure stopped.

During the first and second ECT sessions, we confirmed that 1 mg/kg of propofol and 1 mg/kg of SCC could provide adequate anesthetic conditions and muscle relaxation to all patients. In addition, the intensity of the ECT stimulus required to achieve a minimum seizure duration of more than 20 s was determined during these sessions.

Patients received 1 mg/kg of SCC as the muscle relaxant agent for three of the subsequent ECT sessions and 0.6 mg/kg of rocuronium during the remaining four ECT sessions. Muscle relaxant selection was made in a non-blinded manner. Electroencephalographic (EEG) seizure duration was recorded by a two-channel EEG after the electrical stimulus.

Neuromuscular assessment

Neuromuscular monitoring was performed using the TOF-watch SX (Organon, Roseland, NJ, USA). The tibial nerve in the leg was supramaximally stimulated at the inferolateral aspect of the medial malleolus with square pulses of 0.2-ms duration, delivered as train-of-four pulses, at intervals of 15 s. The resulting contractions of the great toe muscles were quantified by an acceleromyographic monitor. Calibration was performed and baseline responses were recorded after propofol administration and before muscle relaxant administration. Neuromuscular monitoring was continued until recovery of the train-of-four ratio to 0.9. Following the protocol of Lee et al. [2], we compared the time to recovery of T1 to 10 and 90% between relaxants. T1 was zero in all patients when sugammadex was administered.

Patients were also assessed for clinical signs such as the time interval between the first spontaneous breath and administration of muscle relaxant and the time to opening of eyes to verbal commands.

All data are expressed as means ± standard deviation (SD). Paired *t* test was used for the comparisons. Calculations were performed by Stat View 5.0 software (Abacus, Concepts, Berkeley, CA, USA).

Table 1 shows the comparison between the effects of succinylcholine and rocuronium–sugammadex in terms of time from the start of administration of neuromuscular blocking agent to T1 zero, to recovery of T1 to 10% and to recovery of T1 to 90%. Although there was a tendency to a shorter time of onset of muscle relaxant action with succinylcholine compared with that with rocuronium, no significant differences in T1 0% were found between the two relaxants. Further, although there was a tendency to shorter time to recovery of T1 to 10 and 90% with rocuronium–sugammadex as compared to succinylcholine, the difference was not statistically significant.

Table 1 Time from commencement of administration of neuromuscular blocking agent to T1 zero, recovery of T1 to 10% and recovery of T1 to 90%

	Height (cm)	Weight (kg)	T1 0% (s)		Recovery of T1 to 10% (s)		Recovery of T1 to 90% (s)	
			SCC	Ro + Sugam	SCC	Ro + Sugam	SCC	Ro + Sugam
Case 1 (62 years, F)	152	40.9	155	277	507	638	565	664
Case 2 (64 years, M)	165	52.0	67	97	305	173	532	387
Case 3 (53 years, F)	149	57.5	105	135	285	221	540	428
Case 4 (67 years, M)	165	51.0	85	112	484	213	694	278
Case 5 (68 years, M)	165	65.5	148	171	537	267	549	390
Means ± SD	159 ± 8	53.3 ± 9.0	112 ± 38	158 ± 71	423 ± 119	302 ± 190	576 ± 67	429 ± 142
P value			0.07		0.26		0.07	

SCC Succinylcholine, *Ro + Sugam* Rocuronium + Sugammadex

Table 2 Measures of seizure duration, time to first spontaneous breath and eye opening to verbal commands

	Seizure duration (s)		Time to first spontaneous breath (s)		Eye opening to verbal commands (s)	
	SCC	Ro + Sugam	SCC	Ro + Sugam	SCC	Ro + Sugam
Case 1	40	43	234	410	535	675
Case 2	38	41	262	374	471	549
Case 3	39	44	250	208	480	330
Case 4	22	33	189	131	697	224
Case 5	27	36	472	257	543	529
Means ± SD	33 ± 8	39 ± 4	281 ± 110	276 ± 115	545 ± 90	461 ± 181
P value	0.01		0.94		0.48	

SCC Succinylcholine, *Ro + Sugam* Rocuronium + Sugammadex

Table 2 compares the effects of succinylcholine and rocuronium–sugammadex administration in terms of seizure duration, time to first spontaneous breath and time to eye opening in response to verbal commands. Seizure duration with succinylcholine was shorter than that with rocuronium–sugammadex. No significant differences in time to first spontaneous breath and eye opening in response to verbal commands were found with the two muscle relaxants.

Table 3 shows the time from administration of sugammadex to recovery of T1 to 10%, to 90% and time to first spontaneous breath with administration of rocuronium–sugammadex. Quick recovery from the muscle relaxant effect was found with rocuronium–sugammadex.

All patients included in this study had normal renal function, as shown by normal ranges of BUN and plasma creatinine. No adverse effects, such as nausea, vomiting or headache, were found with either relaxant. In addition, no recurarization was seen in any of the patients treated with rocuronium–sugammadex.

Table 3 Time from administration of sugammadex to recovery of T1 to 10%, T1 to 90% and time to first spontaneous breath

	Recovery of T1 to 10% (s)	Recovery of T1 to 90% (s)	Time to first spontaneous breath (s)
Case 1	308	334	43
Case 2	23	237	19
Case 3	30	150	30
Case 4	57	122	47
Case 5	50	173	47
Means ± SD	93 ± 120	203 ± 84	37 ± 12

Discussion

We showed similar efficacy with rocuronium–sugammadex as compared to succinylcholine for muscle relaxation during ECT.

