

Ask the Experts: Addressing Challenges Related to Reversal of Neuromuscular Blockade

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Disclosure of Relevant Financial Relationships

- Michael Aziz
 - Consultant, Merck (has divested himself of this relationship)
- Deborah Wagner
 - Consultant, Fresenius Kabi; consultant, Merck

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Abbreviations

- ASA American Surgical Association
- MUE medication-use evaluation
- NMB neuromuscular blocker
- PACU post anesthesia care unit
- PONV postoperative nausea and vomiting
- RSI rapid sequence induction
- TOF train of four

Learning Objectives

At the conclusion of this application-based educational activity, participants should be able to

- Examine issues related to the management of complications from neuromuscular blockade and reversal
- Use team-based concepts to enhance the practice model for medication management in the perioperative space

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Use the Reflection Sheet

To capture

- Key ideas & insights “The Ah Ha’s”
- What you’ll do differently with this new information?
- Key takeaways to implement after today

Reflection Sheet: READ AND PRINT THIS BEFORE THE WEBINAR BEGINS
Ask the Experts. Addressing Challenges Related to Reversal of Neuromuscular Blockade
Keep on-hand during the webinar and record key ideas – or “Ah Ha’s!” and key “takeaways” for action.

Topic	Key Ideas and Insights – “Ah Ha...”	Key Takeaways for action: What will you do differently?
Special Populations		
Risk of Postoperative Nausea and Vomiting Associated		
Rapid Sequence Intubation		
Team-Based Practice Model		

**If you attended the first webinar in this series, what changes did you make in your practice since then?
(Select all that apply.)**



- Improved the PACU handover procedure
- Addressed the appropriate use of sugammadex 16 mg/kg
- Monitored use of NMB reversal agents or initiated a MUE review of NMB and reversal
- Developed algorithm for use of sugammadex
- Explored options for safer use of NMB agents with interprofessional team

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Special Populations

Michael Aziz

Obesity

- Obese patients are at higher risk of post-operative respiratory complications and airway obstruction
- Residual neuromuscular blockade during recovery impairs both ventilatory function, upper airway patency, and the capacity to reduce microaspiration

Garibaldi RA et al. *Am J Med.* 1981; 70:677-80.

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Obesity: Upper Airway

- Obese patients are at risk for upper airway obstruction due to redundant tissue and features such as obstructive sleep apnea
- Maintaining airway patency when pharyngeal muscles are relaxed becomes paramount or severe acute obstructive events may occur

Obesity: Upper Airway

- Maintaining laryngeal reflexes is important to reduce the risk of aspiration of gastric or pharyngeal contents during recovery
- Upper airway muscular reflexes are difficult to measure and more susceptible to residual neuromuscular blockade than other muscle groups.
- So, even minor impairments of these reflexes predispose patients to microaspiration and subsequent pneumonia

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Obesity: Lower Airway

- Obese patients ventilate with a reduced functional residual capacity
- Under anesthesia, this makes small airways prone to collapse (atelectasis) and predisposes patients to pneumonia
- Surgery of the chest and abdomen further impair ventilatory function

Obesity: Strategies

- Patients should be emerged from anesthesia and extubated awake for full upper airway reflexes
- Residual neuromuscular blockade must be avoided due to the high risk of airway obstruction, microaspiration, and small airway collapse
- Appropriate monitoring and reversal of neuromuscular blockade is imperative

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Postoperative Nausea and Vomiting

Deborah Wagner

The Big Little Problem



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Risk Factor Categorization for Postoperative Nausea and Vomiting

- What do the consensus guidelines say?
 - Evidence conflicting
 - Neuromuscular blocker reversal agents A-2
 - Reduced doses of neostigmine removed to reduce baseline risk

Gan TJ et al. *Anesth Analg*. 2014; 118:85-113.

Neuromuscular Blocking Agent Antagonists



- Clinical trials before 1998
 - Relevant dose-related emetogenic effect
- Clinical trials post 1998
 - No significant difference or higher incidence with higher doses

Fuchs-Buder T et al. *Eur J Anaesthesiol Suppl*. 2001; 23:53-9.
Salmenpera M et al. *Acta Anaesthesiol Scand*. 1992; 36:445-8.

