RSII: sugammadex, the new generation?

Mercoledì, 8 gennaio alle ore 14,30 – Aula 2CR

Baini L. Battaglia C. Mosca A. Toninelli A.

In a “can’t intubate – can’t ventilate” scenario, after failure to oxigenate with an SGA device, which is the best next action?

- Open cricothyrotomy
- Needle cricothyrotomy
- Percutaneous tracheostomy
- Mask ventilation until patient awakens

Vote

American Society of Anesthesiologists

http://education.asahq.org/front - accesso 07/01/2014

Definition of RSII

"Rapid sequence induction and intubation (RSII) is an established method of inducing anaesthesia in patients at risk of pulmonary aspiration and allowing rapid intubation of the trachea."

Sinclair RCF, Luxton MC. Rapid Sequence induction. Continuing Education Anaesthesia, Critical Care & Pain 2005;5:45-48

Rapid sequence induction and intubation (RSII) is an anesthesia induction technique designed to facilitate rapid tracheal intubation in patients at high risk of aspiration. The main objective of the technique is to minimize the time interval between loss of protective airway reflexes and tracheal intubation with a cuffed endotracheal tube. Because the airway is unprotected during this time, it is the most critical period during which aspiration of gastric contents is likely to occur. The concept of RSII gradually evolved after the introduction of succinylcholine in 1951 and the description of cricoid pressure (CP) in 1961. However, the first publication that gathered all the components into a structured RSII technique appeared in 1970 (Stept WJ, Safar P. Rapid induction/intubation for prevention of gastric-content aspiration. Anesth Analg 1970;49:633– 6).

Patient factors associated with a high risk of aspiration

- Abdominal pathology, especially obstruction or ileus;
- Delayed gastric emptying (e.g. pain, trauma, opioids, alcohol);
- Incompetent lower oesophageal sphincter, hiatus hernia, gastro-oesophageal reflux disease;
- Altered conscious level resulting in impaired laryngeal reflexes, neurological or neuromuscular disease;
- Pregnancy;
- Difficult airway;
- Metabolic disturbances.

Sinclair RCF, Luxton MC. Rapid Sequence induction. Continuing Education Anaesthesia, Critical Care & Pain 2005;5:45-48

Patient factors

Patients will be at risk if the stomach is not empty, such as those undergoing emergency surgery. Factors associated with a high risk of aspiration include:
(i) abdominal pathology, especially obstruction or ileus;
(ii) delayed gastric emptying (e.g. pain, trauma, opioids, alcohol, vagotomy);
(iii) incompetent lower oesophageal sphincter, hiatus hernia, gastro-oesophageal reflux disease;
(iv) altered conscious level resulting in impaired laryngeal reflexes;
(v) neurological or neuromuscular disease;
(vi) pregnancy;
(vii) difficult airway;
(viii) metabolic disturbances.
The risk of aspiration in these patients is present throughout the perioperative period, especially during induction and emergence from anaesthesia. Warner and colleagues (Warner MA, Warner ME, Weber JG. Clinical significance of pulmonary aspiration in the perioperative period. Anaesthesiology 1993;78:56–62) reported aspiration in 1 of 8 000 anaesthetics given to ASA grade I and II patients; there was greater incidence in ASA III and IV patients (1/343).

Essential features of RSII

- Position
- Pre-oxygenation with 100% oxygen
- Predetermined induction doses of drugs
- Cricoid pressure
- Cuffed endotracheal tube
- Equipment and strategy to manage failed intubation

Sinclair RCF and Luxton MC. Continuing Education in Anaesthesia, Critical Care & Pain 2005;5:45-48

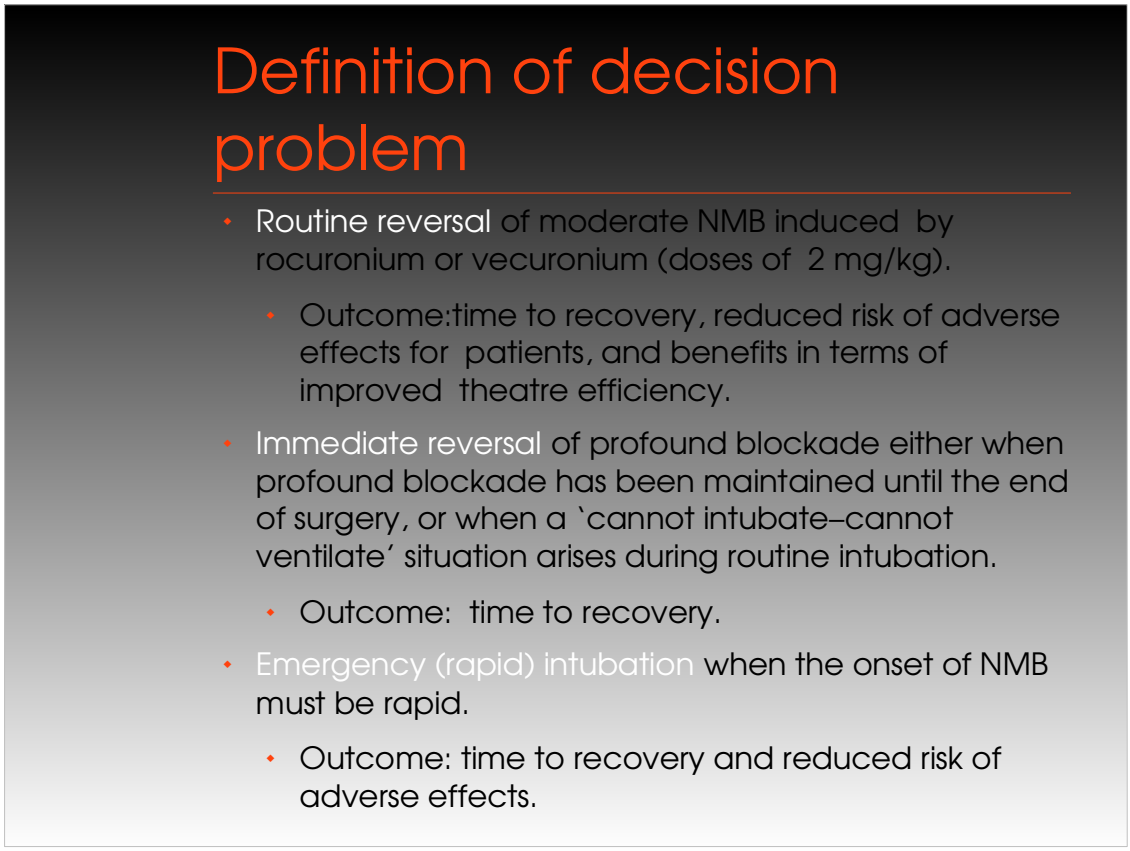
The equipment must be checked and include working suction, capnography, and an adequate selection of endotracheal tubes and laryngoscopes. The trolley must tip to a head-down position easily. A wide bore i.v. cannula is connected to running fluid to ensure speedy circulation of drugs to the brain.

The patient should be positioned in the optimal intubating position.

Pre-oxygenation with oxygen 100% is essential to maximize the oxygen available to the patient from their functional residual capacity during induction. Oxygen is administered for 3–5 min or until the expired oxygen fraction is >85%.

A pre-calculated dose of induction agent is administered, followed immediately by a neuromuscular blocking agent.

Cricoid pressure (at 20–40 N or 2–4 kg) is applied before loss of consciousness. After the jaw has relaxed and succinylcholine-associated fasciculations have ceased, the trachea is intubated. Placement of the endotracheal tube must be confirmed by ventilation, capnography and/or auscultation of the chest. After tube position and adequate seal are confirmed the cricoid pressure may be released.



In the main scenarios for the use of NMB the decision problems relating to the use of sugammadex are:

• Routine reversal of moderate NMB induced by rocuronium or vecuronium (doses of 2 mg/kg). Relevant outcomes are time to recovery, reduced risk of adverse effects for patients, and benefits in terms of improved theatre efficiency.

• Immediate reversal of profound blockade either when profound blockade has been maintained until the end of surgery (routine reversal of profound blockade), or when reversal is needed shortly after administration of rocuronium or vecuronium, for example when a 'cannot intubate–cannot ventilate' situation arises during routine intubation.

There are currently no comparators for this scenario as N&G cannot be used due to the period of spontaneous recovery required before these agents can be administered. The relevant outcome is time to recovery.

• Emergency (rapid) intubation when the onset of NMB must be rapid. The intervention under assessment in this scenario is rocuronium plus sugammadex versus succinylcholine.

The availability of sugammadex 16 mg/kg would allow high-dose rocuronium to be used for rapid intubation in the knowledge that the blockade could be quickly reversed if necessary. In most cases, following rapid intubation, patients would proceed through surgery and their NMB would be reversed as in the routine scenarios, i.e. the 16-mg/kg dose of sugammadex would only be used in the rare cases when the immediate reversal of the rapidly induced block was required. Relevant outcomes are time to recovery and reduced risk of adverse effects for patients.

L'innovazione nei sistemi sanitari

Il livello di sviluppo di un sistema sanitario e l'accessibilità all'assistenza sanitaria che esso garantisce, sono indicatori del livello di sviluppo di un paese e ne sanciscono la caratteristica di paese "avanzato"

Ministero della Salute.Manuale di formazione per il governo clinico: Il governo dell'innovazione nei sistemi sanitari. Dicembre 2012

Il livello di sviluppo di un sistema sanitario e l'accessibilità all'assistenza sanitaria che esso garantisce, sono indicatori del livello di sviluppo di un paese e ne sanciscono la caratteristica di paese "avanzato". La salute di una popolazione e le caratteristiche demografiche sono in parte il risultato della qualità di un sistema sanitario e, a loro volta, hanno ricadute sui costi e sulla sostenibilità del sistema stesso. Il livello di sviluppo di un sistema sanitario determina anche l'interesse che esso esercita sull'industria che produce beni e strumenti (commodities) per la sanità, contribuendo, anche se in maniera indiretta, all'occupazione, allo sviluppo e alla ricchezza di un paese.

Nel settore della sanità si concentrano saperi scientifici e umanistici che concorrono alla ricerca e propongono nuovi strumenti per la cura, la diagnosi, la prevenzione, l'organizzazione e valutazione dell'assistenza sanitaria. Nonostante gli elevati costi, l'innovazione, quando efficace, offre notevoli benefici al sistema, quindi, anche nei momenti di crisi economica e di contrazione della spesa, non è opportuno rinunciarvi, interrompendo gli investimenti di risorse e capitali. Tuttavia, soprattutto nei periodi di crisi e di riduzione della crescita, è necessario valutare attentamente il livello del rischio che si è disposti ad accettare quando si investe in una innovazione che, per sua stessa natura, è accompagnata da un certo grado di incertezza. L'innovazione, come la ricerca, comporta il rischio dell'errore, o meglio del mancato ritorno rispetto all'investimento e alle aspettative.