Use of succinylcholine is associated with a variety of adverse events and contraindications [3]. In addition, succinylcholine is thought to be a potent trigger for malignant hyperthermia (MH) [3]. Although several ultrashort acting non-depolarizing muscle relaxants have been developed, none of these have a shorter duration of action than succinylcholine [1, 4–7].

While Trollor et al. [8] reviewed the possible safety of the use of succinylcholine in cases with neuroleptic malignant syndrome, some researchers examined other neuromuscular agents, such as vecuronium [9, 10], mivacurium [4, 7, 11], rapacuronium [6] and rocuronium [5] during ECT. Kelly et al. [11] showed the safety of mivacurium as an alternative to succinylcholine. In contrast, Cheam et al. [4] reported that a low dose of mivacurium was less effective than succinylcholine. Another report [9] that examined the safety of vecuronium reported that vecuronium shortened the seizure duration and prolonged anesthetic time.

There is only one report evaluating the effects of rocuronium versus succinylcholine on clinical recovery from ECT [5]. Turkkal et al. [5] reported that although the time to first spontaneous breath was longer in the rocuronium group than in the succinylcholine group, no significant differences were detected between the two groups in terms of eye opening, head lift or tongue depressor testing. However, the dosage of rocuronium used in the study of Turkkal et al. [5] was relatively small (0.3 mg/kg), which is thought to be inadequate for muscular paralysis. Rocuronium (0.6–1.2 mg/kg) typically produces complete neuromuscular block within 2 min, as compared with an average of 1 min with 1 mg/kg succinylcholine [12]. However, at this dose, rocuronium has a longer duration of action, making it inappropriate for use in ECT where rapid recovery of neuromuscular function is required. Hence, we selected a clinically more commonly used dosage of rocuronium of 0.6 mg/kg.

Lee et al. [2] compared the time required for sugammadex reversal of profound rocuronium-induced neuromuscular block with time to spontaneous recovery after succinylcholine. In their study, 1.2 mg/kg rocuronium or

1 mg/kg succinylcholine was used for blockade of neuromuscular transmission and facilitation of tracheal intubation. Sugammadex (16 mg/kg) was administered 3 min after rocuronium administration. Mean times to recovery of T1 to 10 and 90% were significantly faster in the rocuronium–sugammadex group as compared with the succinylcholine group. Hence, they concluded that reversal of profound high-dose rocuronium-induced neuromuscular block (1.2 mg/kg) with 16 mg/kg sugammadex was significantly faster than spontaneous recovery from 1 mg/kg succinylcholine. This report implies that the rocuronium–sugammadex combination may be useful for inducing muscle paralysis during ECT. Our study indicated possible equipotent effects of rocuronium- and succinylcholine-induced neuromuscular block for muscle relaxation.

Certain other factors should be considered while analyzing our results.

First, we previously showed that the onset and duration of muscle relaxants were greatly influenced by cardiac output before injection [13]. Hence, the onset and duration of muscle relaxation in each of our patients may have been affected by their individual cardiac outputs.

Second, in this study, sugammadex was infused after the end of the seizure. Puhringer et al. [12] reported that the timing of administration of sugammadex might influence the reversal of profound rocuronium-induced neuromuscular blockade. Thus, it is possible that our results were affected by the timing of administration of sugammadex.

The mechanism of the longer seizure duration with ECT following rocuronium–sugammadex administration as compared to that with SCC administration is unknown. Small differences in the hyperventilation status before electrical stimulation between the two groups might have some effect on seizure duration [1]. Another possibility is that the number of sessions of ECT might have affected the seizure duration because of improvement in the depressive condition resulting from ECT [1].

The dose of 0.6 mg/kg of rocuronium used in this study was half the dosage used by Lee et al. [2]. However, a dose of 16 mg/kg of sugammadex was used as the neuromuscular antagonist in this study. Reportedly, a dose of at least 4–8 mg/kg of sugammadex is needed for recovery from deep neuromuscular blockade, indicated as a post-tetanic count of 1–2 on the TOF monitor [14]. We believe that more profound neuromuscular blockade was induced in our study group by administration of sugammadex as compared to this previous study. In addition, we were afraid of the risk of recurarization with use of a small dose of sugammadex. Hence, a dose of 16 mg/kg of sugammadex was used as the neuromuscular antagonist in this study.

We measured variables only twice during ECT. With subsequent ECT sessions, patients require larger doses of propofol to achieve unconsciousness due to improvement in the depressive condition induced by ECT. Hence, the propofol dosage could have greatly influenced seizure duration and hemodynamic changes induced by ECT in this study. In addition, improvement in the depressive condition by ECT could have led to the anti-depressant agent being changed, which could also have affected the hemodynamic changes induced by ECT.

For unknown reasons, there were some differences in the time to recovery of T1 to 10 and 90% and the time to the first spontaneous breath between case one and the others. One possible speculation for this difference is that case 1 exhibited differential effects to the non-depolarizing neuromuscular agents because of undetectable degeneration, demyelination or axon loss in the motor nerve ending of the neuromuscular junction and infarction or atrophy of the skeletal muscle. This could partly explain why almost twice the time was needed for the recovery of T1 to 10 and 90% in this patient. Another possibility is that the onset and duration of muscle relaxants are greatly influenced by cardiac output before injection [13] be responsible for these differences observed in case 1.

Although the cost of sugammadex may preclude its routine use for ECT, rocuronium–sugammadex may be useful for muscle relaxation during ECT in patients in whom the use of succinylcholine is contraindicated, such as those with severe osteoporosis, amyotrophic lateral sclerosis and a history of neuroleptic malignant syndrome [7].

In conclusion, we demonstrated the potential efficacy of rocuronium–sugammadex as an alternative to succinylcholine for muscle relaxation during ECT.

Conflict of interest None.

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