The Internet Journal of Emergency and Intensive Care Medicine 2003 : Volume 7 Number 1

Dilemma In Rapid Sequence Intubation: Succinylcholine Vs. Rocuronium

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Citation: O. Karcioglu : Dilemma In Rapid Sequence Intubation: Succinylcholine Vs. Rocuronium . *The Internet Journal of Emergency and Intensive Care Medicine*. 2003 Volume 7 Number 1

Keywords: Rapid sequence intubation | rapid sequence induction | neuromuscular blockade | muscle paralysis | succinylcholine | rocuronium

Abstract

Succinylcholine is the single ultra-short acting depolarizing neuromuscular blocking agent (NMBA) used in the rapid sequence intubation protocol with

its rapid onset of effect, complete reliability, short duration of action. Rocuronium is diverse from other non-depolarizing NMBA being the first one with a short onset time and devoid of untoward effects. Despite its widespread use, succinylcholine has several potential hazards including an increase in potassium levels, bradycardia for children and prolonged apnea for those with pseudocholinesterase deficiency. Rocuronium is indicated in subjects with disease states such as known or suspected hyperkalemia, crush injury, non-acute burns, increased intracranial or intraocular pressure and neuromuscular disease. Although succinylcholine has many side effects, it remains to be the first-choice NMBA for the majority of attempts for rapid sequence intubation. Rocuronium may be a suitable alternative to succinylcholine with its short onset time. The objective of this article is to update data from studies comparing the use of succinylcholine and rocuronium in rapid sequence intubation protocol in adults.

Introduction

Rapid sequence intubation (RSI) is developed to secure the airway of a critically ill or injured patient rapidly and safely. RSI applies to virtually all attempts for endotracheal intubation (ETI) in the emergency departments (ED) except for arrest situations. RSI is particularly preferred for ED use because of the simultaneous onset of sedation, paralysis and minimizing the risk of aspiration ([1]). After being launched in the late seventies, the procedure has been dynamically changing in time with introduction of many newer and advantageous agents ([2],[3],[4]).

RSI protocol is still in development in order to minimize the risk of aspiration of gastric contents in case of “full stomach” while preventing secondary brain injury via rendering unconsciousness and paralysis and to achieve higher rates of successful ETI.

Laryngoscopy and ETI are performed after administering rapid and short-acting sedative, hypnotic and amnestic agents in conjunction with

neuromuscular blocking agents (NMBA) ([5]). Short-acting agents like succinylcholine (SCh) are generally preferred for fear of protracted intubation failure ([5],[6]). For decades, SCh used to be the sole agent demonstrated to consistently provide paralysis in less than one minute ([7],[8],[9]). It is still the sole depolarizing NMBA used in the procedure. It is particularly useful in the critically ill or injured with a full stomach for whom a RSI technique is needed ([10]). Patients intubated in emergent conditions generally have full stomach and rapid intubation is critical to prevent aspiration of gastric contents. SCh provides a means for rapid intubation in these high-risk patients. Rocuronium (RCR) is diverse from other non-depolarizing NMBA being the first one with a short onset time devoid of adverse effects. The objective of this article is to review all prospective studies comparing the use of SCh and RCR in RSI protocol in adults.

Clinical And Pharmacological Properties Of Each Agent

Introduced in 1952, SCh depolarizes the neuromuscular membrane and is structurally consisted of two acetylcholine molecules. It acts as a false transmitter of acetylcholine by avidly binding to postsynaptic cholinergic receptors, resulting in persistent depolarization and paralysis ([10]). This action is associated with muscle fasciculation which can lead to increased intracranial and intragastric pressures. The molecule is rapidly hydrolyzed by serine pseudocholinesterase. SCh is rapidly active within 60 seconds of administration by IV bolus. The clinical duration of action is 3 to 10 minutes and normal neuromuscular function returns within 15 minutes. The first report on the administration of SCh for performing ETI in multiple cases in the ED was published by Thompson et al in 1982 ([11]).

Prolonged or repeated use may augment its effects at vagal or sympathetic ganglia. The former action may lead to bradycardia and hypotension that is more severe in children, necessitating atropine premedication ([6],[12]). Muscle fasciculations can increase serum potassium level by 0.5-1.0 meq/L and produce arrhythmias. SCh should be avoided after burns, muscle trauma

etc. between one week and 6 to 12 months after injury ([10]). Although increased intraocular pressure with SCh in patients with globe injuries is a concern, administration of defasciculating dose of a competitive NMBA permits the safe use of SCh in this setting.