A System for Prioritizing Policies

Anticipated Effect of a Policy on Aggregate Health Care Costs	Anticipated Effect of a Policy on Population Health		
	Increase	Minor, if any	Decrease
Increase	May or may not be worthwhile	Avoid	Avoid
Minor, if any	Worthwhile	Not worth analyzing	Avoid
Decrease	Especially high priority	Worthwhile	May or may not be worthwhile

Garber S et al. Challenges to value-enhancing innovation in health care delivery. RAND Corporation 2011

Table illustrates a system for prioritizing policies affecting HCI for (costly) attention by policymakers, whose time and resources are limited. This system classifies policies in terms of their anticipated effects—relative to the status quo—on the expected present values of health (QALYs) and health care costs at the national level. In the table, effects in each dimension are divided into three categories, namely (1) substantial increases, (2) substantial decreases, and (3) insubstantial ("minor") effects. We explicitly refer to minor effects to emphasize that many HCIs are likely to have only small (beneficial or detrimental) effects in at least one of the two dimensions, and such effects might best be ignored in policy analyses to allow more detailed consideration or estimation of effects that seem much more substantial. Thus, for example, the cell in the table corresponding to minor effects in both dimensions is dealt with summarily as "not worth analyzing."

The other eight outcome cells of Table are discussed in groups. First, three cells are labeled "avoid"—these cells correspond to situations in which substantial socially undesirable effects are anticipated in one of the dimensions with no substantial and desirable anticipated effect on the other. Second, two cells are labeled "worthwhile"—these correspond to situations in which it is anticipated that there would be a substantial desirable effect in one of the dimensions and at most a minor effect on the other. Third, two other cells are labeled "may or may not be worthwhile" because they correspond to expected social improvement in one dimension but undesirable effects anticipated in the other; judging whether such HCIs are likely to be socially desirable requires further analysis. Finally, one cell is labeled "especially high priority" to emphasize that policies promoting HCIs that are reasonably believed to offer substantial improvement in both dimensions are likely to receive relatively widespread support in policy debates because they offer something substantial to both advocates focused on cost containment and advocates focused on health promotion.

Evidence-Based Decision Making

- If adoption is delayed, patients may be denied access to clinically important and cost-effective interventions
- Conversely, a premature decision could result in a waste of resources on cost-ineffective or even harmful practices that, once diffused, are hard to eliminate

Chalkidou K et al. Evidence-Based Decision Making: When Should We Wait For More Information? Health Affairs 2008;27:1642–1653

The main problem for decisionmakers is how to balance the costs of waiting for better information against the costs of acting prematurely. If adoption is delayed, patients may be denied access to clinically important and cost-effective interventions, and incentives for research and development (R&D) investment will be reduced. Conversely, a premature decision could result in a waste of resources on cost-ineffective or even harmful practices that, once diffused, are hard to eliminate.

A Proposed Decision-Making Framework

- Question 1: Does current evidence suggest that the innovation is better than current practice?
- Question 2: Is collection of more information worthwhile (value of information)?
- Question 3: Should we wait for more information (options)?

Chalkidou K et al. Evidence-Based Decision Making: When Should We Wait For More Information? Health Affairs 2008;27:1642–1653

From our perspective at NICE, rational decision making requires an assessment of both clinical effectiveness and cost-effectiveness. Proponents of evidence-based medicine require a systematic review with rigorous assessment of research quality, consideration of clinical and statistical significance, and a judgment about the balance between health benefits and harms before concluding that evidence is sufficient to warrant implementation of a new technology.
In decision theory, an innovation should be implemented as long as its expected
net benefit (mean benefits minus mean costs) is positive.
The so-called value of information, or VOI, takes account of both the extent of uncertainty and the size of potential impact on clinical benefits and costs. VOI analysis weighs up four key parameters: (1) How uncertain are we about our decision? (2) What would be the impact of making the wrong decision? (This includes the effect size/magnitude of potential incremental benefit of innovation over standard practice.) (3) To what extent will the research reduce the uncertainty? (4) How much is the research likely to cost?
The third question (the options question) becomes relevant only after it has been established that (1) the innovation has a positive expected net benefit (“yes” to question 1), and (2) further research is worthwhile; that is, the value of information exceeds its cost (“yes” to question 2). Before recommending the innovation in this situation, decisionmakers should consider whether they should wait for additional evidence, weighing the potential costs (including health benefits forgone) of delaying the implementation of an apparently promising innovation against the benefits of preventing its dissemination if this later turns out to have been a false promise. If a delay is deemed appropriate, the technology would, in the meantime, be provided only in the context of appropriate research, and current practice would continue for all other patients (“yes” to question 3). Such research arrangements need not be limited to randomized controlled trials (RCTs). It may be that the required information can be collected fromregistry or prospective cohort study. This option becomes particularly appealing when the innovation has already diffused.

What it is, what it isn't, and are we practicing it?

- STRENGTH: the ability to demonstrate best practce through tools of EBM
- WEAKNESS: the inerzia of the *status quo*
- OPPORTUNITY: to shape health care by insisting on EBM
- THREAT: the continue decline of the US health care system

Metzdorff MT. Evidence-based medicine: What it is, what it isn't, and are we practicing it? ? J Trauma Acute Care Surg 2013;75:927–935

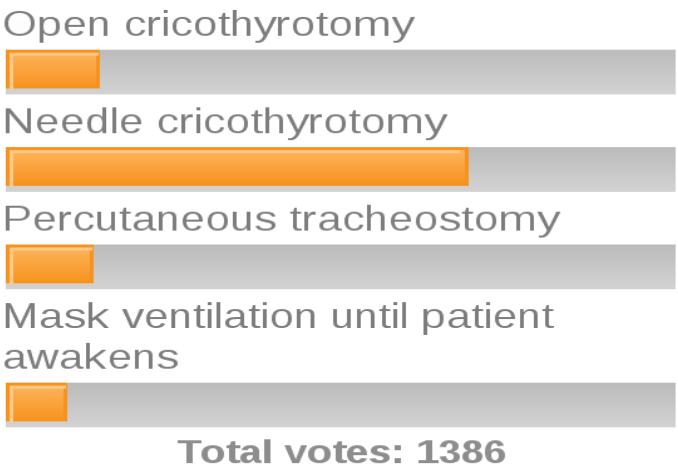
Our strength, the ability to demonstrate best practice through evidence-based medicine;
Our weakness, the inertia of the status quo, especially in the face of multiple responsibilities in our lives;
Our opportunity, to shape health care policy/distribution/reimbursement by insisting on evidence-based medicine in medical and medical policy decision making;
Our threat, the continued decline of the US health care system in the face of the medical/industrial complex and insurance industries driven by greed rather than evidence-based medicine.

Suggested priorities research

- Evaluate the effects of replacing succinylcholine with rocuronium + sugammadex for rapid induction and reversal of NMB on morbidity, mortality, patient-reported outcomes and resource use
- Collect data on the use of sugammadex in clinical practice to obtain better estimates of the incidence and implications of rare major adverse events, for example allergic / anaphylactic reactions

Chambers D et al. Sugammadex for the reversal of muscle relaxation in general anaesthesia: a systematic review and economic assessment. Health Technology Assessment 2010;14:No. 39

In a “can’t intubate – can’t ventilate” scenario, after failure to oxigenate with an SGA device, which is the best next action?



American Society of Anesthesiologists

http://education.asahq.org/front - accesso 07/01/2014

utilizzo del **rocuronio** nell’ intubazione a sequenza rapida

dr. Luca Baini

caratteristiche di un **curaro** ideale

- rapido onset
- non influenzare il consumo di ossigeno
- durata d’azione breve
- reversibile facilmente con un antagonista
- non avere effetti cardio/respiratori
- non triggerare l’ipertermia maligna

Pro: rocuronium should replace succinylcholine for rapid sequence induction

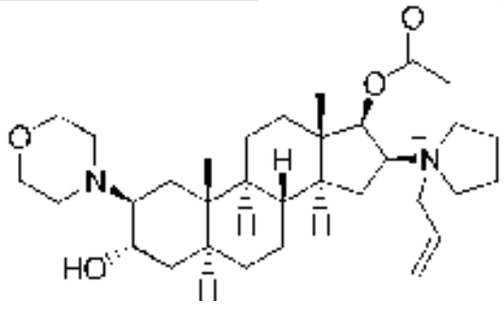
Thierry Girard

European Journal of Anaesthesiology **2013**, 30:585–589

inoltre…

- non avere effetti sulla pressione intra cranica
- non avere effetti sulla pressione endogastrica
- non avere effetti sulla pressione endoculare

ROcuronio



Il **Rocuronio** è un farmaco bloccante neuromuscolare non depolarizzante di tipo amminosteroideo ad azione miorilassante intermedia usato in anestesia, per facilitare l'intubazione e per fornire un adeguato rilassamento della muscolatura striata.

Dosaggio: intubazione a rapida sequenza 1 - 1.2 mg/Kg;
le dosi supplementari per mantenere uno stato di miorisoluzione sono di 0.1 mg/Kg.

Metabolismo: è principalmente eliminato dal fegato (80%) ed una piccola quota (20%) è escreta dal rene.

effetti collaterali del **rocuronio**

- tachicardia
- ipotensione

} Effetti rari
> 1/10.000

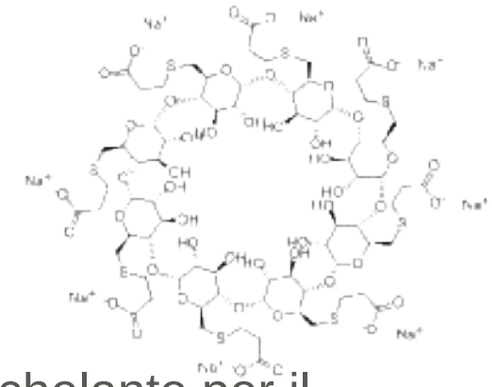
- orticaria
- broncospasmo

} Effetti molto rari
< 1/10.000

caratteristiche di un **decurarizzante** ideale

- Recupero del respiro spontaneo in maniera rapida
- Azione antagonista diretta
- Onset rapido
- Assenza di effetti collaterali

