

Sugammadex

(bridion)

Prepared By The Anesthesia Team

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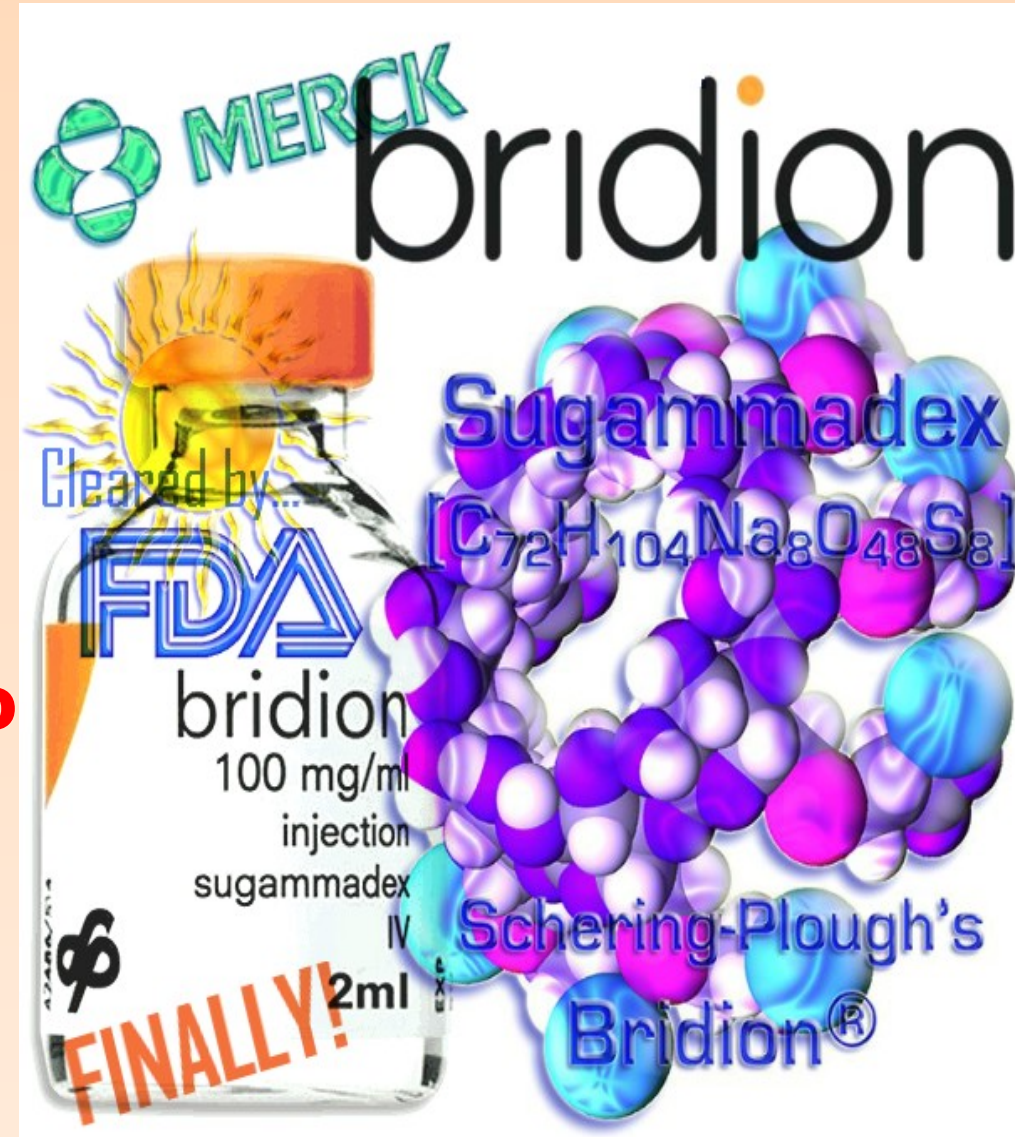
Palestine