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Early and Delayed PONV

Outcome	Anticholinergics	Number of Studies	Number of Participants	Relative Risk
Early nausea (0-6 hr)	Atropine and glycopyrrolate	6	584	1.24
Early vomiting (0-6 hr)	Atropine	1	79	0.67
	Glycopyrrolate	5	505	1.39
	Atropine and glycopyrrolate	8	768	1.05
Delayed nausea (6-24 hr)	Atropine	2	199	0.75
	Glycopyrrolate	6	568	1.35
	Glycopyrrolate	4	337	1.09
Delayed vomiting (6-24 hr)	Glycopyrrolate	4	337	1.01

Cheng C et al. *Anesth Analg*. 2005; 101:1349-55.

How do neostigmine and sugammadex compare?



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Postoperative Outcomes with Residual Neuromuscular Blockade

- Retrospective analysis of 1,444 patients receiving a nondepolarizing NMB
 - 722 sugammadex, 212 neostigmine, 510 no reversal
- Endpoints of unwanted events in the PACU
- Doses
 - Sugammadex 2.7 mg/kg (1.1-7.4 mg/kg)
 - Neostigmine 2.4 mg (0.8-3.8 mg)
- NMB – 97.5% rocuronium
- Incidence of PONV 21.5% (neostigmine) vs. 13.6% (sugammadex), $p < 0.05$



Ledowski T et al. *Eur J Anaesthesiol.* 2014; 31:423-9.

Effects on Postoperative Nausea and Vomiting

- 98 ASA class I or II patients undergoing general surgery with reversal
 - Sugammadex 2 mg/kg or neostigmine 50 mcg/kg + 0.2 mg atropine
- Outcomes: early postoperative nausea/vomiting, 24 hours post and use of rescue agents

Yagan O et al. *Rev Bras Anesthesiol.* 2017; 67:147-52.

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Recovery Characteristics

- Single center, randomized, blinded, parallel trial
 - Laparoscopic gynecologic surgery
 - 304 patients
 - Reversal with sugammadex 2 mg/kg or neostigmine 40 mcg/kg + glycopyrrolate 400 mcg
- Outcome: incidence of nausea/vomiting in first 6 hr postop

Paech MF et al. *Anaesthesia*. 2018, 73:340-7.

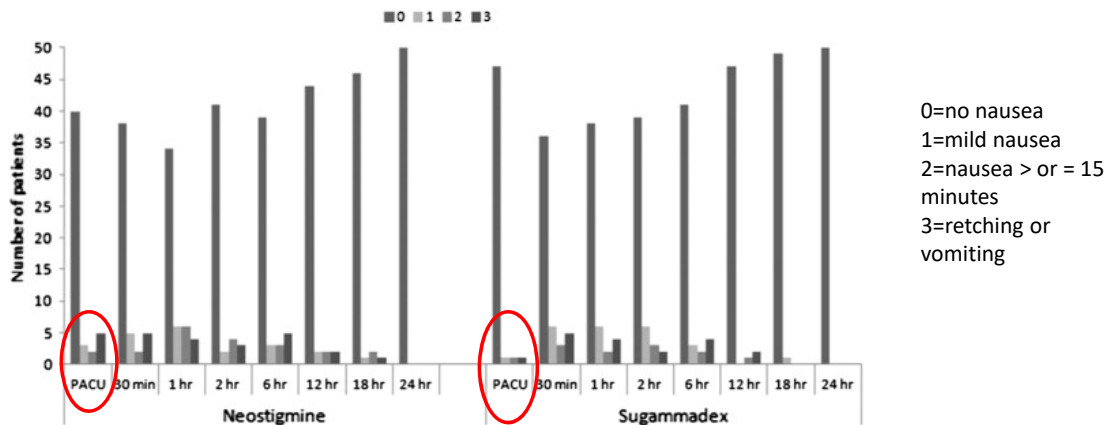
Comparison Between the Two

- Prospective, randomized, double blind study
 - 100 ASA class I or II patients, risk for PONV assessed before surgery
 - Reversal with sugammadex 2 mg/kg or neostigmine 70 mcg/kg + 0.4 mg atropine
- Outcomes: PONV, antiemetic use, and adverse effects

Koyuncu O et al. *J Clin Anesth*. 2015; 27:51-6.

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Postoperative Nausea/Vomiting Scores



Koyuncu O et al. *J Clin Anesth.* 2015; 27:51-6.