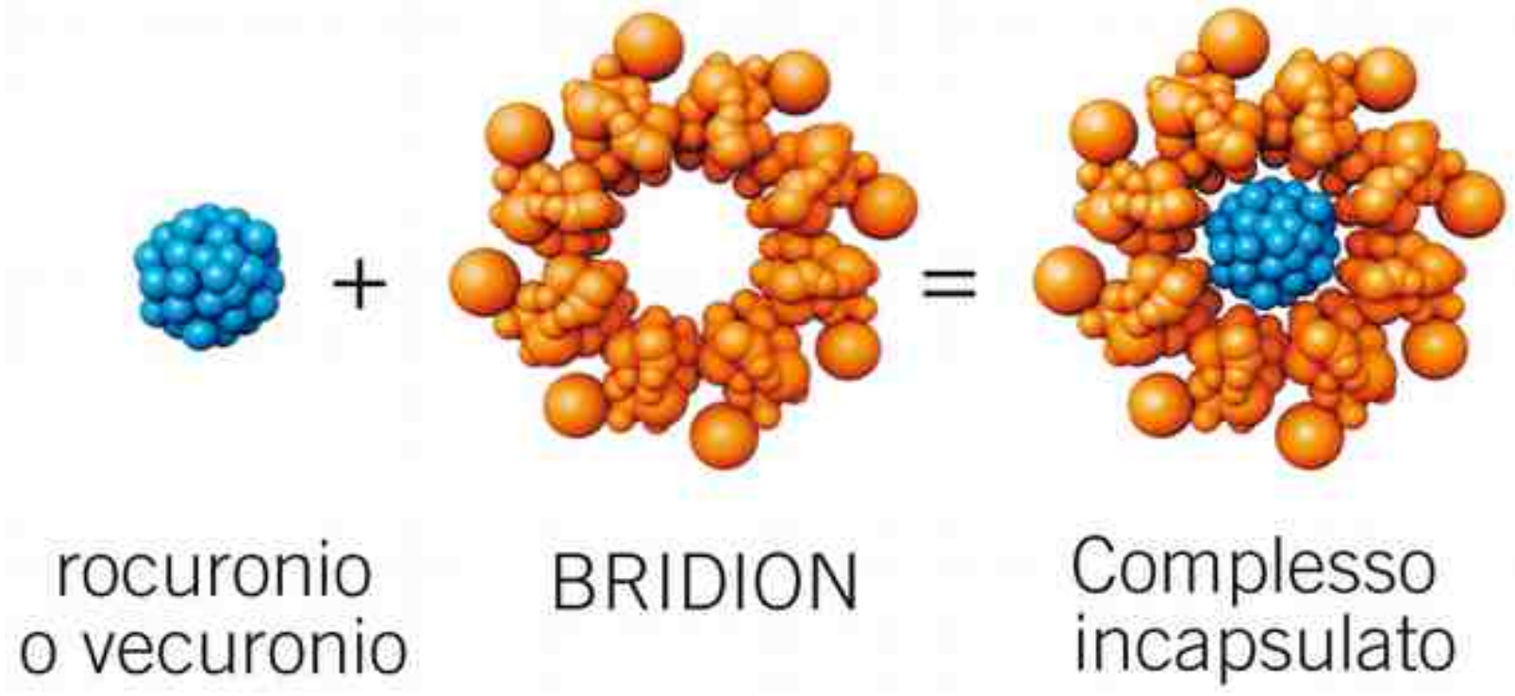
sugammadex



il **Sugammadex** è un’alfa - ciclodestrina che funge da chelante per il rocuronio;
lo antagonizza e lo elimina per via renale in maniera rapida.
Il legame che si forma tra sugammadex e rocuronio è di tipo irreversibile.

Dosaggio: per l’antagonismo immediato dopo somministrazione di rocuronio, è raccomandata una dose di 16 mg/kg di peso corporeo di sugammadex; dopo una dose in bolo da 1,2 mg/kg di peso corporeo di bromuro di rocuronio è lecito attendersi un tempo mediano al ripristino di un valore di 0,9 del rapporto T4/T1 di circa 1,5 minuti.

Controindicazioni: non somministrare il sugammadex in pazienti con grave alterazioni della funzione renale, con Cl Creatinina < 30 ml/min.



rocuronio
o vecuronio

BRIDION

Complesso
incapsulato

Reversal of rocuronium-induced neuromuscular blockade with sugammadex in pediatric and adult surgical patients.

Plaud B, Meretoja O, Hofmockel R, Raft J, Stoddart PA, van Kuijk JH, Hermens Y, Mirakhur RK.

Anesthesiology. **2009** Feb;110(2):284-94

Efficacy, safety, and pharmacokinetics of sugammadex for the reversal of rocuronium-induced

neuromuscular blockade in elderly patients.

McDonagh DL, Benedict PE, Kovac AL, Drover DR, Brister NW, Morte JB, Monk TG.

Anesthesiology. **2011** Feb;114(2):318-29. doi: 10.1097/ALN.0b013e3182065c36.

Effective reversal of muscle relaxation by rocuronium using sugammadex in a patient with

myasthenia gravis undergoing laparoscopic cholecystectomy.

Komasawa N, Noma H, Sugi T, Sukenaga N, Kakiuchi H.
Masui. **2011** Apr;60(4):476-9.

Safety and efficacy of sugammadex for the reversal of rocuronium-induced neuromuscular blockade in cardiac patients undergoing noncardiac surgery.

Dahl V, Pendeville PE, Hollmann MW, Heier T, Abels EA, Blobner M.
Eur J Anaesthesiol. **2009** Oct;26(10):874-84. doi: 10.1097/EJA.0b013e32832c605b.

gravidanza

Non esistono dati relativi all'uso del Rocuronio bromuro durante la gravidanza nell'uomo, che consentano di valutare i potenziali danni per il feto. Nel corso di studi sugli animali non sono state osservate né **embriotossicità** né **teratogenicità** che potessero essere attribuite al trattamento con il rocuronio bromuro.
L'uso del **rocuronio bromuro durante il parto cesareo a dosi pari a 0,6 mg/kg di peso corporeo non influenza il punteggio di Apgar, il tono muscolare** o l'adattamento cardiorespiratorio fetale. Da un campione di sangue del cordone ombelicale è evidente che **si verifica solo un limitato trasferimento placentare** di Rocuronio bromuro, il quale non determina l'osservazione clinica di alcun effetto negativo per il neonato.

Rocuronium and sugammadex for rapid sequence induction of obstetric general anaesthesia
Williamson RM, Mallaiah S, Barclay P.

Acta Anaesthesiol Scand. 2011 Jul;55(6):694-9. doi: 10.1111/j.1399-6576.2011.02431.x. Epub **2011** Apr 11

Modified rapid sequence induction for Caesarian sections:

case series on the use of rocuronium and sugammadex
Nauheimer D, Kollath C, Geldner G.

Anaesthesist. **2012** Aug;61(8):691-5. doi: 10.1007/s00101-012-2065-6.

Effetti collaterali **sugammadex**

- disgeusia
- PORC
- reazioni allergiche

Rocuronium versus succinylcholine for rapid sequence induction intubation (Review)

Abstract

BACKGROUND: Patients requiring emergency endotracheal intubation often require a rapid sequence induction (RSI) intubation technique to protect against aspiration or increased intracranial pressure, or to facilitate intubation. Succinylcholine is the most commonly used muscle relaxant because of its fast onset and short duration; unfortunately, it can have serious side effects. Rocuronium has been suggested as an alternative to succinylcholine for intubation. This meta-analysis is an update since our initial Cochrane systematic review in 2003.

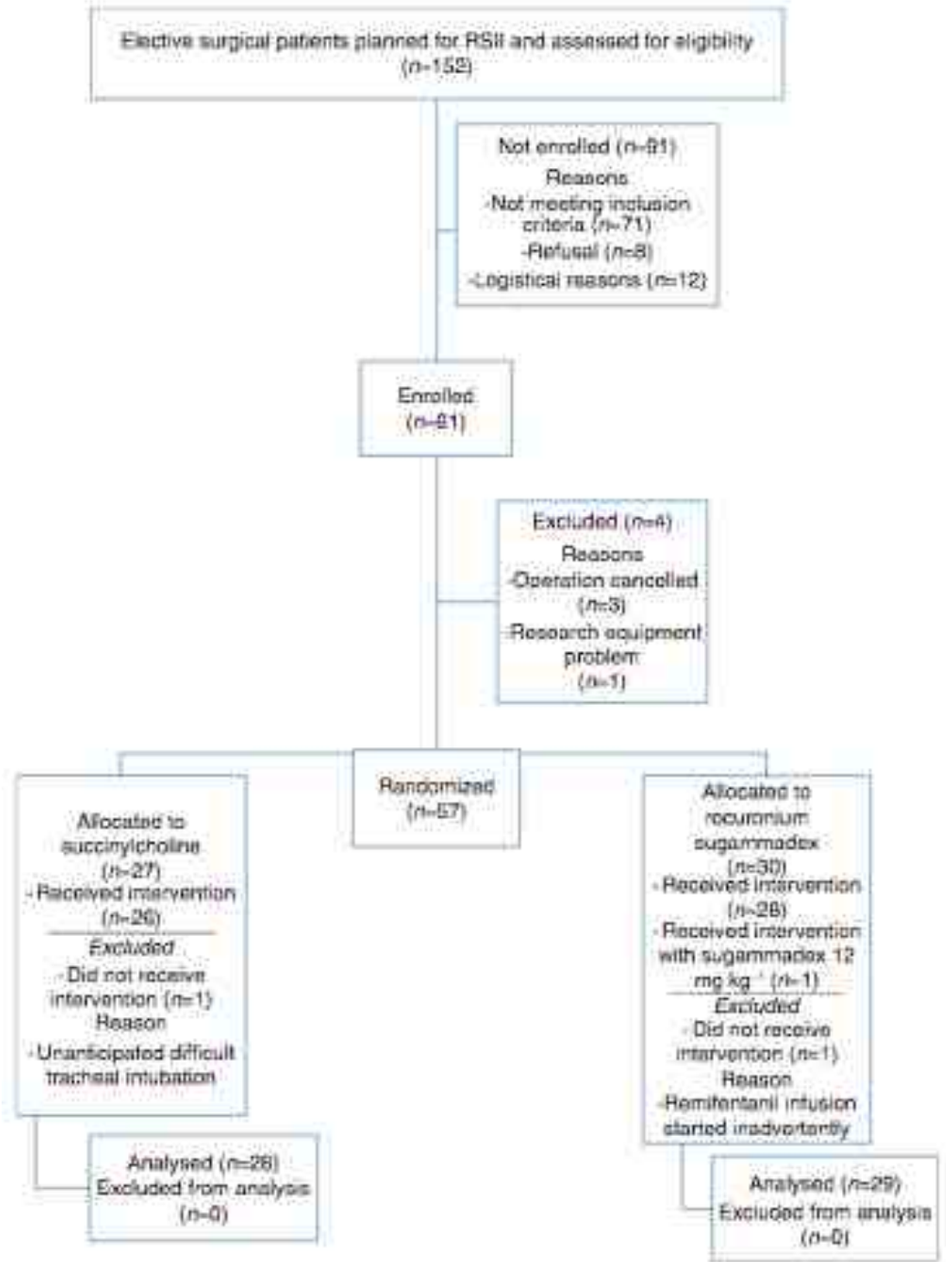
OBJECTIVES: To determine if rocuronium creates comparable intubating conditions to succinylcholine during RSI intubation. Comparisons were made based on dose of rocuronium, narcotic use, emergency versus elective intubation, age and induction agent. The primary outcome was excellent intubation conditions. The secondary outcome was acceptable conditions.