RCR, a structural analog of vecuronium, is a recently synthesized non-depolarizing NMBA that has been demonstrated to have a faster onset of action than the other non-depolarizing drugs. This drug produces rapid paralysis allowing it to be used for RSI ([6]). RCR is the first non-depolarizing NMBA having an onset time comparable to that of SCh without adverse effects. Other non-depolarizing NMBA are reserved for maintenance infusion to cause prolonged apnea and paralysis. There are sparse data regarding usage of RCR for emergent tracheal intubation in the ED ([1]). Despite its short onset, the duration of action of RCR in doses like 1.2 mg/kg is sufficiently long to represent a clinical disadvantage when a short-acting NMBA is required. This, on the other hand, necessitates preparation for advanced and surgical airway maneuvers like cricothyroidotomy should the attempts for ETI failed. Most of the published data comparing the two agents involve use in the operating suite ([9],[13],[14],[15],[16],[17],[18],[19],[20],[21],[22],[23],[24],[25]). Table I indicates 16 randomized controlled studies (RCT) which had compared the two agents in adults with the clinical endpoint of intubating conditions so far.

Author, year	Number of eligible subjects	Treatment groups and characteristics*	Premedication medications	Induction medications**	True RSI
Cooper, 1992 (35)	40	SCH 1 (20); RCR 0.6 (20)	Temazepam	Fentanyl .001-.003 Thiopental 3-5	-
Huizinga, 1992 (36)	60	SCH 1.5 (30); RCR 0.6 (30); Control (10)		Alfentanil 1 Propofol 1.5-2.5	-
Magorian, 1993 (9)	40	SCH 1 (10); RCR 0.6 (10); RCR 0.9 (10); RCR 1.2 (10); Vecuronium 0.1 (10)	Midazolam Fentanyl	Thiopental 2-7	+
Tryba, 1994 (37)	80	SCH 1.5 (20); RCR 0.6 (20) X 3 groups	Lormetazepam Chlorazepate	Fentanyl .002 Thiopental 6	+
Dubois, 1995 (31)	24	SCH 1 (12); RCR 0.6 (12)	Midazolam Droperidol	Fentanyl .001-.01 Thiopental 3-5	-
Tang, 1996 (25)	75	SCH 1 (23); SCH 1 (25); RCR 0.6 (27)	Midazolam	Fentanyl .0015 Thiopental 4	-
Stevens, 1996 (38)	70	SCH 1 (10); RCR 0.6 (30); RCR 0.6 (30)	Midazolam	Fentanyl .003 Thiopental 7	-
Sparr, 1996 (39)	150	SCH 1 (50); RCR 0.6 (25) X 4 groups		Control: Thiopental 5; I: thiopental 5; II: Propofol 2.5; III: Propofol 2.5, Alfentanil .02; IV: Thiopental 5, Alfentanil .02	+
Sparr 1996 (7)	50	SCH 1 (25); RCR 0.6 (25)		Thiopental 6	+
Latorre, 1996 (40)	40	SCH 1 (20); RCR 0.6 (20)	Oxazepam	Fentanyl .002-.003 Propofol 1.5-2	-
Weiss, 1997 (23)	45	SCH 1.5 (14); RCR 0.7 (15); RCR 0.9 (16)		Fentanyl .002 Thiopental 4-5	+
Nelson, 1997 (24)	42	SCH 1 (22); RCR 0.6 (20)	Midazolam Fentanyl	Thiopental 4-5	+
McCourt, 1998 (41)	314	SCH 1 (127); RCR 0.6 (57); RCR 1.0 (130)	Fentanyl	Thiopental 3-5	+
Viinik, 1999 (18)	30	SCH 1-1.5 (15); RCR 0.6 (15)		Midazolam .025 Alfentanil .025 Propofol 1.5	-
Andrews, 1999 (20)	272	SCH 1 (139); RCR 1 (133)		Propofol 2.5	+
Lam, 2000 (14)	30	SCH 1 (15); RCR 0.6 (15)	Midazolam	Fentanyl 2 Propofol 2.5	-

* NMB type, dose (mg/kg), and number of subjects in group (N).
** Name, dose (mg/kg).

Table I. RCTs comparing the intubating conditions after utilization of SCh and RCR in adult humans.

Developed within the last decade, RCR is indicated in subjects with known or suspected hyperkalemia, crush injury, burns (non-acute) increased

intracranial or intraocular pressure, chronic neuromuscular disease and in whom the physicians avoid administering a second dose of SCh ([1],[3]).

Sakles et al conducted the first study and thus pioneered in the use of RCR in RSI in ED patients and in this prospective study, 58 cases (22%) out of 261 were administered RCR for RSI. The most common reason reported for use of RCR was suspected hyperkalemia (53%). The mean dose used was 1.0 +/- 0.2 mg/kg. None of the complications appeared to be related to RCR. The authors concluded that the use of RCR in the ED setting appears to be useful ([26]). Table II summarizes the main features and side effects of both agents. Some of the side effects of SCh are unique to specific populations.

agent	Dose (mg/kg)	onset of effect	duration	adverse effects	maximum paralysis
Succinylcholine	1-1.5	30-60 sec	3-10 min	hyperkalemia, increased intracranial, intraocular and intragastric pressures, histamine release, fasciculation, malignant hyperthermia, stimulation of autonomic ganglia and their effects, masseter spasm, long bone fractures	24-84 sec (1 mg/kg)
Rocuronium	0.6-1.2	1-1.5 min	30-110 min	none	89 and 55 sec respectively

Table II. Clinical and pharmacological features of both agents.