Effects on PONV Following Laparoscopic Surgery

- Prospective, double blind, randomized study
 - 80 patients for elective laparoscopic cholecystectomy surgery
 - Sugammadex 2 mg/kg or neostigmine 0.04 mg/kg + 0.15 mg atropine
- Outcomes: PONV at 0-24 hr and antiemetic use

Tas Tuna A et al. *Surg Laparosc Endosc Percutan Tech.* 2017; 27:237.

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Results

	Number of Patients		
	Sugammadex (n = 40)	Neostigmine (n = 40)	Difference Between Groups
0-2 hours			
0	15	9	NS
1	19	21	NS
2	1	3	NS
3	4	7	NS
2-6 hours			
0	30	25	NS
1	7	9	NS
2	2	3	NS
3	1	3	NS
6-24 hours			
0	38	34	NS
1	2	4	NS
2	0	2	NS
3	0	0	NS

Tas Tuna A et al. *Surg Laparosc Endosc Percutan Tech.* 2017; 27:237.

Based on the information presented, use of current reversal agents increases the risk for postoperative nausea and vomiting.



- a. True
- b. False

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Rapid Sequence Induction (RSI)

Michael Aziz



What is rapid sequence induction?

- A technique of anesthetic induction aimed at reducing the risk of aspiration of gastric contents
- Performed during emergency airway management when the stomach is full (not-fasted) or the patient is predisposed to aspiration from poor gastric emptying or reduced gastric volume

El-Orbany M et al. *Anesthesia Analg.* 2010; 110:1318-25.

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Principles of Rapid Sequence Induction

- Avoid or reduce the use of face mask ventilation, which entrains air into the stomach and predisposes the patient to aspiration
- Application of cricoid pressure during induction of anesthesia to occlude the esophagus
- Administer a rapidly acting neuromuscular blocker to create the fastest intubation conditions

RSI: Neuromuscular Blockade

- Succinylcholine takes potent effect in 1 min and typically lasts at least 5 min
- Rocuronium at high doses (1.2 mg/kg) has similar onset and efficacy but may last hours

Perry JJ et al. *Cochrane Database Syst Rev.* 2008; 10:CD002788.

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Reversal of RSI Neuromuscular Blockade

- Succinylcholine cannot be reversed chemically
- Clinical reversal depends on pseudocholinesterase metabolism, which is rarely absent in some inherent conditions
- Reversal of rocuronium can be achieved in 2 min with sugammadex (16 mg/kg) compared with 2 hr by metabolism

de Boer HD et al. *Anesthesiology*. 2007; 107:239-44.

Emergency Reversal During RSI

- When difficult airway management is encountered, restoration of spontaneous ventilation may be life saving
- Compared with succinylcholine, reversal of rocuronium with sugammadex may be achieved faster, and this technique has been applied in case reports
- However, it takes several minutes to identify that failed intubation is encountered, so reversal with sugammadex may not restore ventilation in time for safe recovery

Curtis R et al. *Br J Anaesth*. 2012; 108:612-14.

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Which drug to use during RSI?

- Jury is still out
- Despite a difficult adverse effect profile with succinylcholine and several contraindications, rocuronium and sugammadex are also associated with anaphylaxis
- We cannot say that one induction drug is preferred over another for safe RSI care

A Team-Based Practice Model

Deborah Wagner



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Pharmacoeconomic Considerations – Many Worlds Collide

Pharmacy POV

Acquisition costs
Use patterns



Lowest drug cost
(*with acceptable outcomes)

OR POV

Turn-over times
Patient safety



Best OR-PACU
efficiency with
safe outcomes

Hospital POV

Bundled payments
Patient safety



Best LOS efficiency
with safe
outcomes

Pharmacoeconomic Considerations – What is Missing Here?

Pharmacy POV

Acquisition costs
Use patterns



OR POV

Turn-over times
Patient safety



Hospital POV

Bundled payments
Patient safety



Shared Mental Models

Budgetary ROI data for actual costs vs. savings
Identification of where causal relationships exist
What is the cost of patient experience?

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Creating an Environment for Medication Safety and Quality

- Culture
- Shared accountability
- Integration into the anesthesiology department
- Collaboration

Inception: 2017



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Who are the members?

