National Essential Medicine List Medication Review Process
Adult Hospital Level
Component: Anaesthesia

Date of Review: March 31st 2015

Medication: Rocuronium

Indication: Rocuronium is a non-depolarising, neuromuscular blocking agent (NMB) used to induce muscular paralysis during general anaesthesia.

Current Status: New medicine. Not currently on Essential Medicines List (EML).

Executive summary: Currently the only muscle relaxant for use in rapid sequence intubation (RSI) on the EML is the depolarising muscle relaxant, suxamethonium.

This can be problematic as suxamethonium is contraindicated in certain conditions e.g.:

- Congenital and acquired medical conditions associated with severe, potentially lethal hyperkalaemia.[1]
- Malignant hyperthermia.[2]

There is in addition a global problem with lack of availability of suxamethonium.

Rocuronium and RSI

In a rapid sequence induction (RSI), the patient is assumed to have a full stomach. For this reason, after IV induction of anaesthesia the patient must not be mask and bag ventilated until intubated with an endotracheal tube, lest gastric insufflation causing regurgitation of gastric contents occurs. It is therefore necessary when performing an RSI to use a muscle relaxant with a speed of onset of 60 seconds or less so that intubation can be performed before hypoxia develops.

Suxamethonium has been used for this purpose for about 50 years, as it has a speed of onset of 45-60 seconds. Furthermore, in the event of a failed intubation, suxamethonium wears off after approximately 5-10 minutes so this enables the patient to start breathing spontaneously once more and woken up.

Rocuronium is an alternative to suxamethonium in certain circumstances because, if given in a sufficiently high dose (≥0.9mg/kg), it has a sufficiently rapid onset of action for rapid sequence intubation to be performed.
(In standard, non-RSI conditions, a dose of 0.5 -0.6mg of rocuronium is used to provide muscle relaxation for intubation. At this dose the onset time is 2-3 minutes and duration of action approximately 30 minutes.

However, unlike suxamethonium, which wears off after 5 minutes, rocuronium has a duration of action in RSI doses of over 45-60 minutes, so if the patient cannot be intubated he/she will remain paralysed and unable to breathe spontaneously for a long time. If it is then not possible to bag-mask ventilate the patient or perform a surgical airway, the patient could die of hypoxia.

The long duration of action of rocuronium (in comparison with suxamethonium) must be acknowledged when administering it so due care and attention is made to not trying to wake up the patient before the rocuronium has worn off. Failure to do so could result in awareness or respiratory difficulties on extubation. A neuromuscular monitoring device is recommended for use whenever a NMB agent is used to prevent this occurring.

Rocuronium should also not be used if the patient has a difficult airway and bag-mask ventilation is predicted as not being possible in the event of failed intubation.

Other neuromuscular blocking drugs on the EML

For RSI - suxamethonium.

For neuromuscular blockade when RSI not required– vecuronium and cisatracurium. The onset of both of these drugs is too slow for RSI, although vecuronium has been trialled for this purpose (see below).