SEARCH STRATEGY: In our initial systematic review we searched all databases until March 2000. We have updated that search and searched the Cochrane Central Register of Controlled Trials (The Cochrane Library, 2007 issue 3), MEDLINE (1966 to June Week 3 2007), EMBASE (1988 to 2007 Week 26) for randomized controlled trials or controlled clinical trials relating to the use of rocuronium and succinylcholine. We included foreign language journals and handsearched the references of identified studies for additional citations.

SELECTION CRITERIA: We included all trials meeting the inclusion criteria (comparison of rocuronium and succinylcholine, main outcomes of intubation conditions).

DATA COLLECTION AND ANALYSIS: Two authors (JP, JL or VS) independently extracted data and assessed methodological quality for allocation concealment. We combined the outcomes in RevMan using relative risk (RR) with a random-effects model.

MAIN RESULTS: In our initial systematic review we identified 40 studies and included 26. In this update we identified a further 18 studies and included 11. In total, we identified 58 potential studies; 37 were combined for meta-analysis. Overall, succinylcholine was superior to rocuronium, RR 0.86 (95% confidence interval (95% CI) 0.80 to 0.92) (n = 2690). In the group that used propofol for induction, the intubation conditions were superior with succinylcholine (RR 0.88, 95% CI 0.80 to 0.97) (n = 1183). This is contrary to our previous meta-analysis results where we reported that intubation conditions were superior in the rocuronium group when propofol was used. We found no statistical difference in intubation conditions when succinylcholine was compared to 1.2mg/kg rocuronium; however, succinylcholine was clinically superior as it has a shorter duration of action.



Rapid sequence induction and intubation with rocuronium–sugammadex compared with succinylcholine: a randomized trial

M. K. Sørensen[1*], C. Bretlau2, M. R. Gäke[2], A. M. Sørensen[1] and L. S. Rasmussen[1]

British Journal of Anaesthesia 108 (4): 682–9 (2012) Advance Access publication 6 February **2012**

Obiettivi dello studio:

1. corretto posizionamento del tubo endotracheale

2. tempo di ripristino della ventilazione spontanea

(frequenza di almeno 8 atti - Vt di 3 ml/Kg - SpO2 del 90% per 30 secondi)

5. durata d’azione del blocco neuromuscolare
(misurata con l’utilizzo del TOF)

	Patients given succinylcholine ($n = 26$)	Patients given rocuronium and sugammadex ($n = 29$)
Age (yr)	49 (46–53)	53 (48–56)
Gender (male/female)	6/20	11/18
Weight (kg)	76 (68–80)	79 (72–85)
BMI (kg m^{-2})	26.8 (23.7–28.9)	25.5 (24.1–27.7)
ASA PS class		
I	5 (19%)	9 (31%)
II	19 (73%)	18 (62%)
III	2 (8%)	2 (7%)
Mallampati score		
1	15 (57%)	18 (62%)
2	9 (35%)	9 (31%)
3	2 (8%)	2 (7%)
Neck movement		
≤90°	0 (0%)	0 (0%)
>90°	26 (100%)	29 (100%)
Ability to prognath		
Yes	26 (100%)	27 (93%)
No	0 (0%)	2 (7%)
Indication for RSII		
Gastrooesophageal reflux disease	20 (76%)	21 (73%)
Hiatus hernia	1 (4%)	7 (24%)
Nausea or vomiting within 24 h of surgery	3 (12%)	0 (0%)
Previous gastric bypass	1 (4%)	1 (3%)
Oesophageal diverticulum	1 (4%)	0 (0%)


-3 min
• Pre-oxygenation
-2 s
• Alfentanil injection (10 µg kg⁻¹)
-90 s
• Propofol injection (2 mg kg⁻¹)
-30 s
• Propofol infusion start (3 mg kg⁻¹ h⁻¹)
-15 s
• Calibration of TOF-Watch®SX
0 s
• Injection of neuromuscular blocking agent (Succinylcholine 1 mg kg⁻¹ or Rocuronium 1 mg kg⁻¹)
60 s
• Cricoid pressure applied
• Start of tracheal intubation
• Endotracheal tube placement verified; sugammadex given in the rocuronium group
• Entrance of blinded investigator — time measurement to spontaneous ventilation
• Time measurement to plateau of T_1 in train-of-four
• Re-calibration of TOF-Watch®SX

	Succinylcholine (1 mg kg^{-1}) ($n=26$)	Rocuronium (1 mg kg^{-1}) Sugammadex (16 mg kg^{-1}) ($n=29$)	P-value
Time from start of procedure to tracheal intubation (s)	330 [313–351]	324 [312–343]	0.45
Intubation conditions			0.13
Excellent	20 (76%)	27 (93%)	
Good	6 (24%)	2 (7%)	
Poor	0 (0%)	0 (0%)	
Intubation difficulty score			0.23
≤5	24 (92%)	28 (100%)	
>5	2 (8%)	0 (0%)	
Time from tracheal intubation to spontaneous ventilation (s)	406 [313–507]	216 [132–425]	0.002
Time from tracheal intubation to T_1 90% (s)	518 [451–671] ($n=17$)	168 [122–201] ($n=27$)	<0.0001
Time from injection of NMBA to T_1 90% (s)	719 [575–787] ($n=17$)	282 [242–319] ($n=27$)	<0.0001

conclusioni:

- pazienti in cui la succinilcolina è controindicata
- NON aumenta la pressione endogastrica
- reversal per una RSII
- reversal di un blocco neuromuscolare

utilizzo del **rocuronio** nell’ intubazione a sequenza rapida

dr. Luca Baini

EJA

Eur J Anaesthesiol 2013; **30**:583–584

INVITED COMMENTARY

The never ending story or the search for a nondepolarising alternative to succinylcholine

Thomas Fuchs-Buder and Denis Schmartz

EJA

Eur J Anaesthesiol 2013; **30**:590–593

EDITORIAL

Con: succinylcholine should not be replaced by rocuronium for rapid sequence induction

Jan-Uwe Schreiber

EJA

Eur J Anaesthesiol 2013; **30**:585–589

EDITORIAL

Pro: rocuronium should replace succinylcholine for rapid sequence induction

Thierry Girard

'So long, succinylcholine!' concluded Lee and Katz[1] in a review article in 2009 after discussing why this agent should be sent out to retirement 60 years after its clinical introduction. During this time, clinical appraisal has changed from 'close to ideal' into 'pharmacologically dirty and dangerous'.[2] Probably unlike any other drug in clinical anaesthesia, succinylcholine has been subject to controversies due to its number of side effects. Life-threatening complications such as malignant hyper-

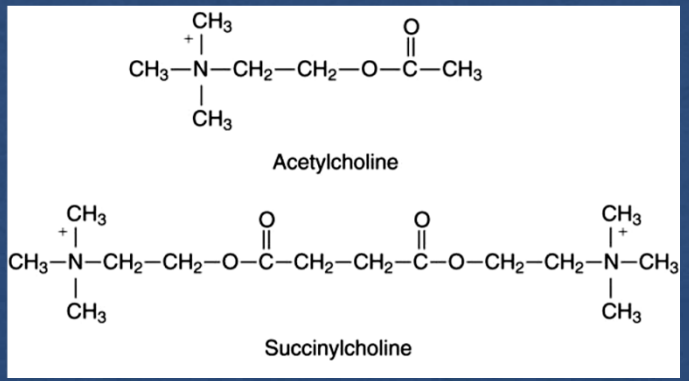
ANNALS OF EMERGENCY MEDICINE MARCH 2011

Evidence-Based Emergency Medicine

Clinical Synopsis

Why look for an alternative to succinylcholine for ED rapid sequence intubation? There is no best neuromuscular

SUCCINYLCHOLINE



introduced by Thesleff and Foldes and colleagues in 1952, changed anesthetic practice drastically.

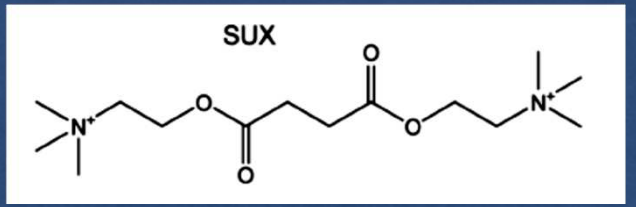
a bis-quaternary ammonium compound

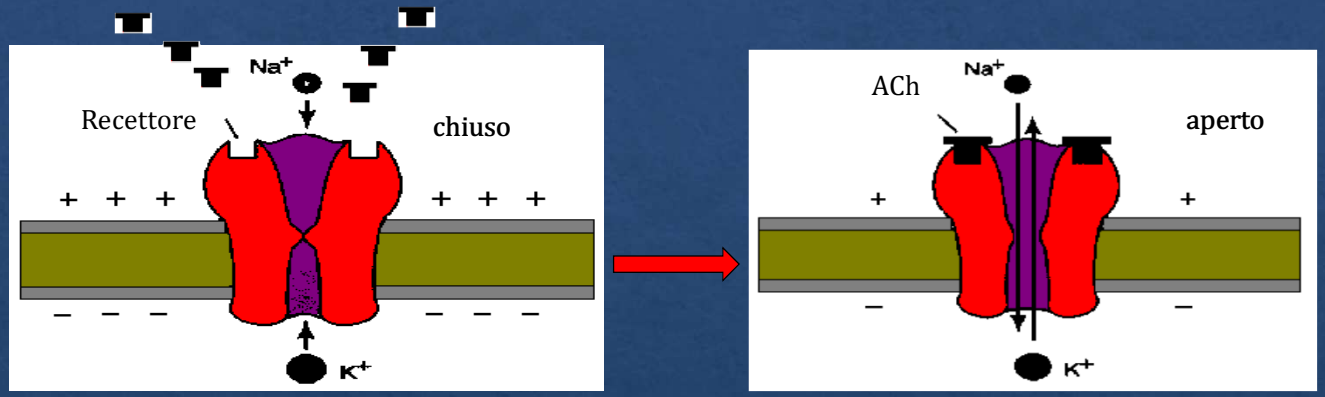
the only available neuromuscular blocker with a rapid onset of effect (0,5-1 min) and an ultrashort duration of action (9-13 min)

The ED_{95} is 0.51 to 0.63 mg/kg

Administration of 1 mg/kg of succinylcholine results in complete suppression of response to neuromuscular stimulation in approximately 60 seconds

Like acetylcholine, succinylcholine stimulates cholinergic receptors at the neuromuscular junction and at nicotinic (ganglionic) and muscarinic autonomic sites, thereby opening the ionic channel in the acetylcholine receptor.





The produced prolonged depolarization of the end-plate region results in:
(1) desensitization of the nAChR,
(2) inactivation of voltage-gated sodium channels at the neuromuscular junction,
(3) increases in potassium permeability in the surrounding membrane.

