

Clinical Pearls Session: Neuromuscular Blockers - What to Use in the Face of a Drug Shortage

Jeremy P. Hampton, PharmD, BCPS
Clinical Assistant Professor – UMKC
School of Pharmacy
Clinical Specialist-Emergency
Medicine – Truman Medical Center

The speaker has no conflict to disclose.



Objectives

- Identify the most commonly used neuromuscular blocking agents (NMBA) for rapid sequence intubation (RSI).
- Compare the pharmacokinetic profiles and therapeutic uses of succinylcholine and rocuronium
- Determine strategies for obtaining optimal paralyzing conditions using rocuronium



Drug Shortages

- Per Institute of Safe Medication Practices (ISMP)
 - Recent number of shortages “unprecedented”
 - Difficult to anticipate
 - Potential for medication errors



Drug Shortages

- Potential for dramatic impact
 - Propofol
 - Epinephrine
 - Dextrose (D50%)
 - Succinylcholine



Rapid Sequence Intubation (RSI)

- Process in which pharmacologic agents administered to facilitate endotracheal intubation
 - Induction
 - Paralysis
 - Post-intubation sedation and analgesia

Emerg Med Clin N Am. 2008; 26:1043-1068




Paralysis


- Frequently utilized agents
 - Non-Depolarizing
 - Succinylcholine: 82%
 - Depolarizing
 - Rocuronium: 12%
 - Vecuronium: 5%

Ann Emerg Med. 2005; 35(2):328-36




| Paralytic Pharmacokinetics | | | | |
|----------------------------|-----------------|------------|------------|-------------|
| | Succinylcholine | Rocuronium | Vecuronium | Pancuronium |
| Onset (sec) | 45 | 60 | 120 - 180 | 120 - 180 |
| Duration (min) | 6 - 10 | 40 - 60 | 45 - 65 | 60 - 100 |

Neuromuscular blocking agents, in: "Manual of Emergency Airway Management" 


| Contraindications/precautions | |
|---|---|
| <ul style="list-style-type: none"> • Succinylcholine <ul style="list-style-type: none"> – Malignant Hyperthermia – Hyperkalemia* – Glaucoma • Rocuronium <ul style="list-style-type: none"> – No absolute contraindications |  |

Succinylcholine chloride [package insert]
Rocuronium bromide [package insert]

| Monday morning in the ED | |
|--|---|
| <ul style="list-style-type: none"> • Pharmacy buyer pages you <ul style="list-style-type: none"> – Succinylcholine is on backorder – Only have 20 vials in house – Hospital uses an average of 10 vials per day • Time to scramble |  |

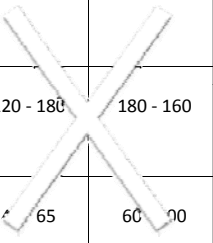

Succinylcholine shortage

- Affects multiple departments
 - Emergency Department
 - Critical care
 - Surgery
- Therapeutic alternatives
 - Rocuronium vs. Vecuronium




Choices for RSI

| | Succinylcholine | Rocuronium | Vecuronium | Pancuronium |
|----------------|-----------------|------------|------------|-------------|
| Onset (sec) | 45 | 60 | 120 - 180 | 180 - 160 |
| Duration (min) | 6 - 10 | 40 - 60 | 65 | 60 - 90 |

MALLON WK, ET AL. ROCURONIUM VS. SUCCINYLCHOLINE IN THE EMERGENCY DEPARTMENT: A CRITICAL APPRAISAL
***J EMERG MED.* 2009; 37:183-88**



Mallon, et. Al.

- Evidence based review of succinylcholine vs. rocuronium
- 3 clinical studies, 1 Cochrane review
- Rate of acceptable conditions, no significant difference
- Succinylcholine judged superior due to short duration



Rocuronium

- Non-depolarizing neuromuscular blocker
 - Onset: 45 – 60 seconds
 - Duration: 40 – 60 minutes
- Dose: 0.6 – 1.2 mg/kg
 - 1 mg/kg is ideal



Rocuronium

- Considerations
 - Slower time to onset
 - Longer acting
- Potential problems
 - Inability to secure airway
 - Post-intubation management



Rocuronium

- Post-intubation management
 - Adequate sedation vitally important
 - Vital sign monitoring
 - Risk of post-traumatic stress disorder (PTSD)

General Hospital Psychiatry 2001; 23(4):198



Rocuronium – Reversal Options

- Neostigmine 0.5 – 2.5 mg IV (Max 5 mg total)
- Pretreat with atropine 25-30 mcg/kg
- Average 17.4 minutes for reversal