- Director of Anesthesiology Quality
- Anesthesia staff: faculty, residents, CRNAs (adult and pediatric)
- Pharmacy representation
 - Purchasing
 - Clean room
 - Operations
 - Clinical
 - Medication use policy
 - Medication safety officer



CRNAs = certified registered nurse anesthetists

Key Drivers

- Begin prioritization process for themes and strategies
- Integrate drug use with availability and develop a shared access point for pharmacy and anesthesia
- Create drug equivalency matrices
- Develop provider communication plans
- Perform a GAP analysis

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Formal Actions

- Preemptively respond to drug shortages
- Review supply of prefilled products and/or ready-to-use products
- Review of medication errors and mitigating factors
- Stocking of medications
- Drug-use reviews (e.g., i.v. acetaminophen, sugammadex)

Using Internal Data



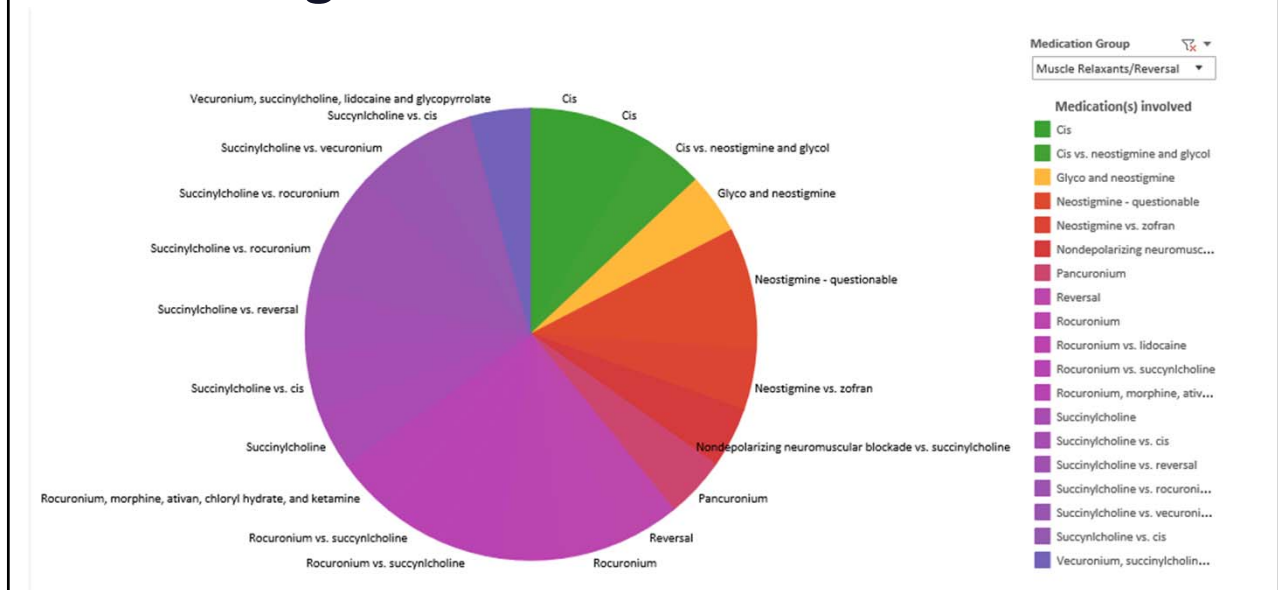
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Making Sense of Big Data

- Data stewardship
 - Development of universal EHR data concepts
 - Continuous assessments of data quality for accuracy and completeness
 - Transformation of data into clinically meaningful measures
 - Self-serve and intuitive access to EHR data
- Development of implementation science within anesthesiology to facilitate a community of engaged clinical providers

Shen B et al. *J Cardiothorac Vasc Anesth.* 2019 Nov 18. pii: S1053-0770(19)31159-0.

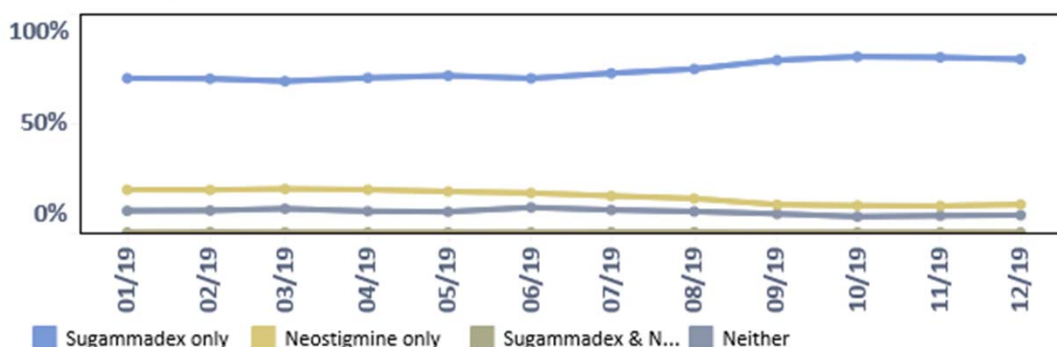
Tracking Where Errors Occur with NMBs



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Tracking the Use of Reversal Agents