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Outlines

- Introduction.
- Mechanism of action.
- Pharmacokinetics
- **Dosing.**
- **Side effects and precautions**
- **Eligibility.**
- **Specific populations**



Introduction

- ❑ Sugammadex, a modified cyclodextrin molecule.
- ❑ It is a unique, **selective relaxant binding agent** (SRBA) which reverses aminosteroid-induced neuromuscular blockade.
- ❑ It provide an impressive **rapid and reliable reversal** of neuromuscular block.
- ❑ It is reversing moderate block around **17 times faster** and with fewer episodes of partial reversal in recovery.
- ❑ It can provide **reversal from deep blockade** ,a feature not possible with neostigmine.
- ❑ It can potentially speed recovery and improve turnaround time in surgical lists.
- ❑ With isolated case reports in the literature suggesting an almost immediate reversal of the **rocuronium-induced anaphylaxis** when sugammadex was administered.

Mechanism of action

□ Sugar **gamma** cyclod**ex**trins = (sugammadex).

□ Sugammadex works via two mechanisms:

1- **firstly** in plasma: it encapsulates the circulating aminosteroid rendering it inactive.

2- **secondly, in the neuromuscular junction (NMJ)** it promotes dissociation of the aminosteroid by creating a concentration gradient from the NMJ to the plasma where it is also encapsulated.

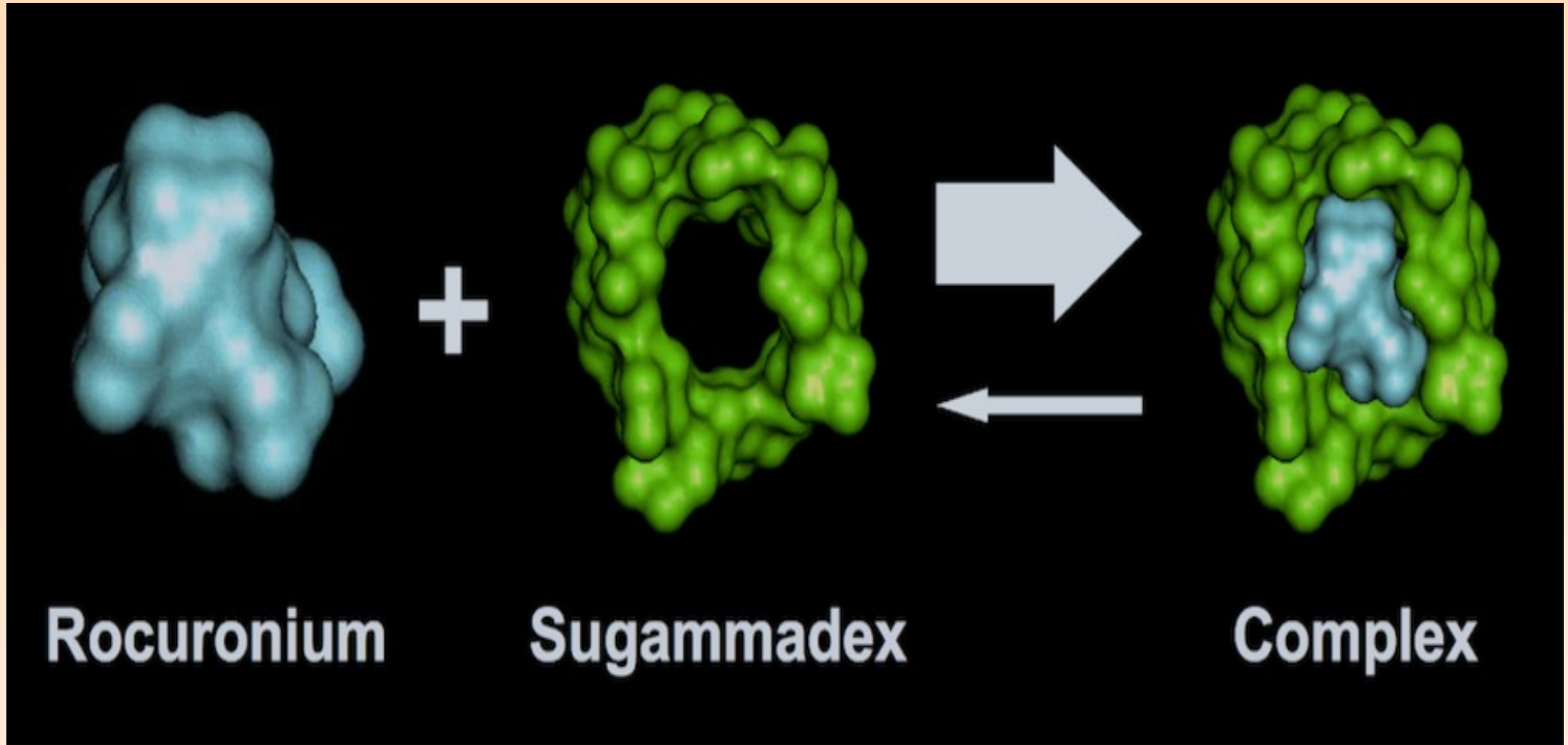
□ Sugammadex also diffuses out of the plasma into the extracellular fluid compartment, encapsulating any unbound aminosteroid it encounters.