The end result is failure of action potential generation, and blockade ensues

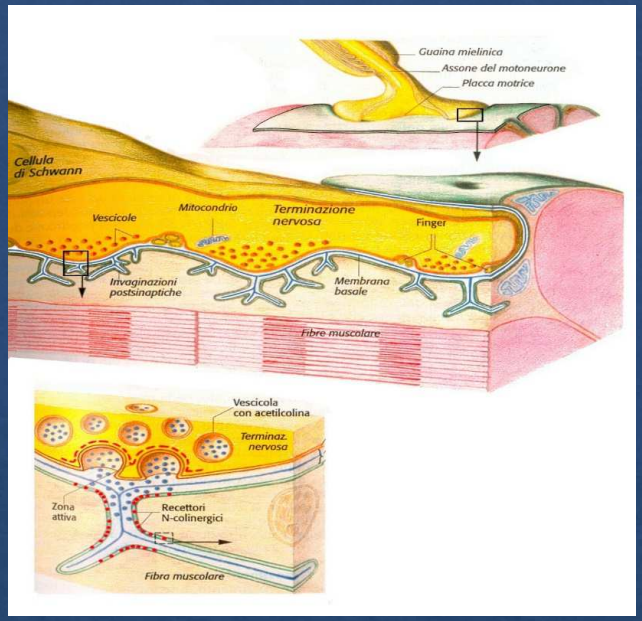
BUTYRYLCHOLINESTERASE
(plasma cholinesterase or pseudocholinesterase)

Hydrolilys to succinylmonocholine and choline

Short duration of action of succinylcholine

The $t_{½}^{\beta} = 47$ seconds

Recovery to 90% muscle strength from 9 to 13 minutes (sux 1mg/Kg)



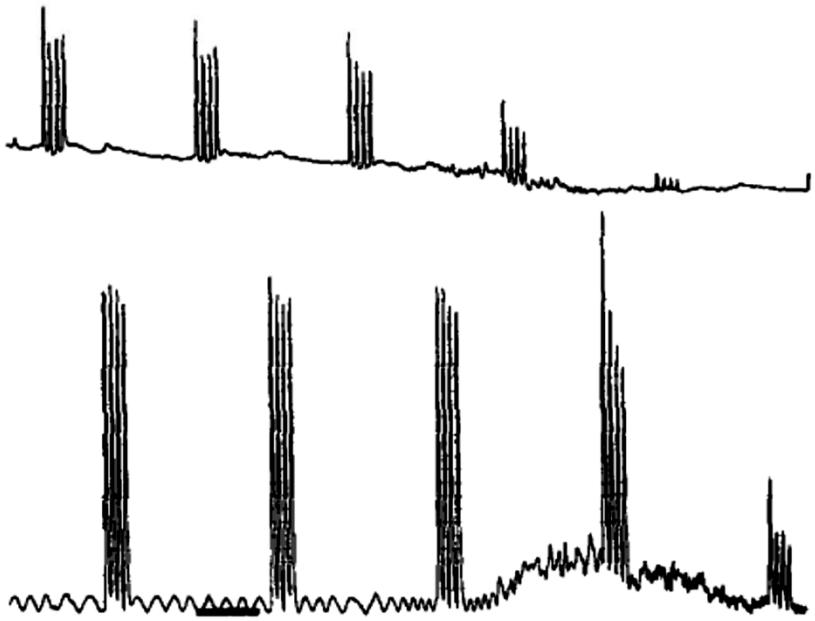


Figure 1. Response to train-of-four stimulation applied every 10 s of the recurrent laryngeal nerve (*top*) and ulnar nerve (*bottom*) after 0.5 mg/kg of succinylcholine (given at the *solid horizontal bar*).

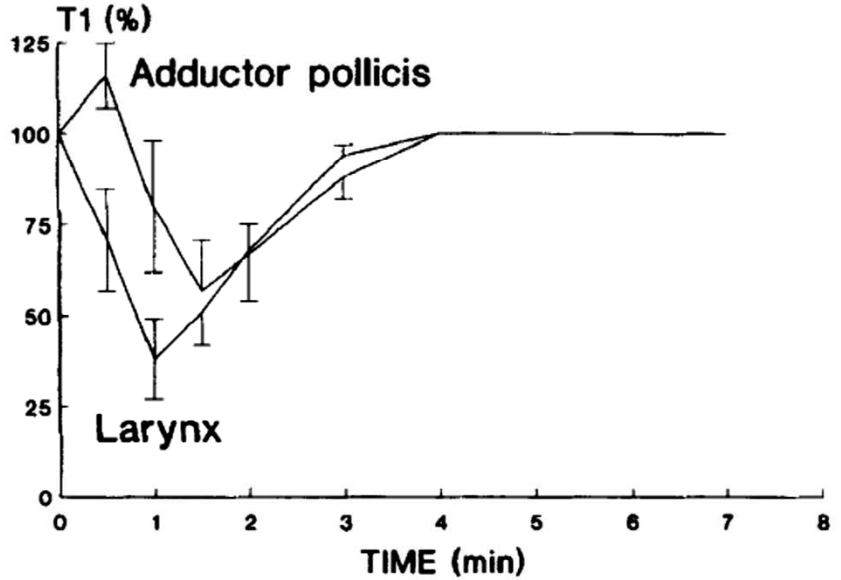


Figure 2. First twitch height (T1) at the larynx and adductor pollicis versus time after 0.25 mg/kg of succinylcholine.

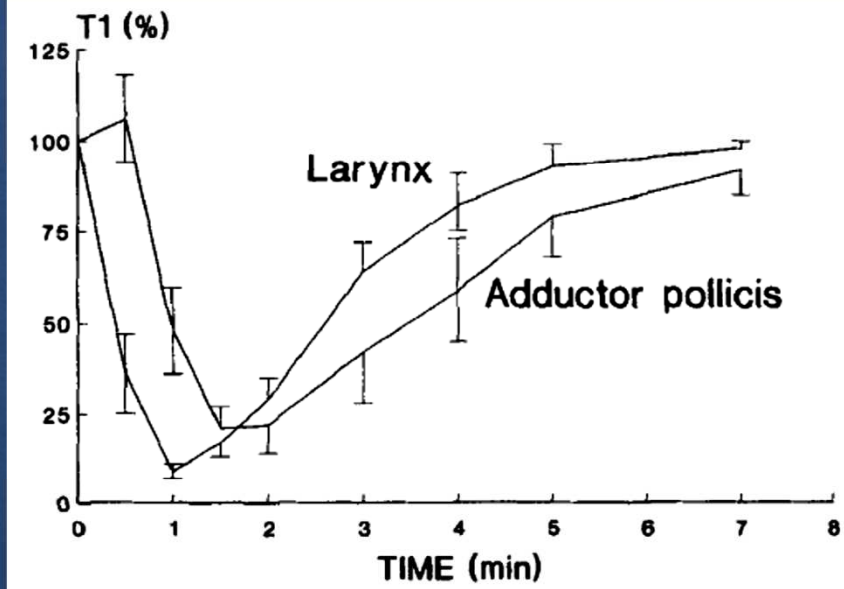


Figure 3. First twitch height (T1) at the larynx and adductor pollicis versus time after 0.5 mg/kg of succinylcholine.

	Maximum blockade			Onset		
Dose (mg/kg)	Larynx (%)	Adductor pollicis (%)	*P*	Larynx (min)	Adductor pollicis (min)	*P*
0.25	66 ± 10	45 ± 13	0.01	0.9 ± 0.1	1.4 ± 0.1	0.01
0.50	93 ± 2	84 ± 6	NS	0.9 ± 0.1	1.7 ± 0.2	0.001

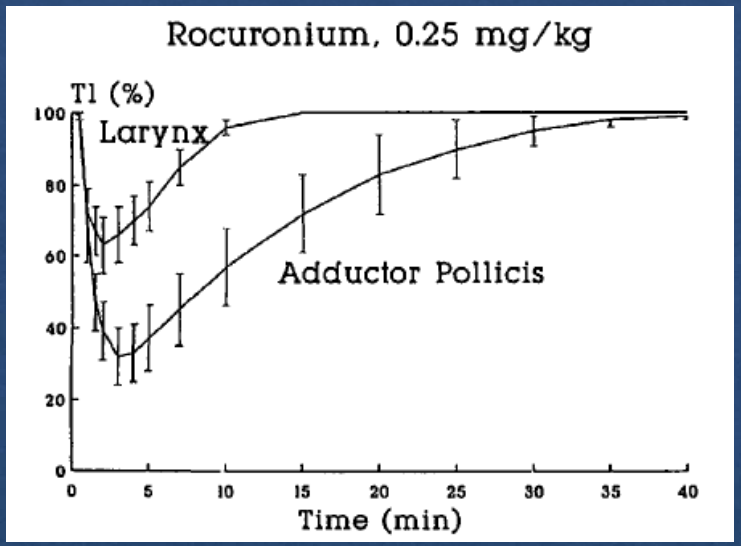
NS, not significant.

Rocuronium (ORG 9426) neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis in humans

CAN J ANAESTH 1992 / 39: 7 / pp 665–9

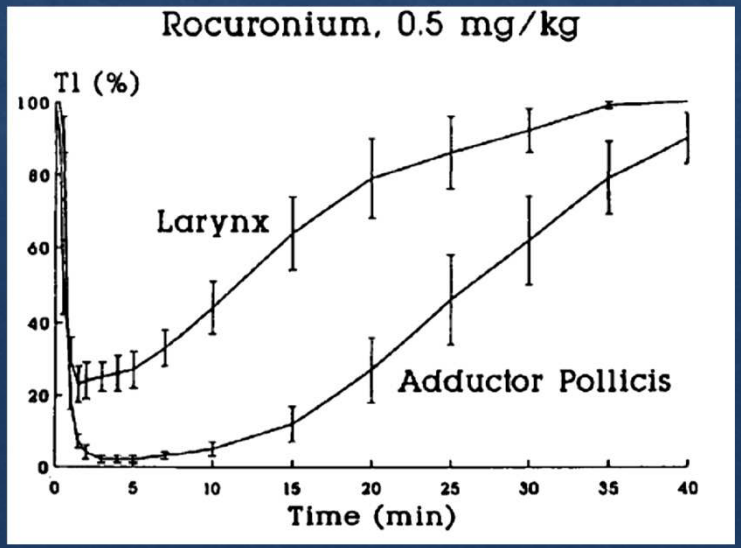
	Maximum blockade (%)		*Onset time (min)*	
	Larynx	*Add poll*	*Larynx*	*Add poll*
Rocuronium 0.25 mg · kg^{-1}	37 ± 8	69 ± 8	1.6 ± 0.1	3.0 ± 0.3
Vecuronium* 0.04 mg · kg^{-1}	55 ± 8	89 ± 3	3.3 ± 0.1	5.7 ± 0.2
Rocuronium 0.5 mg · kg^{-1}	77 ± 5	98 ± 1	1.4 ± 0.1	2.4 ± 0.2
Vecuronium* 0.07 mg · kg^{-1}	88 ± 4	98 ± 1	3.3 ± 0.2	5.7 ± 0.3

*Vecuronium data from Donati *et al.*[1]



Onset time P<0,01

Maximum blockade P<0,05



Onset time P<0,001

Maximum blockade P<0,01

Rocuronium versus succinylcholine for rapid sequence induction intubation (Review)

Perry JJ, Lee JS, Sillberg VAH, Wells GA

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2008, Issue 2

http://www.thecochranelibrary.com

WILEY

Search Metods

- Cochrane Central Register of Controlled Trials *(The Cochrane Library, 2007 issue 3)*
- MEDLINE *(1966 to June Week 3 2007)*
- EMBASE *(1988 to 2007 Week 26)*
- References of selected articles were also hand searched to identify any pertinent additional citations missed by the electronic search

Selection criteria:

- the study compared rocuronium and succinylcholine;
- randomized controlled trials
- the study used a scoring system to assess the main outcome of intubation condition at 60 seconds;
- the dose of rocuronium administered was at least 0.6mg/kg and the dose of succinylcholine was at least 1 mg/kg

The search identified 58 potential studies; 37 trials met the inclusion criteria.