Reversal Agent



Education from Quality Assurance Committee



- Links
- QA Committee Handbook
- QA Focus
- Quality Update
- Report A Safety Event★
- Quick-Reference
- QA Committee Member Spotlight
- Next QA Committee Meeting: TBD

The "QA focus" is a quarterly newsletter published by the QA staff which is meant to be a resource for all staff and providers of the UMHS department of Anesthesiology.

If you have feedback on an issue of the "QA focus" or if you have some suggestions for future content, please let us know anytime by contacting [Nathan Kirkpatrick](#), 734-615-4390.

Current Edition



Ask the Experts: Addressing Challenges Related to Reversal of Neuromuscular Blockade

Michigan Medicine Drug Utilization Evaluation

	Count of Cases by Train of Four (TOF) Value Before Reversal		
	Neostigmine 2016*	Neostigmine 2017**	Sugammadex 2017**
0 / 4	137	74	584
1 / 4	160	87	809
2 / 4	244	147	697
3 / 4	250	205	396
4 / 4	5502	4062	2933
Sustained Tetany	479	429	311
Blank	44	443	478
Total	6816	5447	6208

* Jan 2016 to Oct 2016

** Jan 2017 to Oct 2017

Sugammadex mg/kg per patient	# Cases
0.06 mg/kg - 1 mg/kg	9
1.01 mg/kg - 1.499 mg/kg	52
1.50 mg/kg - 1.749 mg/kg	151
1.75 mg/kg - 2.499 mg/kg	10340
2.501 mg/kg - 3 mg/kg	669
3.001 mg/kg - 3.49 mg/kg	303
3.50 mg/kg - 3.75 mg/kg	209
3.751 mg/kg - 4.499 mg/kg	2749
4.5 mg/kg - 5 mg/kg	236
5.01 mg/kg - 5.45 mg/kg	69
5.46 mg/kg - 5.99 mg/kg	48
6 mg/kg - 8 mg/kg	78
8.001 mg/kg - 10 mg/kg	20
10.001 mg/kg - 15 mg/kg	24
15.001 mg/kg - 17.02 mg/kg	34
Total	14991

* Based on a prior sugammadex analysis from 11/2016 through 2/28/2018

Standardizing the Dose

UM RX SUGAMMADEX ROUNDING

✓ Accept

- ☐ sugammadex (BRIDION) injection - weight <= 50 kg
100 mg, Intravenous, ONCE
- ☐ sugammadex (BRIDION) injection - weight 50 - 120 kg
200 mg, Intravenous, ONCE
- ☐ sugammadex (BRIDION) injection - weight > 120 kg
500 mg, Intravenous, ONCE