□ This encapsulation allows for neuromuscular blockade to be rapidly terminated.

□ Unlike anticholinesterase drugs, sugammadex has no effect on acetylcholinesterase.

□ This obviates the need for anticholinergic drugs, thus avoiding their side effects

Mechanism of action



Pharmacokinetics

- The pharmacokinetics of sugammadex shows a dose dependent linear relationship over the dose range of 0.1–32 mg/kg.
- In a healthy adult sugammadex has an estimated volume of distribution of 11–14 litres.
- An elimination half-life of 1.8 hours.
- Clearance of 88 ml/min.
- It is not metabolized and is excreted almost exclusively unchanged by the kidneys with more than 90% being renally excreted within 24 hours.
- Excretion via faeces or expired air was < 0.02% of the dose.
- The rocuronium-sugammadex complex behaving in a similar manner to sugammadex.
- The elimination of rocuronium being shifted from the biliary system to be renal.

Dosing

1-rocuronium:

- Sugammadex has the ability to reverse any depth of rocuronium induced neuromuscular blockade. (One-to-one binding capacity with rocuronium)

- **The dose of sugammadex is dependent upon:**

- 1- The timing and dose of rocuronium.
- 2- The depth of block.

Depth of block: (routine, moderate and profound)

- It is the response to neuromuscular monitoring, train-of-four (TOF) and post-tetanic count (PTC).

A- Routine block is represented by a TOF of 2 or more.

B- Moderate block is a deeper level of block and corresponds to a TOF of 0 and PTC 1-2.

C- Profound block is the deepest level of neuromuscular block and occurs 3-5 min. post NMBDs when there is no response on neuromuscular monitoring to TOF or PTC.

- **Adequate reversal** is determined by a TOF of >0.9 , where the height of the fourth twitch is 90% of the height of the first twitch.

Type of Block	Dose of Sugammadex	Time to TOF >0.9
Routine – TOF count 2	2mg/kg	2 minutes
Moderate – Post tetanic count 1-2	4mg/kg	3 minutes
Profound – 3-5 minutes post NMBDs	16mg/kg	1.5 minutes

Figure 2: Table showing dose of sugammadex required to reverse different levels of rocuronium neuromuscular blockade.⁴

Time since 4mg/kg sugammadex administration	Dose of NMBD
5 minutes	1.2mg/kg rocuronium
4 hours	0.6mg/kg rocuronium or 0.1mg/kg vecuronium

Figure 3: Table showing the dose of rocuronium required after administration of sugammadex.⁴

Dosing

2- Vecuronium:

- For reversal of routine and moderate rocuronium and also vecuronium-induced blockade, similar doses of sugammadex are required.
- the dose of sugammadex for reversal of profound vecuronium induced block has not been studied and therefore has not been formally determined.

