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ESSENTIAL NOTES

Suxamethonium or rocuronium for rapid sequence induction of anaesthesia?

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Since its introduction in 1951, the use of the neuromuscular blocking agent (NMBA) suxamethonium during the rapid sequence induction (RSI) of anaesthesia has long been regarded as 'gold standard' practice. This is because suxamethonium produces profound neuromuscular block (NMB) with rapid onset and (usually) rapid recovery. These properties were unmatched by the available non-depolarising NMBAs, even when their action is reversed using an anti-cholinesterase drug, as onset is typically slower and offset is very much slower; reliable reversal with an anti-cholinesterase is only possible at relatively light degrees of NMB. However, in the past decade, the place of suxamethonium has been challenged by the popularity of using a combination of rocuronium (a low-potency non-depolarising NMBA with a rapid onset of action) and sugammadex (which provides rapid and reliable reversal from both light and deep NMB).[1]

This article compares the current options available for NMB for RSI (Table 1):

(i) Suxamethonium (usually 1–2 mg kg^{-1}) and await spontaneous reversal of NMB in the event of failed tracheal intubation

(ii) Rocuronium (usually 0.6–1.2 mg kg^{-1}) reversed in the event of failed tracheal intubation with sugammadex up to 16 mg kg^{-1}.

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The RSI of anaesthesia forms a cornerstone of our practice and is one of the earliest practical skills acquired during training. It is used principally in emergency anaesthesia, but it is also used in obstetric anaesthesia or for patients with gastro-oesophageal reflux. The theory behind RSI is essentially two-fold. Firstly, it aims to minimise the time from loss of consciousness to the onset of profound NMB, with placement of a cuffed tracheal tube to secure the airway and protect the lungs from the increased risk of aspiration of gastric contents, blood, or other fluids. Secondly, the prompt offset of NMB and return of consciousness and protective reflexes should minimise the risk of the 'can't intubate, can't oxygenate' scenario.

However, the optimum NMBA for RSI is still currently debated. Whilst suxamethonium does reliably produce rapid onset of NMB, the author believes that the classical teaching of its rapid offset is incorrect. Many anaesthetists have been taught that, by using suxamethonium, adequate spontaneous ventilation will recur *before* the onset of hypoxaemia if attempts at tracheal intubation fail; this assumption is unreliable and potentially hazardous. Although genetic or acquired differences of plasma cholinesterase activity do cause different pharmacokinetic effects between patients, there are also major physiological issues to consider. The quality of the prior preoxygenation and denitrogenation of the lungs has a major effect. As the only effective lung storage capacity for oxygen is limited to the functional residual capacity (FRC), ineffective pulmonary denitrogenation reduces the time from apnoea to the onset of hypoxaemia, and this time will be reduced further in patients with a reduced FRC or in patients with high oxygen consumption (e.g. obstetric patients).[2,3]

The adverse effects of suxamethonium are well described.[1] The transient increase in serum K^+ (usually <0.5 mmol L^{-1}) with suxamethonium is usually of little or no consequence. However, in patients in whom there may be a large number of extrajunctional acetyl choline receptors (e.g. major burns and

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Table 1 Characteristics of suxamethonium and rocuronium. NMB, neuromuscular block. *Approximates to 95% depression of first twitch of train of four. †Approximates to 25% recovery of first twitch of train of four. ‡Determined by plasma cholinesterase activity

	Suxamethonium	Rocuronium
Action at neuromuscular junction	Depolarising	Non-depolarising
Time to onset of NMB* (satisfactory intubating conditions)	60 s	Dose-dependent, larger doses can produce block in 60–75 s
Time to spontaneous return of neuromuscular function†	Typically approximately 10 min‡	Dose-dependent, but typically in excess of 30 min
Drug reversal of NMB	Not possible	Anticholinesterase (e.g. neostigmine 50 μg kg^{-1}) only effective at light NMB (partial recovery); sugammadex effective at any level of NMB
ED_{95} (dose causing 95% twitch depression)	0.3 mg kg^{-1}	0.3 mg kg^{-1}
I.V. 'intubating dose'	1–2 mg kg^{-1} ($3\times ED_{95}$); can be given i.m.: 3 mg kg^{-1})	0.6–1.2 mg kg^{-1} (at least $2\times ED_{95}$)
Common adverse effects	Myalgia, small increase in serum K^+, skin flushing, cardiac arrhythmias, and increase in intraocular pressure	
Rarer adverse effects	Anaphylaxis, marked hyperkalaemia, very prolonged NMB duration,‡ and trigger for malignant hyperthermia	Anaphylaxis, hypotension, tachycardia, and bradycardia
Cost	Very cheap	Rocuronium: moderate cost (sugammadex: high cost)