POPULATION

(n=2690)

- males and females
- any age
- rapid sequence induction and intubation (RSII) or modified RSII
- electively or emergently intubation

INTERVENTIONS

- All of the studies compared rocuronium to succinylcholine for neuromuscular blockade
- Sedative used for induction anaesthesia was thiopental, propofol, benzodiazepines or etomidate
- With or without narcotic agents
- Use of pre-treatment sedatives (e.g. low dose benzodiazepines).

COMPARATIONS:

Dose of Rocuronium - Induction Agent - Narcotic use – Age - Emergency vs elective intubations

OUTCOMES

Primary outcome:

Excellent intubation conditions

Secondary outcome:

Acceptable intubation conditions

ADDITIONAL TABLES

Table 1. Intubating conditions

Score	Ease of laryngoscopy	Vocal cords	Intubation response
(1) Excellent	Good	Open	None
(2) Good	Fair	Open	Diaphragmatic movement
(3) Poor	Difficult	Movement	Moderate coughing
(4) Impossible	Poor	Closed	Severe coughing or bucking

TOTAL SCORE

3: excellent intubation conditions

4 - 6: good intubation conditions

7 - 9: poor intubation conditions

10 - 12: inadeguate or impossibile intubation conditions

Golberg et al.
Comparison of tracheal intubating conditions and neuromuscular blocking profiles after intubating doses of mivacurium chloride or succinylcholine in surgical outpatients.
Anesthesia and Analgesia 1989;**69**(1):93–9.

Primary Outcome

Excellent vs other intubation conditions.

Secondary Outcome

Acceptable (excellent or good) vs suboptimal intubation conditions.

TOTAL SCORE

3: excellent intubation conditions

4 - 6: good intubation conditions

7 - 9: poor intubation conditions

10 - 12: inadeguate or impossibile intubation conditions

Data collection & analysis:

Two authors independently extracted data and assessed methodological quality for allocation concealment.

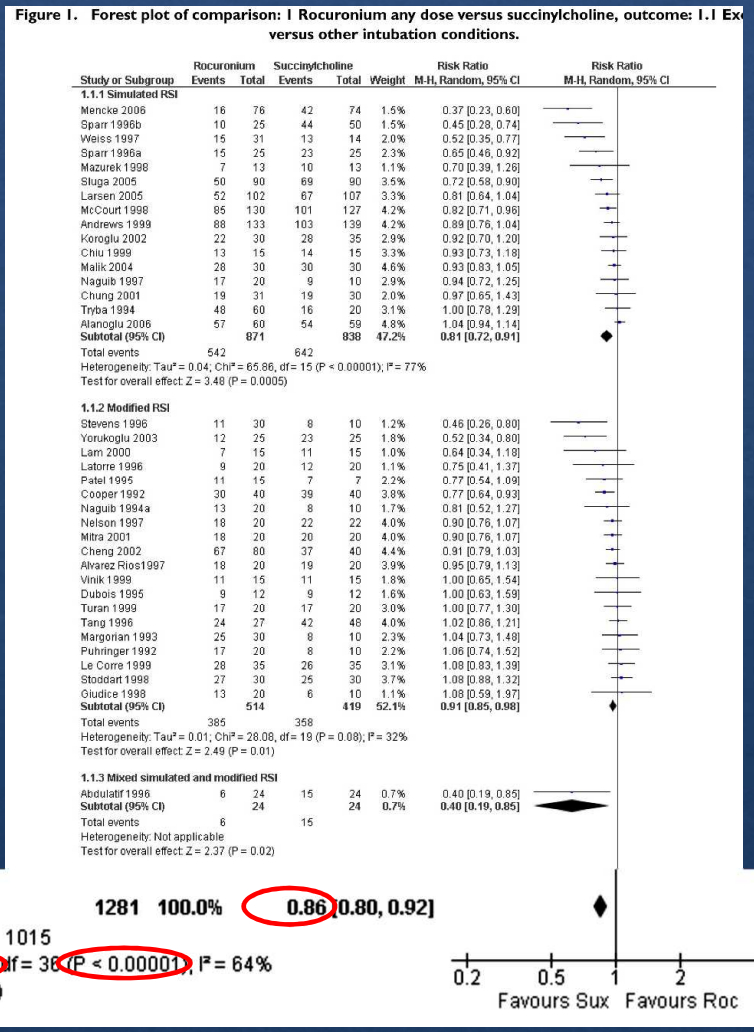
The outcomes were combined in Review Manager software using dichotomous variables, which were calculated as relative risks (RRs) for both excellent and acceptable intubation conditions, both with 95% confidence intervals (95%CIs) with a random-effects model.

Results

Primary outcome of excellent intubation conditions

There was a statistically significant RR favouring succinylcholine when comparing the primary outcome of excellent intubating conditions.
RR of 0.86, (95% CI 0.80 to 0.92).
The chi-squared for heterogeneity was significant.

(Analysis 1.1, Figure1)



Results

Secondary outcome of clinically acceptable intubations

There was also a statistically significant difference found using the less stringent endpoint of clinically acceptable conditions (excellent or good, excluding poor or failed) (RR 0.96, 95% CI 0.93 to 0.99) The chi-squared test for heterogeneity was significant for this group of studies.

(Analysis 1.2)

Comparison 1. Rocuronium any dose versus succinylcholine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Excellent versus other intubation conditions	37	2690	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.80, 0.92]
1.1 Simulated RSI	16	1709	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.72, 0.91]
1.2 Modified RSI	20	933	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.85, 0.98]
1.3 Mixed simulated and modified RSI	1	48	Risk Ratio (M-H, Random, 95% CI)	0.4 [0.19, 0.85]
2 Acceptable versus suboptimal intubation conditions	36	2571	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.93, 0.99]
2.1 Simulated RSI	15	1590	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.89, 1.00]
2.2 Modified RSI	20	933	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.95, 1.01]
2.3 Mixed simulated and modified RSI	1	48	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.55, 0.93]

Results

… effects of interventions

Subgroup analysis for the primary outcome of excellent intubation conditions:

- ✓ Simulated versus modified RSII
- ✓ Comparing the dose of rocuronium
- ✓ Induction agents
- ✓ Use of narcotics
- ✓ Age groups
- ✓ Emergency intubation

Results

Comparing the dose of rocuronium

The subgroup using a dose of rocuronium of 0.6-0.7 mg/kg had a RR favouring succinylcholine for excellent conditions (RR 0.81, 95% CI 0.73 to 0.90).

There were no statistical differences for acceptable intubation conditions in the group that received 0.9-1.0 mg/kg of rocuronium or the group that received 1.2 mg/kg of rocuronium.

Comparison 2. Rocuronium specific dose versus succinylcholine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Excellent versus other intubation conditions	37	2791	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.81, 0.93]
1.1 Rocuronium 0.6-0.7mg/kg	30	1782	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.73, 0.90]
1.2 Rocuronium 0.9-1.0mg/kg	11	923	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.89, 1.02]
1.3 Rocuronium 1.2mg/kg	3	86	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.75, 1.15]
2 Acceptable versus suboptimal intubation conditions	36	2672	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.93, 0.99]
2.1 Rocuronium 0.6-0.7mg/kg	30	1782	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.90, 1.00]
2.2 Rocuronium 0.9-1.0mg/kg	10	804	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.95, 1.01]
2.3 Rocuronium 1.2mg/kg	3	86	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.80, 1.25]

Results

Emergency intubation

…there was a significant RR favouring succinylcholine (RR 0.79, 95%CI 0.71 to 0.88).
(Analysis 7.1)

Analysis 7.1. Comparison 7 Rocuronium versus succinylcholine in emergency intubation, Outcome 1 Excellent versus other intubation conditions.

Review: Rocuronium versus succinylcholine for rapid sequence induction intubation

Comparison: 7 Rocuronium versus succinylcholine in emergency intubation

Outcome: 1 Excellent versus other intubation conditions

Study or subgroup	Rocuronium n/N	Succinylcholine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Larsen 2005	52/102	67/107		20.6 %	0.81 [0.64, 1.04]
Mazurek 1998	7/13	10/13		3.5 %	0.70 [0.39, 1.26]
McCourt 1998	85/130	101/127		50.7 %	0.82 [0.71, 0.96]
Sluga 2005	50/90	69/90		25.2 %	0.72 [0.58, 0.90]
Total (95% CI)	**335**	**337**		**100.0 %**	**0.79 [0.71, 0.88]**

Total events: 194 (Rocuronium), 247 (Succinylcholine)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.10$, $df = 3$ ($P = 0.78$); $I^2 = 0.0\%$

Test for overall effect: $Z = 4.23$ ($P = 0.000023$)

0.1 0.2 0.5 1 2 5 10

Favours Sux Favours Roc

Results

… effects of interventions

Subgroup analysis for the primary outcome of excellent intubation conditions:

- ✓ Simulated versus modified RSII (RR 0.81, 95% CI 0.72 to 0.91) vs (RR 0.91, 95%CI 0.85, 0.98)
- ✓ Induction agents [propofol RR 0.88, (95% CI 0.80 to 0.97)] [tiopenthal RR 0.83 (95% CI 0.76 to 0.92)]
- ✓ Use of narcotics [with narcotic RR of 0.85 (95% CI 0.78 to 0.92)] [without narcotic NS]
- ✓ Age groups [The paediatric subgroup demonstrated no statistical difference for both excellent and clinically acceptable conditions.]