In general

- 1- neuromuscular monitoring is recommended until complete reversal is clinically achieved.(there is great variability in recovery times).
- 2- Reduced doses of sugammadex (<2mg/kg)
 - is associated with prolonged recovery times.
 - incomplete reversal and not recommended.

Side effects and precautions

1- Hypersensitivity

- Although it **is rare**, but far the most concerning side effect of sugammadex.
- The incidence is **less than 1%**.
- It can be **rapid(five min.) and severe** in nature **(anaphylaxis)** with most cases .
- The mechanism of this reaction is not clear .
- It may be involve previous food and pharmaceutical CD exposure.
- Incidence increase with higher drug dose (16 mg/kg), frequent and repeated use.
- Sugammadex has been used in some cases of **rocuronium induced anaphylaxis**.

2- Coagulation

- A transient **increase in activated APTT and prothrombin time (PT) at 10-30min**.
- Normalizes by one hour in doses of 4 mg/kg ,not associated with adverse clinical consequences.
- **Further studies are needed** to review the effect of higher doses of sugammadex.

Side effects and precautions

3- Arrhythmia:

- The most notable being **bradycardia** but generally less than that of neostigmine.
- Prolongation of QTc interval ,but with the same rate as in the placebo group.

4- Neurotoxic: Animal studies suggested that sugammadex may be neurotoxic,

5- renal: Sugammadex is not recommended for patients with severe renal impairment (CrCl<30ml/min).

6- Sugammadex is physically incompatible with verapamil, ranitidine and ondansetron.

7- Sugammadex may decrease the progesterone levels in women taking oral contraceptives.

8- block recurrence with Flucloxacillin, fusidic acid and toremifene because they may displace rocuronium or vecuronium from sugammadex.

therefore patients should be monitored post-operatively for signs of B. recurrence.

9-Laryngeal spasm- strong adduction of the vocal cords following reversal and lasting 2 - 3 minutes in non-intubated patients.

Eligibility

- ❑ Due to its high cost each dose should be carefully considered.
 - ❑ (In some countries)The approved indications are as follows:
1. Immediate reversal is required in an **emergency situation** e.g. when laryngoscopy is difficult and there is a decision to wake the patient up.
 2. There is **residual blockade** despite standard doses of neostigmine/glycopyrrolate.
 3. When a rapid complete reversal is desirable e.g. frail patients in the colorectal enhanced recovery program.
 4. The patient **is morbidly obese** and there is concern of prolonged residual NMB despite 5 mg neostigmine.
 5. The patient has **severe respiratory or neuromuscular compromise**.
 6. When Neostigmine/glycopyrrolate is contra-indicated.
 7. short procedures needs NMB (less 20min) when suxamethonium is contra-indicated.
 8. For treatment of **anaphylaxis where rocuronium** is the suspected culprit.

Specific populations

☐ **Elderly:**

- ☐ The dose of sugammadex for the elderly is the same as younger adult.
- ☐ Onset of action may be slower (reduced CO in the elderly population.)

☐ **Paediatrics:**

- ☐ Routine reversal of TOF count 2 with sugammadex 2mg/kg in children is recommended.
- ☐ Sugammadex use is not endorsed in neonates or infants.

☐ **Obesity:**

- ☐ There is an ongoing debate surrounding the dosing of sugammadex .
- ☐ Currently dosing is based on actual body weight.
- ☐ Dose based on ideal body weight (IBW) plus 40% appears to be safe.
- ☐ Dosing based on IBW alone has been associated with prolonged recovery.

☐ **Pregnancy and breastfeeding:**

- ☐ Need more studies.

☐ **Neurological disease:**

- ☐ Sugammadex is shown to be a safe and effective alternative of neostigmine in most neurological disorders including myasthenia gravis.

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you