Sugammadex: A Revolutionary Drug for Clinical Anesthesia Practice

Michael Murray, S-AA, Nova Southeastern University

Introduction:

Neuromuscular blockade is used to help with endotracheal intubation, make sure the patient doesn't move during surgery, and improve the surgical exposure. Muscle relaxants are a key component to anesthesia, but just as important is reversing neuromuscular blockade once the surgery is completed. Sugammadex is a relatively new drug in the clinical setting, which is gaining popularity every year among hospitals. The drug is a neuromuscular reversal agent that has been considered the ideal drug to reverse a patient, at least compared to other drugs on the market. The drug is known for having a quick onset and its ability to reverse quickly for patients with a varying degree of neuromuscular blockade. In this review, it will be discussed why Sugammadex is an ideal reversal agent, compare it to other reversal agents on the market, and discuss why it isn't the leading reversal agent in clinical practice.

Sugammadex, an Ideal Reversal Agent:

Sugammadex is a synthetic cyclodextrin molecule, that is used to reverse the non-depolarizing muscle relaxants Rocuronium and Vecuronium. The main advantage of Sugammadex is that it can rapidly reverse the effects of Rocuronium and Vecuronium, compared to other anticholinesterase reversal drugs. An example of when this drug is beneficial when you have a difficult airway where you can't ventilate or intubate the patient. If you use Sugammadex you can rapidly reverse the effects of the muscle blockade to get the patient spontaneously ventilating again. This can be useful in scenarios where a large dose of Rocuronium was given, such as a modified RSI. Sugammadex can reverse any degree of blockade, even if the patient has no twitches on the train of four test, within 2-3 minutes. It is good to use when the patient has a post tetanic count of 1 or 2. This can be very useful for guaranteeing a much safer emergence process for the patient. It is also good for quick cases that require deep anesthesia and neuromuscular blockade, such as a laryngeal microscopy.

Sugammadex vs Neostigmine:

Neostigmine, a cholinesterase inhibitor, is the most common reversal agent today. What drug is more beneficial to patients? Why is Neostigmine currently the most popular reversal agent? In a study that compared the two drugs for post-operative pulmonary complications, it was found that the administration of Sugammadex was associated with a 30% reduced risk of pulmonary complications, 47% reduced risk of pneumonia, and 55% reduced risk of respiratory failure (Kheterpal 2020). Sugammadex is also more effective for reversing deeper neuromuscular blockade and has a faster onset than Neostigmine. One study showed how much quicker Sugammadex works than Neostigmine. 2 mg/kg of Sugammadex was 6.6 times faster in reversing a moderate neuromuscular blockade and 4 mg/kg Sugammadex was 16.8 times faster reversing a deep blockade. The same study also found that Sugammadex had 40% fewer adverse events than Neostigmine (Hristovsaka 2017). It also does not have the side effect of bradycardia like Neostigmine. The main reason Neostigmine is more widely used is because of how expensive Sugammadex is. Neostigmine is more cost-efficient for hospital and performs an adequate job in reversing patients. Neostigmine can also reverse more NDMR's while Sugammadex only reverses Rocuronium and Vecuronium.

Qualitative peripheral nerve stimulator	Neostigmine	Sugammadex	Quantitive peripheral nerve stimulator
PTC 0–15	Wait	4 $mg.kg^{-1}$	PTC 0–15
TOF count 1 or 2	Wait	2 $mg.kg^{-1}$	TOF count 1 or 2
TOF count 3 or 4	50 $\mu g.kg^{-1}$	2 $mg.kg^{-1}$	TOF count 3 or 4
Fade	50 $\mu g.kg^{-1}$	2 $mg.kg^{-1}$	TOF ratio < 0.5
No fade	30 $\mu g.kg^{-1}$	2 $mg.kg^{-1}$	TOF ratio 0.5–0.9
	No reversal	No reversal	TOF ratio > 0.9

(Bailey, 2017)