Articles on the use of rocuronium for RSI

Author	Type of trial	Intervention	Primary Outcome	Results	Comments
Perry 2008[3]	Systematic review. 58 studies. 37 combined for meta-analysis.	RCTs or controlled clinical trials from 1966 to June 2007	Overall suxamethonium superior to rocuronium especially when propofol used for induction. (Contrary result to previous Cochrane review). Rocuronium dose of 1.2mg/kg produced same intubating conditions as suxamethonium at expense of long duration of action.		
Sharp 2009[4]	Review. Non-systematic.	Concerning suxamethonium: "Faith that spontaneous recovery will be sufficiently rapid to allow retrieval of a failed ventilation scenario is misplaced". Dose of rocuronium licensed for Caesarean section is 0.6mg/kg. Evidence this dose gives poorer intubating conditions than with suxamethonium. Use higher doses to get similar onset, 0.9-1.2mg/kg. Sugammadex 16mg/kg can reverse rocuronium faster than suxamethonium wears off.			
Herbstritt 2012[5]	Review. 94 papers. 7 relevant.	Trials where doses of suxamethonium and rocuronium at least 1mg/kg for RSI.	Intubating conditions at 60 seconds similar although trend for suxamethonium to be better. Patients can still become critically hypoxic in the 5-10 mins for suxamethonium to wear off and one should not depend on this "safety net" before proceeding to alternate means to secure the airway. Movements as suxamethonium starts to wear off may make this difficult.		
Mason 2013[6]	Review. Non-systematic.	Dose of rocuronium for RSI: 0.6-1.2mg/kg, onset 1-2 minutes and duration of action 30-90 minutes. Imperative to sedate patients until muscle relaxant effect worn off.			
Stollings 2014[7]	Review.	Medline articles 1966-2013 of RSI with rocuronium.	Pharmacotherapy of drugs used with RSI	Dose of 0.6mg-1.2mg/kg used.	Caution in patients who may be difficult to bag-

					mask ventilate. Notes drug shortages are growing problems. Caution in use of off-label drugs for RSI.

These articles highlight that although suxamethonium provides better intubating conditions than rocuronium, if suxamethonium cannot be used then rocuronium can be used for RSI - providing the patient is given a sufficiently high dose (≥0.9mg/kg), the patient can be mask ventilated in the event of a failed intubation and the patient is kept anaesthetised until the muscle relaxant can be reversed.
(If suggamadex were to become available in South Africa, it could be used to rapidly reverse the muscle relaxant effect of rocuronium in the event of a failed intubation).

Articles comparing speed of onset of rocuronium (roc) and vecuronium (vec)

Author	Type of trial	Intervention	Primary Outcome	Results	Comments
Smith 2002[8]	Prospective blinded study. 100 adults requiring air medical transport and intubation.	RSI with either roc1.0mg/kg or vec0.15mg/kg -alternate days.	Intubating conditions on laryngoscopy.	Intubation success 95% vec and 100% roc. 5 vec patients had inadequate NMB versus 1 roc patient.	More coughing and bucking after intubation with vec.
Nava-Ocampo 2006[9]	Meta-analysis. 21 studies; 29 effect sizes.	Studies comparing the T_{Max} at the adductor policis after IV boluses of roc and vec	Time to onset of action of NMB.	T_{Max} of roc 20-70 secs faster than vec. Subset analysis: roc 0.6mg/kg onset times 50-300secs, (40%>120secs); vec 0.1mg/kg 95 – 290 secs.	At dose 0f 0.6mg/kg roc not much faster than vec 0.1mg/kg. Need higher doses of roc for RSI. Roc 7x more expensive (in Mexico).

These articles show that vecuronium has been investigated for use in RSI and been shown not be as suitable as rocuronium, due to the slower onset time of vecuronium.

Conclusion

Rocuronium should be included in the EML as an alternative muscle relaxant for use in RSI when suxamethonium is contraindicated or not available, provided the practitioner is trained in its use and aware of the contraindications to its use.

Suxamethonium remains superior to rocuronium for RSI but rocuronium is the most appropriate alternative to use if suxamethonium is not available or contraindicated, in terms of outcomes of clinically acceptable intubation conditions and time to onset.

In addition, erratic supply of suxamethonium globally warrants availability of a second agent for RSI.

Alternative anaesthetic techniques for RSI are problematic, as these techniques require either avoiding muscle relaxants completely by administering a high dose of a short acting opiate with propofol (which does not provide consistently good intubation conditions) or administering a fraction of a non-depolarising muscle relaxant before inducing anaesthesia and then rapidly administering the rest of the non-depolarising muscle relaxant (The patient often experiences a suffocating feeling as the first dose of muscle relaxant starts working prior to anaesthesia being induced).

Level of Evidence: I Systematic review

References

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[8] Smith CE, Kovach B et al. Prehospital intubating conditions during rapid sequence intubation: rocuronium versus vecuronium. Air M J 2002; 21(1): 26-32.
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