Micromedex Healthcare Series [Internet database]
Anesth Analg 2007;104(3):575

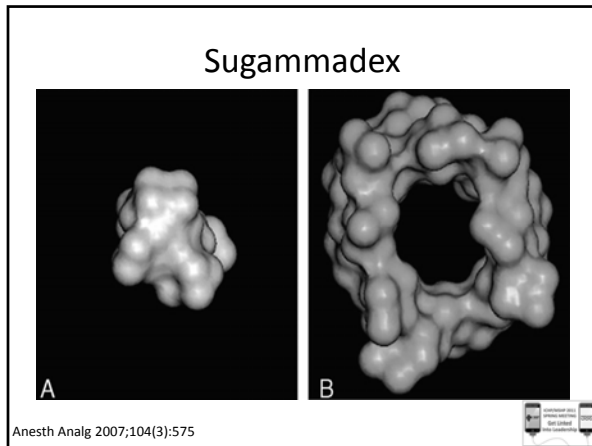


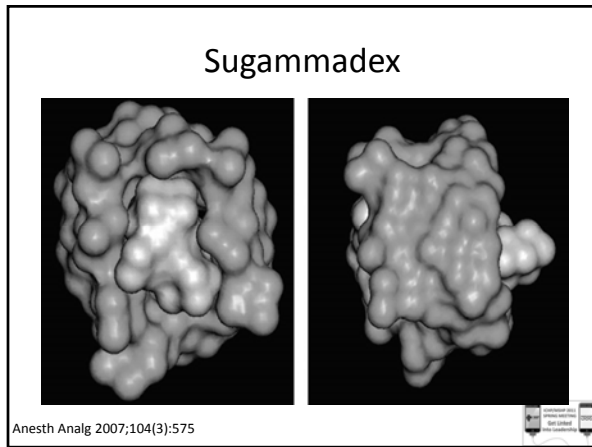
Sugammadex

- Modified cyclodextran
 - Reversal agent for rocuronium and vecuronium
- Originally submitted to FDA 1/3/2008
 - Denied 8/2008 citing need for safety study
- New Drug Application submitted 1/2/2011
 - Assigned priority review status by FDA

Anesth Analg 2007; 104(3):575







Sacan O, White PF. Sugammadex reversal of rocuronium-induced neuromuscular blockade: a comparison with neostigmine-glycopyrrolate and edrophonium-atropine. Anesth Analg 2007;104:569-74

Sugammadex vs. Neostigmine vs. Edrophonium

- 60 patients undergoing elective surgery
- Sugammadex 4 mg/kg IV: N=20 (group S)
- Neostigmine 70 mcg/kg IV: N=20 (group N)
- Edrophonium 1 mg/kg IV: N=20 (group E)
- Primary outcome: TOF ratio of 0.7 and 0.9



Sugammadex vs. Neostigmine vs. Edrophonium

- Significantly faster reversal group S (vs. N and E, $P < 0.05$)
- All in group S reversed < 5 min
- None in group N reversed < 5 min
- 5% in group E reversed < 5 min



Recommendation

- Rocuronium 1 mg/kg IV
 - Allow 60 seconds before intubating
- Keep neostigmine and atropine on hand
- Closely monitor vital signs post-intubation
- Ensure adequate sedation and analgesia



Summary

- Drug shortages have large impact on practice
- Succinylcholine shortage has had direct effect
- Rocuronium indicated in absence
 - 1 mg/kg
- Sugammadex may render succinylcholine obsolete



References

1. Mace E., Challenges and advances in intubation: rapid sequence intubation. *Emerg Med Clin N Am.* 2008; 26:1043-1068.
2. Sagarin MJ, Barton ED, Chung YM, et al. Airway management by US and Canadian emergency medicine residents: a multicenter analysis of more than 60,000 endotracheal intubation attempts. *Ann Emerg Med.* 2005; 35(2):328-36.
3. Caro DA, Laurin EG. Neuromuscular blocking agents. In: Walls RM, Murphy MF, eds. *Manual of Emergency Airway Management.* 3rd ed. Philadelphia: Lippincott, Williams & Wilkins; 2008:248-262.
4. Succinylcholine chloride [package insert]. Lake Forest, IL: Hospira, Inc.;2004.
5. Rocuronium bromide [package insert]. Lake Forest, IL: Hospira, Inc.;2008
6. Mallon WK, et al. Rocuronium vs. Succinylcholine in the Emergency Department: A Critical Appraisal. *J Emerg Med.* 2009; 37:183-88
7. Micromedex Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically.
8. Sacan O, White PF, Tufanogullari B, Klein K. Sugammadex reversal of rocuronium-induced neuromuscular blockade: A comparison with neostigmine-glycopyrrolate and edrophonium-atropine. *Anesth Analg.* 2007; 104(3):569



ICHP/MSHP 2011 Spring Meeting

Clinical Pearls Session: Neuromuscular Blockers - What to Use in the Face of a Drug Shortage

Jeremy P. Hampton, PharmD, BCPS

UAN: 121-000-11-015-L01-P

Post Test Questions:

1. The most commonly utilized neuromuscular blocker for rapid sequence intubation is _____.
 - a. Succinylcholine
 - b. Rocuronium
 - c. Vecuronium
 - d. Pancuronium

2. The most appropriate paralytic for rapid sequence intubation, in the absence of succinylcholine is _____.
 - a. Vecuronium
 - b. Pancuronium
 - c. Rocuronium
 - d. Cisatracurium

3. The optimal paralytic dose of rocuronium in rapid sequence intubation is _____.
 - a. 1.2 mg/kg
 - b. 0.6 mg/kg
 - c. 1 mg/kg
 - d. 1.5 mg/kg

4. The non-depolarizing neuromuscular blocker with the shortest duration of action currently on the market is _____.
 - a. Vecuronium
 - b. Rocuronium
 - c. Pancuronium
 - d. Rapacuronium

5. Pending FDA approval, a potential future option for rocuronium-induced paralysis is _____.
 - a. Sugammadex
 - b. Saflutan
 - c. Epanova
 - d. Aflibercept