Neostigmine	Sugammadex
Co-administered with glycopyrrolate	Single drug
Widely available	Limited availability
Cheap	Expensive
Reverses all non-depolarising agents	Only reverses rocuronium and vecuronium
Cannot reverse deep blockade	Can reverse deep blockade
Slow onset, short duration	Fast onset
Problems if given in a repeated dose	May be given repeatedly
Worsens neuromuscular function if given after full recovery	No problems if given after full recovery
May increase PONV	Does not increase PONV
Non-allergenic	Allergenic

(Bailey, 2017)

Limitations of Sugammadex:

As mentioned earlier, Sugammadex only works on reversing the effects of Rocuronium and Vecuronium, not other NDMR's like Neostigmine. The major drawback is how expensive Sugammadex is. For example, in Belgium, Sugammadex has an average cost of 82.70 euro for a 200 mg vial, while the cost for a comparable amount of Neostigmine and Glycopyrrolate is 4.05 euros (Cammu, 2018). The high cost of Sugammadex combined with the fact that Neostigmine is adequate for most case has limited its usage. Another known is issue, although rare, is hypersensitivity. It is also reccomended to avoid this drug in patients with severe renal impairment or on dialysis. Another problem is if you underdose Sugammadex, it is possible to have the recurrence of neuromuscular blockade.

Fun Facts about Sugammadex:

1. Sugammadex inactivates Rocuronium by encapsulating the free molecule to form a stable complex.
2. Sugammadex can reduce the clinical efficacy of hormonal contraceptive drugs and should be explained to female patients.
3. There are 3 different doses for Sugammadex, 2 mg/kg, 4 mg/kg, and 16 mg/kg. 2 mg/kg is the standard dose given if we have response on a TOF test. 4 mg/kg is if there is a PTC of 0-15. 16 mg/kg is the emergency dose if you need to reverse a large dose of rocuronium that was just given.
4. The tradename of Sugammadex is Bridion.
5. The concentration of Sugammadex is 100 mg/mL. It comes either as 200 mg/ 2L or 500 mg/ 5mL.
6. Recovery could be delayed in patients using the drug Toremifene.

Conclusion:

Sugammadex is the most effective drug on the market for reversing neuromuscular blockade. It has a very quick onset and can reverse deep levels of blockade at any point in the surgery, even right after the administration of Rocuronium. It also has less adverse side effects than Neostigmine. However, it is not viable at the current time to overtake Neostigmine as the most used reversal agent. This is since Sugammadex is much more expensive than Neostigmine and Neostigmine can still do an adequate job with reversal. Sugammadex should still be used in emergency situations and certain procedures or patients when indicated but is probably not the best option for routine cases with healthy patients due to cost.

References:

1. Bailey, C. R. (2017). Sugammadex: When should we be giving it? Anaesthesia, 72(10), 1170–1175. https://doi.org/10.1111/anae.13960

2. Kheterpal, S., Vaughn, M. T., Dubovoy, T. Z., Shah, N. J., Bash, L. D., Colquhoun, D. A., Shanks, A. M., Mathis, M. R., Soto, R. G., Bardia, A., Bartels, K., McCormick, P. J., Schonberger, R. B., & Saager, L. (2020). Sugammadex versus neostigmine for reversal of neuromuscular blockade and postoperative pulmonary complications (stronger). Anesthesiology, 132(6), 1371–1381. https://doi.org/10.1097/aln.0000000000003256

3. Cammu, G. (2018). Sugammadex: Appropriate use in the context of budgetary constraints. Current Anesthesiology Reports, 8(2), 178–185. https://doi.org/10.1007/s40140-018-0265-6

4. Singh, D. R., Sivashanmugam, T., Kumar, H., Nag, K., Parthasarathy, S., & Shetti, A. N. (2013). Sugammadex: A revolutionary drug in Neuromuscular Pharmacology. Anesthesia: Essays and Researches, 7(3), 302. https://doi.org/10.4103/0259-1162.123211

5. Hristovska, A.-M., Duch, P., Allingstrup, M., & Afshari, A. (2017). Efficacy and safety of sugammadex versus neostigmine in reversing neuromuscular blockade in adults. Cochrane Database of Systematic Reviews, 2017(9). https://doi.org/10.1002/14651858.cd012763