

Preparation for Premedication Recommendations for Premedication in Rapid Sequence Intubation

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Objectives

- Describe the physiological response to laryngoscopy and intubation
- Discuss the evidence for premedications in rapid sequence intubation (RSI)
- Select appropriate premedications in adult and pediatric patient cases



Reviewing RSI



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MAYO CLINIC

7 P's of RSI





Mace, SE. Emerg Med Clin N Am 2008. 24(4) Walls RM, et al. Manual of Emergency Airway Management. 3. Lipincott, Williams, and Wilkins; 2008 ©2017 MFMER | slide-5

Why do we premedicate? – RSRL

- Reflex sympathetic response to laryngoscopy (RSRL)
 - Mechanical stimulation of sympathetic and parasympathetic nerves within the airway



MAYO CLINIC

Self-Assessment Question #1

Which of the following describes the RSRL (reflex sympathetic response to laryngoscopy)?

- A. Decreased cough
- **B.** Decreased intraocular pressure
- C. Decreased laryngospasm
- **D.** Increased intracranial pressure



Pathophysiological response

Physiologic Variable	RSRL	
Intracranial pressure (ICP)	Increase (5 mmHg)	
Mean airway pressure	Increase	
Bronchospasm/Laryngospasm	Increase	
Mean arterial pressure (MAP)	Increase (20-25 mmHg)	
Heart rate (HR)	Increase/Decrease (30 BPM)	

Paralysis does not alter response



RSRL: reflex sympathetic response to laryngoscopy BPM: beats per minute

Pediatric Airways are Different

 Pediatrics have larger tongue/cavity ratio, longer epiglottis, higher and more anterior trachea, small mandible, narrower vocal cords





Kerrey BT, et al. *Ann Emerg Med* 2012; 60(3):251-9 Image: Basow DS (Ed), *UpToDate*, Waltham, MA 2013. Accessed January 11, 2017 ©2017 MFMER | slide-9

Physiologic Variable	Airway Pressure	Spasm	ICP	HR	MAP
RSRL Response	1	1	↑ (5 mm Hg)	↑↓ (30 BPM)	↑ (25 mm Hg)
Populations at Risk	Asthma COPD		Ocular Trauma Cranial Trauma	Myocardia Aortic dissecti Trauma/I Pedia	l ischemia on/aneurysm Bleeding atrics

Α	"Asthma"
В	"Brains and babies"
С	"Cardiac"

MAYO CLINIC MAP: mean arterial pressure ICP: intracranial pressure

Schofer, JM. Cal J Emerg Med 2006;7(4):75-9

"The difficult emergency airway is far more likely to be the result of challenging <u>physiology</u> than the result of challenging anatomy"

Dr. Sam Ghali, Emergency Medicine Physician

Can we alter the physiologic response with (pre)medications or is it a waste of time?



Premedications – "LOAD"

- No specific recommendations given on pharmacologic agents for RSI by EAST, ACEP
- Historical acronym ingrained in medical training

L	Lidocaine	1.5 – 2 mg/kg
0	Opioids (fentanyl)	2 – 5 mcg/kg
Α	Atropine	0.01 – 0.02 mg/kg
D	Defasciculating dose of NMB	10% of intubation dose

MAYO CLINIC MB: Non-depolarizing neuromuscular blocker

Mayglothling J, et al. *J Trauma Acute Care Surg* 2012. 73(5):333-340 ACEP, Clinical & Practice Management Policy. *Rapid Sequence Intubation, April* 2012. Schofer, JM. *Cal J Emerg Med* 2006;7(4):75-9

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<u>LOAD – Lidocaine</u>

Indications

- Prevention of bronchospasm/cough reflex
- Prevention of ICP elevation
- MOA: attenuation of sympathetic surge, reduction of cough reflex
- Mostly used in traumatic brain injury populations



Lidocaine in asthma?

- Many studies show IV lidocaine promotes bronchodilation
- Does IV lidocaine prevent bronchospasm after intubation?



Promotion of bronchodilation *≠* Prevention of bronchospasm



Maslow AD, et al. Anesthesiology 2000; 93:1198-1204

Intubation raises ICP?

 ICP increases during endotracheal intubation, suctioning in elective neurosurgical patients



Lidocaine and ICP

Design	Prospective, RCT
Question	Does lidocaine blunt ICP increases associated with endotracheal intubation?
Intervention	Lidocaine 1.5 mg/kg vs. placebo; 2 minutes prior to RSI
Population	20 patients w/ brain tumors, elective neurosurgical cases
Results	ICP increases seen with both, more modest increases with lidocaine than placebo -12.1 mm Hg; 95% CI [-22.8 – -1.4 mm Hg; p = 0.03]
Conclusion	Lidocaine 1.5 mg/kg given 2 minutes prior to intubation blunts intubation-related ICP elevations more significantly than placebo



Lidocaine dosing



QD

Yukioka H, et al. Anesth Analg 1985;64:1189-92

Is lidocaine safe?