ⓘ Next Required

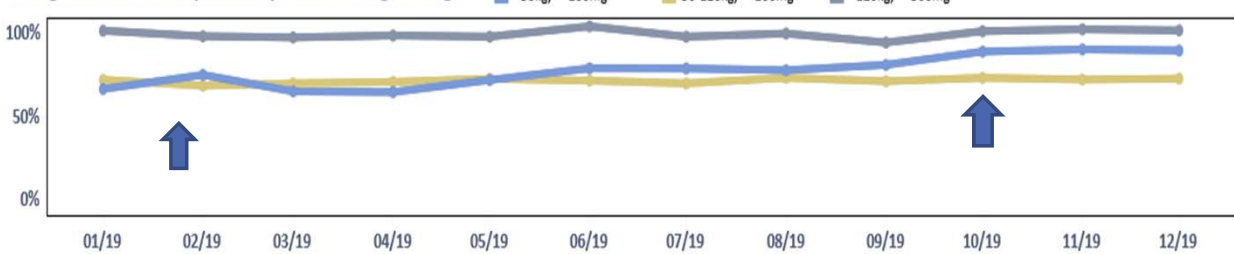
✓ Accept

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Effect of Dose Rounding

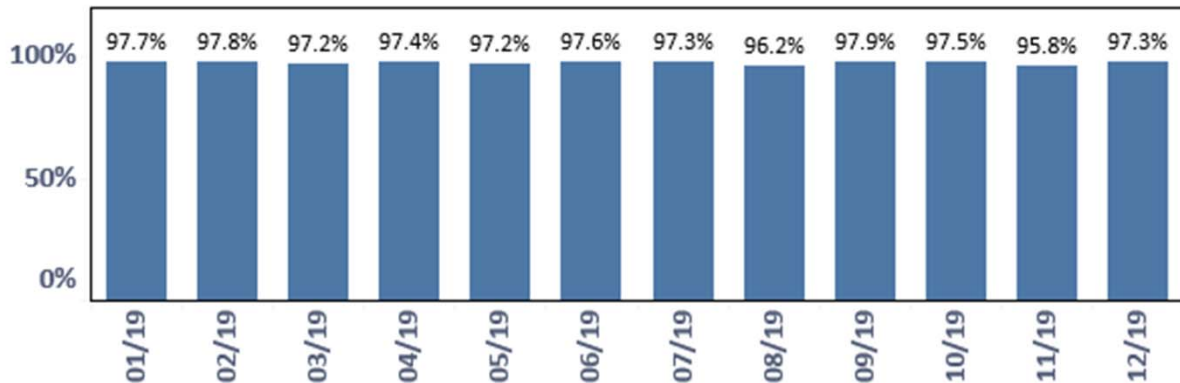
Sugammadex

Dosage Guideline Compliance by Patient Weight Range



Are we following our guidelines?

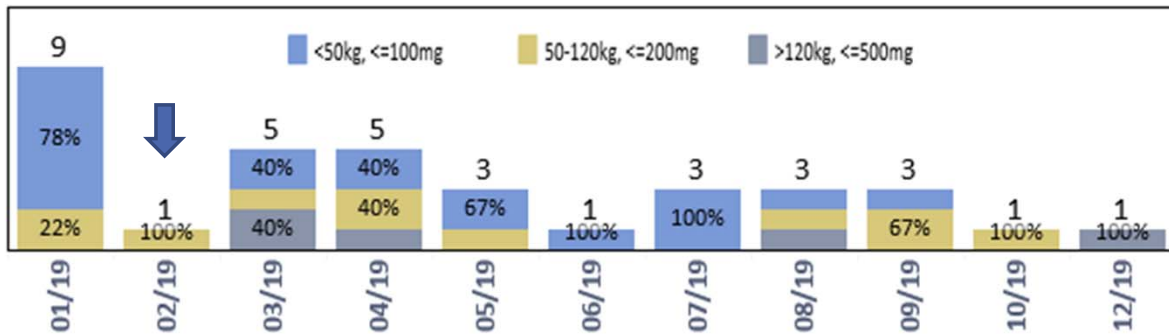
Documentation of High Risk Criteria for Sugammadex Use



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Change in Reintubation Rates Following Standardized Reversal Practices

Reintubations and Reversal Agents



How to Optimize Neostigmine Use

- Keep doses less than 50 mcg/kg
- Monitor train of four
- Ensure 2 twitches are present before reversal
- Use correct ratio of glycopyrrolate in combination
- Understand variability of response to both neuromuscular blockers and reversal agents

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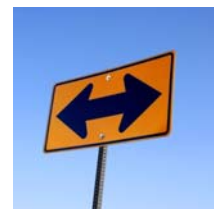
How to Optimize Sugammadex Use

- Create an algorithm
- Monitor train of four
- Review doses administered relative to
 - Weight
 - Neuromuscular blocker used
 - Provider
- Monitor high risk patients
- Review all high doses for appropriateness
- Avoid drift towards higher doses of neuromuscular blockers



Hospitals That Have Both Neostigmine and Sugammadex

- Choice of reversal agent
 - Neostigmine
 - Reversal at TOFc of 4 at the adductor pollicis
 - Optimize dosing and allow sufficient time to work
 - Sugammadex
 - Indicated for deeper levels of NMB at reversal – TOFc < 4
 - Prioritize for patients with limited physiologic reserves to handle postoperative complications



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Key Takeaways

- Use your Reflection Sheet as a guide!
- Engage your interprofessional team

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Rapid Sequence Intubation		
Team-Based Practice Model		

Consider these other practice changes – What will you do?

- a. Assess patients at high risk for PONV relative to reversal agents
- b. Examine high risk populations for complications of NMB
- c. Review access to reversal agents for moderate/deep block and rapid sequence induction
- d. Integrate a broad practice model in perioperative space for medication management

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