major nerve injures) or in whom there is intra-abdominal sepsis or severe metabolic acidosis, increases in serum K^+ may be more extreme and lead to dysrhythmias or even cardiac arrest.[1,4] Many patients commonly requiring RSI in anaesthetic practice, such as those undergoing emergency laparotomy, have these risk factors. Suxamethonium has also been associated with more rapid oxygen desaturation during RSI in patients who are obese, compared with rocuronium.[5] Another area of concern is allergy; suxamethonium is nearly twice as likely to cause anaphylaxis as any other NMBAs (approximately one in 9,000), although the next most likely drug is rocuronium (one in 17,000).[6] Although the incidence of anaphylaxis is lower, the 6th National Audit Project report found that the severity was greater with rocuronium than suxamethonium.[6] Overall, combined with concerns over other adverse effects (potential trigger for malignant hyperthermia, and effects on intragastric, intraocular, and intracranial pressures), these issues have resulted in a decline in the popularity of suxamethonium.

Non-depolarising NMBAs have traditionally been viewed as having no place in RSI because of their slower onset and offset of action. The speed of onset of NMB is related to both drug potency and the dose used.[7] NMBAs with a lower potency generally have a faster onset of action because higher doses are given, and therefore, higher concentrations are achieved more quickly at the neuromuscular junction (NMJ). However, the use of high doses of benzylisoquinolinium compounds (atracurium and cisatracurium) is limited in practice by them causing histamine release. Aminosteroid NMBAs with intermediate duration of action, such as vecuronium and rocuronium, allow larger doses to be given safely, with little or no histamine release. Of these NMBAs, rocuronium is less potent and so appears more favourable for use in RSI.

The onset of adequate NMB (and therefore, quality of conditions for tracheal intubation) of rocuronium and suxamethonium has been compared in a recent Cochrane review, with the minimum doses of suxamethonium 1 mg kg^{-1} and rocuronium 0.6 mg kg^{-1}. Compared with lower doses of rocuronium, suxamethonium produced better intubating conditions. However, at higher doses of rocuronium (0.9–1.2 mg kg^{-1}), the intubating conditions were similar to suxamethonium.[8] However, the offset of rocuronium-induced block is crucial for its safety profile in RSI, and it is only relatively recently, with the widespread availability of sugammadex, that rapid reversal from deep NMB has become possible. Sugammadex encapsulates free plasma rocuronium, which in turn rapidly facilitates the offset of action of the drug from the NMJ down a concentration gradient. The dose of sugammadex required depends on the depth of block from 2 to 16 mg kg^{-1}. The introduction of sugammadex has been limited to some degree by its high cost. Although rare, some adverse effects have been described, including anaphylaxis, hypotension, tachycardia, and bradycardia. Sugammadex has been suggested as a potential treatment for rocuronium-induced anaphylaxis, but this is not generally supported.[9]

Other issues should be considered. The choice of i.v. anaesthetic agent during RSI is important; for example, the combination of thiopental and suxamethonium provides better conditions than thiopental with rocuronium.[8] It should be noted that many younger anaesthetists have very limited experience of thiopental as it is rarely used now.

A key area is the scenario of difficult or failed tracheal intubation, where rapid *offset* of NMB may be viewed as more hazardous than NMB being still present; the atypical variants of plasma cholinesterase include a hyperactive form resulting in more rapid or premature offset.[1] This is compounded by the classical teaching that a second dose of suxamethonium should not be given, as it is safer to wake the patient up than continue with prolonged attampts at intubation. With the many options available, including videolaryngoscopy and supraglottic airway device insertion (including intubation guided fibreoptically using an Aintree catheter), these are probably all undertaken more easily with deep NMB. Even bag–mask ventilation, once presumed to be more effective

without NMB, has recently been shown to produce greater delivered tidal volumes when rocuronium was used.[10]

In summary, RSI requires swift and profound NMB, continuing until either the airway is secured or a decision has been made to wake the patient up. Suxamethonium very often provides these requirements inexpensively, but the rocuronium–sugammadex combination may prove ultimately more preferable in a number of scenarios. Whilst a more costly alternative, this combination has both fewer adverse effects and a bespoke rapid offset of NMB. However, in order to undertake this safely, a large dose of sugammadex (up to 16 mg kg^{-1}) must always be directly available if needed.

Declaration of Interest

WJF is an editor of *BJA Education*. He has received lecturer's honoraria from Merck Sharp & Dohme within the past 5 yrs.

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