Discussion

- succinylcholine creates better intubation conditions than rocuronium
- this meta-analisys does not find conclusive evidence that increasing doses of rocuronium led to better intubating conditions

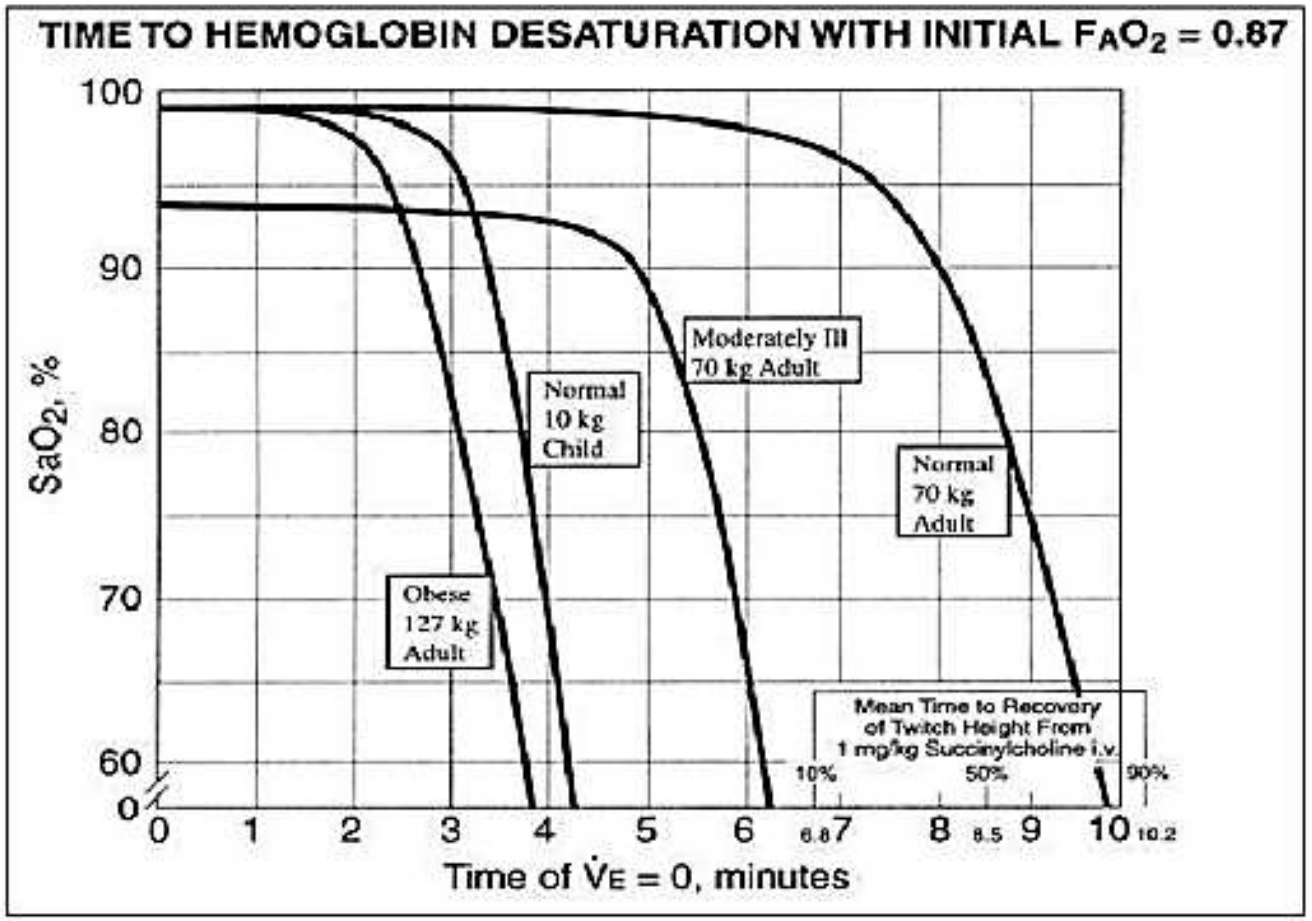
Implications for research

Future studies should be done about:

- patients undergoing emergency RSII
- effects of the larger doses (i.e. 0.9mg/kg and 1.2mg/kg) of rocuronium vs succinylcholine.

Discussion

« However it should be noted that rocuronium has a longer duration of action compared to succinylcholine and that increasing the dose of rocuronium increases its duration of action which can result in an increased incidence of adverse outcomes *(i.e. increased duration of paralysis in a patient who cannot be successfully intubated).*»



Benumof, J., R. Dagg, and R. Benumof, Critical hemoglobin desaturation will occur before return to an unparalyzed state following 1 mg/kg intravenous succinylcholine. Anesthesiology, 1997. 87(4): p. 979-1061

‘Can’t intubate – Can’t ventilate’ (CICV)

Laparoscopic
Cholecystectomy
Sex F
Age 40 aa
Weight 113kg
Height 169 cm

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland

Anaesthesia, 2010, **65**, pages 936–941 doi:10.1111/j.1365-2044.2010.06455.x

ORIGINAL ARTICLE

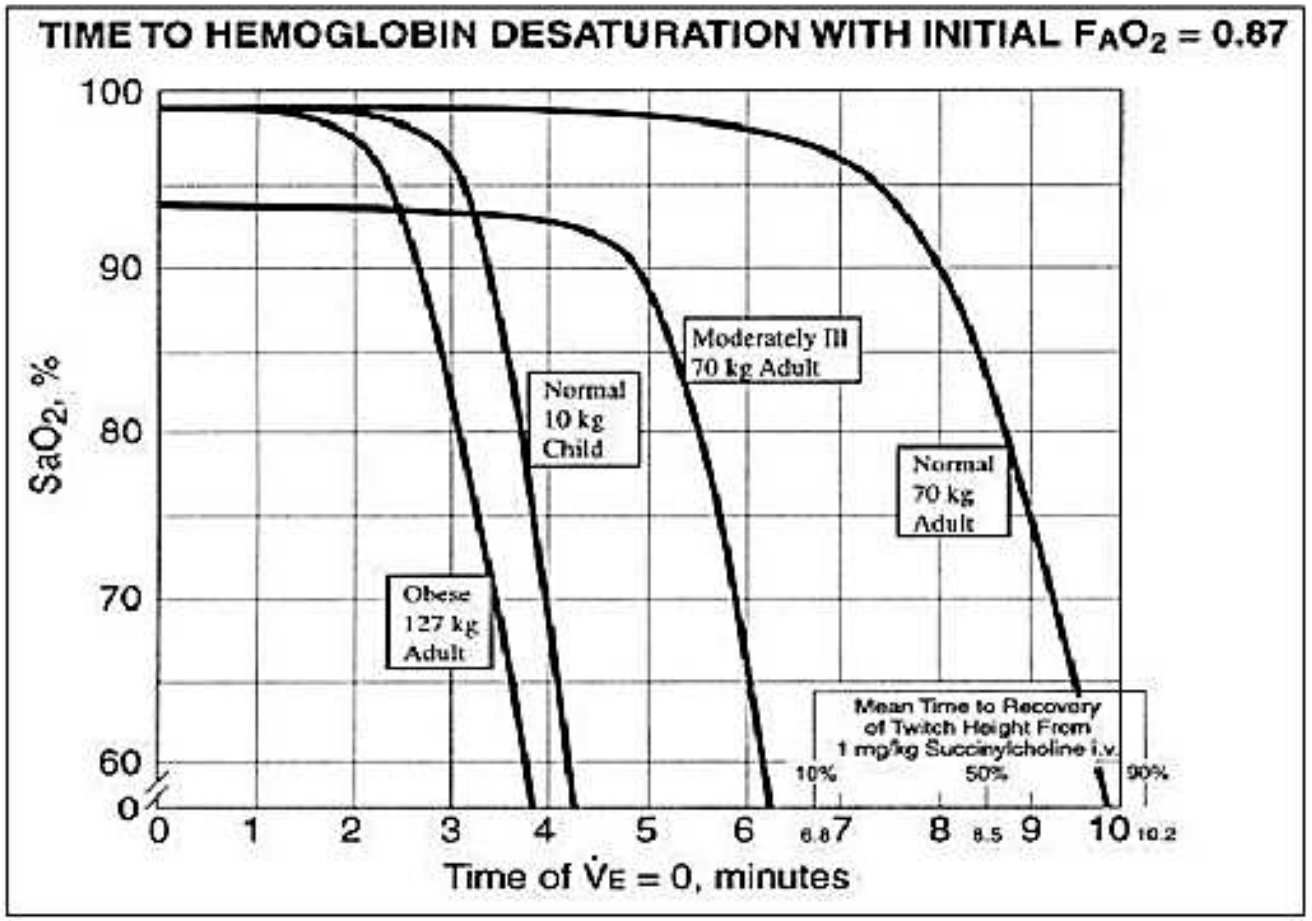
Can sugammadex save a patient in a simulated ‘cannot intubate, cannot ventilate’ situation?

M. M. A. Bisschops,[1] C. Holleman[2] and J. M. Huitink[3]

1 Senior Registrar, 2 Trainee Nurse Anaesthetist, 3 Staff Anaesthetist, Department of Anesthesiology, VU University Medical Centre, Amsterdam, Netherlands

Summary

Recent studies have shown that the use of high dose rocuronium followed by sugammadex provides a faster time to recovery from neuromuscular blockade following rapid sequence induction than suxamethonium. In a manikin-based ‘cannot intubate, cannot ventilate’ simulation, we studied the total time taken for anaesthetic teams to prepare and administer sugammadex from the time of their initial decision to use the drug. The mean (SD) total time to administration of sugammadex was 6.7 (1.5) min, following which a further 2.2 min (giving a total 8.9 min) should be allowed to achieve a train-of-four ratio of 0.9. Four (22%) teams gave the correct dose, 10 (56%) teams gave a dose that was lower than recommended, four (22%) teams gave a dose that was higher than recommended, six (33%) teams administered sugammadex in a single dose, and 12 (67%) teams gave multiple doses. Our simulation highlights that sugammadex might not have saved this patient in a ‘cannot intubate, cannot ventilate’ situation, and that difficulties and delays were encountered when identifying, preparing and administering the correct drug dose.



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'Can't intubate – Can't ventilate' (CICV)

While our anaesthetic teams knew where to find the drug, important time was lost while collecting it from the fridge and calculating and preparing the correct dose.

This decision was made at a managerial level because sugammadex is an expensive drug that is used infrequently.

Anaesthesia
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Summary

time of their initial decision to use the drug. The mean (SD) total time to administration of sugammadex was 6.7 (1.5) min, following which a further 2.2 min (giving a total 8.9 min) should be allowed to achieve a train-of-four ratio of 0.9. Four (22%) teams gave the correct dose, 10 (56%) teams gave a dose that was lower than recommended, four (22%) teams gave a dose that was higher than recommended, six (33%) teams administered sugammadex in a single dose, and 12 (67%) teams gave multiple doses. Our simulation highlights that sugammadex might not have saved this patient in a 'cannot intubate, cannot ventilate' situation, and that difficulties and delays were encountered when identifying, preparing and administering the correct drug dose.