For example, increase in potassium levels can be clinically significant in cases with known or suspected hyperkalemia, bradycardia is a real threat for children and prolonged apnea is a risk for the pseudocholinesterase deficient. However, the clinical consequences of some untoward effects such as increased intraocular or intracranial pressure have not yet been defined. Thus many authors advocate the utilization of the drug even in the 'risky' situations like open eye surgery or head trauma ([6],[27],[28]). In a one-year cohort study by Laurin et al. only one complication in 382 subjects, widening of the QRS complex secondary to SCh use in a patient with unsuspected hyperkalemia, could be attributed to the choice of NMBA ([1]). Although SCh has many side effects, it remains to be the first-choice NMBA for a vast majority of ED attempts for ETI.

Role Of Succinylcholine And Rocuronium In RSI And Comparison Studies

In a recent study Morris et al reported that SCh and thiopental were the most commonly chosen agents in RSI in the operating room ([29]). Silber et al questioned directors of 100 EDs in the United States and put forth that SCh and vecuronium were the agents most commonly used to achieve NMB ([30]). Most departments employed defasciculating dose of vecuronium before SCh to prevent fasciculation-related muscle pain and other complications seen postoperatively.

RCR has been advocated as a proper NMBA with its short-acting non-depolarizing properties in RSI in many studies ([1],[14],[18],[20],[23],[25],[31]). Several clinical studies demonstrated RCR's brief onset time ([32],[33]). The utilization of RCR in high doses (e.g 1.2 mg/kg) present a disadvantage when a short duration of action is necessary ([9]). It is typical to administer SCh or RCR after sedative hypnotic agents in RSI procedures. On the other hand, timing principle was tried and shown to compensate the delayed effect of RCR by infusing the agent before the hypnotic ([24],[34]).

Neuromuscular blockade has been an integral component of the RSI protocol, although there are some techniques for ETI without using NMBA. Thus, to compare the use of different paralytic agents in RSI necessitates the exclusion of other anesthetic, sedative and hypnotic agents in order to merely determine the degree of paralysis achieved and scoring intubation conditions. Thus most of the studies comparing the two agents have the disadvantage of confounding effects of other adjuncts.

One of the broadest prospective studies on ED use of both agents was conducted by Laurin et al in 2000 ([1]). In this one-year cohort comprising 520 patients the physician's overall satisfaction with the extent of paralysis was found to be higher for SCh (mean = 9.4 +/- 1.3) than RCR (mean = 8.8 +/- 2.0) ($p < 0.01$). The authors concluded that both agents produced fast and reliable paralysis for RSI.

Lam et al carried out a prospective, open-label, parallel group comparative, randomized study. They reported that despite a shorter onset time with SCh, paralysis was successfully antagonized in both groups, and the recovery profile was similar ([14]).

Magorian et al compared three different doses (0.6, 0.9 and 1.2 mg/kg) of RCR with 1 mg/kg SCh in 50 ASA 1-3 patients ([9]). Onset times of RCR in 0.9 and 1.2 mg/kg were similar to that of SCh. The authors suggested that RCR might be an alternative for SCh during RSI, particularly in those at risk for the adverse sequelae of SCh.

Andrews et al compared the muscle-relaxant effect of the two agents under propofol anesthesia in 349 patients undergoing surgery. Usage of RCR 1 mg/kg in RSI protocol was found to be clinically equivalent to SCh 1 mg/kg ([20]).

Mazurek et al assessed the quality of muscle paralysis and intubation conditions with SCh 1.5 mg/kg or RCR 1.2 mg/kg during RSI. The two agents were shown to produce comparable intubation conditions in children ([22]).

The problem of slightly longer onset time of RCR compared to SCh was addressed by Nelson et al in a prospective randomized, double-blind comparison study in 42 patients undergoing elective surgery ([24]). SCh group received 1 mg/kg SCh concurrent with thiopental 4 to 5 mg/kg while RCR group was administered RCR 20 seconds after thiopental. The authors recommended application of this “timing principle” as the practice provided equivalent intubation conditions.

To compare the pharmacodynamics of two commonly recommended doses of RCR (0.7 mg/kg and 0.9 mg/kg) and SCh (1.5 mg/kg) in RSI with fentanyl and thiopental, Weiss et al. conducted a prospective, double-blind, randomized study of 45 patients. Authors indicated that patients who received RCR 0.7 mg/kg displayed a significantly lower intubation score than the other two groups; 60% were rated as poor. RCR at a dose of 0.9 mg/kg provides intubating conditions similar to SCh 1.5 mg/kg at 1 minute

([23]).

Conclusion

Optimal airway management requires utilization of a variety of pharmacologic adjuncts proved useful in obtaining a secure airway and minimizing risk to the patient. SCh has been shown to cause many adverse effects including fatal bradycardia, fasciculation and hyperkalemia. Despite these drawbacks, it remains to be the first-choice NMBA for a vast majority of ED attempts for ETI. A non-depolarizing muscle relaxant, RCR that is free of side effects and has comparable onset time may be viewed as a suitable alternative to SCh.

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