We found that costly time was lost because sugammadex was not directly available in the operating theatre.

Sugammadex is dosed on real body weight and not on lean body weight

Anaesthesia
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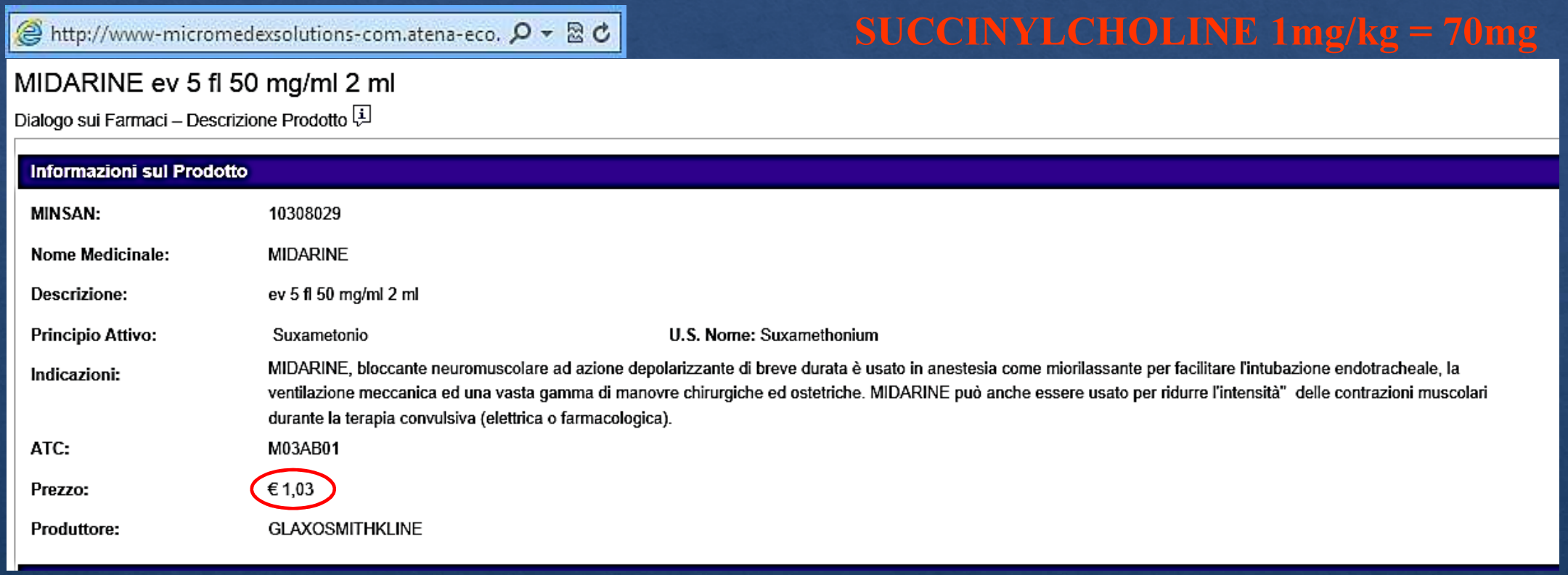
"Our patient required a dose of 1800 mg, which meant that nine ampoules of 2 ml (200 mg) needed to be prepared.

Our findings underline the fact that it is important to have sugammadex directly available at the site where high dose rocuronium is administered to patients. "

Rapid Sequence Induction: Adulto 70 kg

SUCCINYLCHOLINE 1mg/kg = 70mg

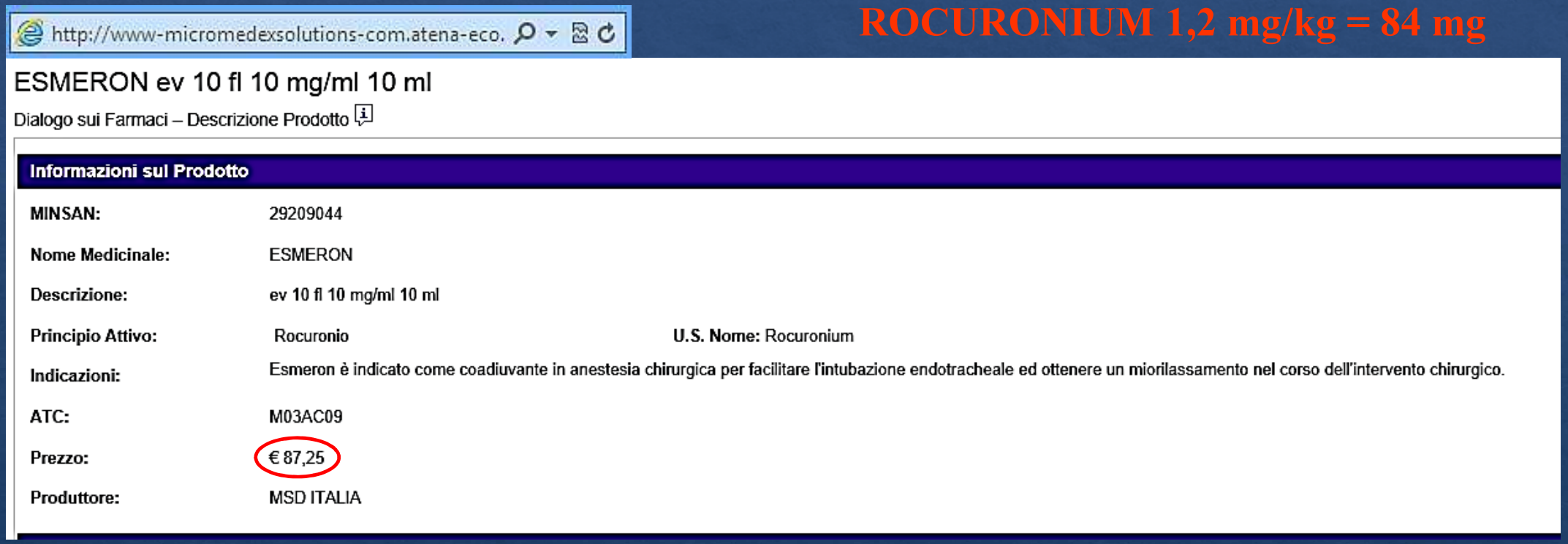


1 fl (100mg) = 0,20 € = 0,002 €/mg

Adulto 70 kg = <u>0,14 €</u>

Rapid Sequence Induction: Adulto 70 kg

ROCURONIUM 1,2 mg/kg = 84 mg

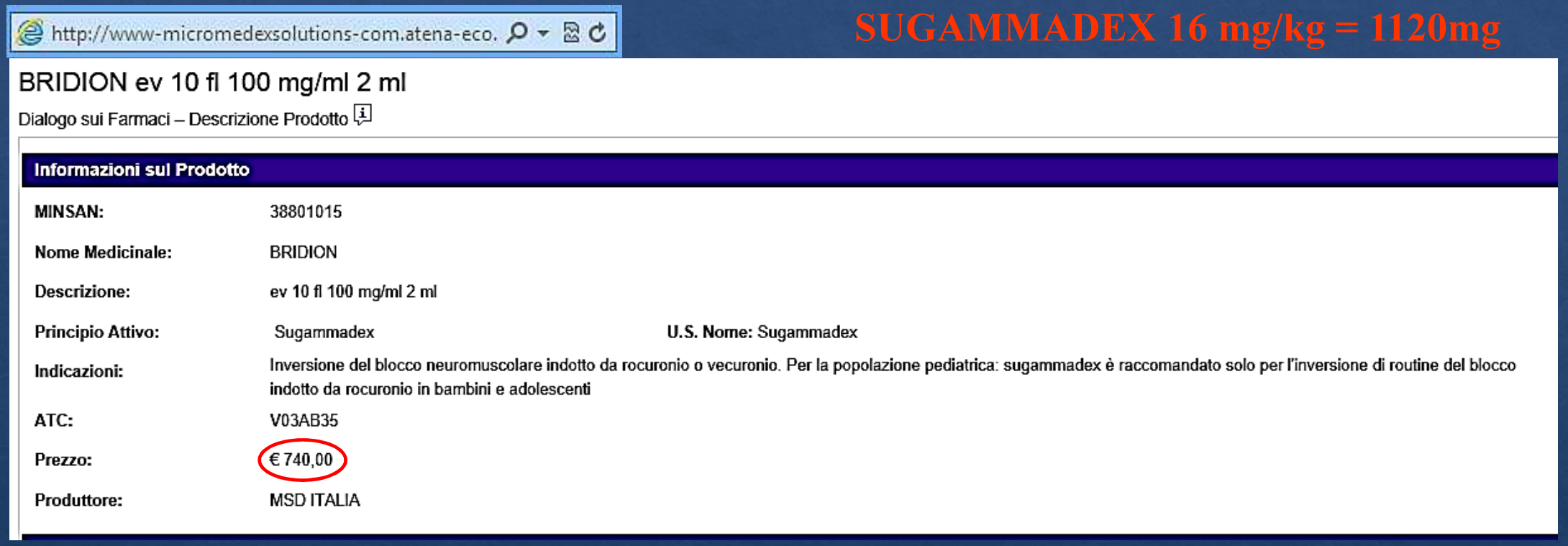


1 fl (100mg) = 8,72 € = 0,0087 €/mg

Adulto 70 kg = 7,33 €

Rapid Sequence Induction: Adulto 70 kg

SUGAMMADEX 16 mg/kg = 1120mg



1 fl (200mg) = 74 € = 0,37 €/mg

Adulto 70 kg = 414 €

from 'close to ideal' into 'pharmacologically dirty and dangerous'

Concerns related to adverse effects:

Cardiac dysrhythmias: sinus bradycardia, junctional rhythms, and ventricular dysrhythmias.
Hyperkaliemia
Increased Intraocular Pressure (IOP)
Increased Intragastric Pressure
Increased Intracranial Pressure
Masseter Spasm
Malignant hyperthermia
Myalgias

Disease-related concerns:

Plasma pseudocholinesterase disorders
Burn injury
Pre-existing Hyperkalemia

EJA

Eur J Anaesthesiol 2013; **30**:590–593

EDITORIAL

Con: succinylcholine should not be replaced by rocuronium for rapid sequence induction

Jan-Uwe Schreiber

Conclusion

The famous Dutch football player Johan Cruijff once said that 'every disadvantage has its advantage'. The disadvantage of succinylcholine as an old drug should be seen as an advantage. Over the years, the number of side effects has led to intensive research on their prevention and treatment. Anaesthesiologists are experienced and aware of the problems that the agent can cause, which may result in additional alertness and careful selection of patients.

Is it, therefore, now justified to say 'so long' to succinylcholine? In case of a RSI, the answer should be 'not yet'.

Eur J Anaesthesiol 2013; **30:**590–593