Design	Retrospective Chart Review
Question	Is lidocaine before RSI associated with poor hemodynamic changes in severe TBI patients?
Population	101 patients w/ severe TBI 46 - Lidocaine 55 - No Lidocaine
Results	MAPs unchanged regardless of lidocaine administration
Conclusion	Lidocaine in RSI was not associated with significant hemodynamic changes in patients with severe TBI

However, Asfar et al. saw a \downarrow 30 mm Hg in MAP in patients who received 1mg/kg lidocaine vs. placebo



Lin CC, et al. Am J Emerg Med 2012; 30(9):1782-87 Asfar SN, et al. Acta Anaesthesiol Belg 1990;41:17-24 ©2017 MFMER | slide-18

Lidocaine in pediatrics

- Evidence extrapolated mostly from adults
- Recent systematic review concludes topical and IV lidocaine is effective for prevention of laryngospasm
 - All studies underpowered, performed in operating rooms, non-RSI
 - Safety remains unknown, controversial



Does it improve outcomes?

International practice variations: US > Europe

Can RSI increase ICP?	CONFIRMED
Can lidocaine attenuate ICP rise?	PLAUSIBLE
Is it safe?	PLAUSIBLE
Does it improve outcomes?	BUSTED
Use in pediatrics?	BUSTED

"<u>No evidence</u> in acute head injury that lidocaine before RSI reduces ICP or improves neurological outcomes"

> Silber SH, et al. *Am J Emerg Med* 1997;15:263–7 Butler J, et al. *Emerg Med J* 2001;18(5):343-8 Robinson N, et al. *Emerg Med J* 2001; 18:453-7 ©2017 MFMER | slide-20



Lidocaine Recommendations

- Poor external validity for RSI in ED populations
- May reduce ICP, no effect on long-term outcomes in acute trauma patients
- Avoid use in pediatrics
- If used, at least make sure you have correct dose:

"Lidocaine 1.5 – 2.0 mg/kg 1–5 minutes prior to RSI"



LOAD – Opioids (Fentanyl)

- Indications
 - Prevention of ICP elevation
 - Prevention of MAP increase
- MOA: attenuates sympathetic activation (pain) to laryngoscopy
- Mostly used in traumatic brain injury patients



Fentanyl effects on intubation

- Decreases cardiovascular effects associated with laryngoscopy
- Prevents release of norepinephrine



Dose finding study





Hosalli, V et al. J Clin Diagn Res 2014;8(9):1-3

Fentanyl dosing

- Pain: 1 mcg/kg
- Premedication for RSI
 - Young, healthy: 3-5 mcg/kg
 - Elderly: 1.5-3 mcg/kg
- Optimally given 3-4 minutes prior to intubation
- 1.5-3 mcg/kg 4 minutes prior to intubation effectively attenuates increases in BP, HR
- >5 mcg/kg: 11%45% incidence of hypotension (MAP < 70 mm Hg)

Hosalli, V et al. *J Clin Diagn Res* 2014;8(9):1-3 Iyer V, et al. *Anaesth Intens Care* 1988;16:411-7 Kovac, AL. *J Clin Anesth* 1996;8(1):63-69 Splinter W, et al. *Can J Anaesth* 1989;36: 3704 Chung F, et al. *Can J Anaesth* 1985;32:622-8

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How often do we use it?

Design	Retrospective Chart Review
Question	How often are neuroprotective agents used in the ED in RSI patients w/ neurological injury?
Population	RSI patients intubated for neurological indication (stroke, TBI)
Results	 77 patients RSI for neuro indication - 74% (57) had indication for neuroprotective premeds - Lidocaine: 84.2% - Fentanyl: 33.3%
Conclusion	Despite potential benefit, significant underutilization exists. Barriers include: lack of knowledge of fentanyl efficacy, concern for hypotension with high doses, and fear over intubation delays



Fentanyl Recommendations

 3-5 mcg/kg 3 minutes prior to intubation in patients:

Indications

With \uparrow ICP (TBI, meningitis, stroke)

With CAD or aortic dissection

Without hemodynamic instability (sepsis)

- Not recommended in children
- <u>Do not delay</u> intubation for fentanyl administration



Kuzak N, et al. Can J Emerg Med 2006;8(2):80-4

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Self-Assessment Question #2

34 year old male (100kg) presents with a severe TBI after a MVC; BP 82/44. Prior RSI, the provider asks for premedication. Which of the following is the correct recommendation for fentanyl in this patient?

- A. Avoid fentanyl
- B. Fentanyl 100 mcg; 3 minutes prior to RSI
- C. Fentanyl 300-500 mcg; simultaneous with paralytic
- D. Fentanyl 300-500 mcg; delay RSI so fentanyl can reach peak effect



LO<u>A</u>D – <u>A</u>tropine

- Indication
 - Reduces bronchial and salivary secretions
 - Increase in HR
- MOA: Non-selective, competitive antagonist of muscarinic receptors; increases HR by antagonizing acetylcholine in the sinoatrial node
- Vagal response most common in pediatrics



Stollings JL, et al. Ann Pharmacother 2014; 48(1):62-76



Atropine recommendations

0.01-0.02 mg/kg for <u>all pediatric</u> patients
Previously 0.1mg minimum dose, toxicity concerns in low-weight neonates (<5kg)

*Per SCCM:

Prior to intubation; critically ill neonates

- \leq 5 y.o w/ first succinylcholine dose
- > 5 y.o w/ multidose succinylcholine

Prior to intubation; septic shock

If given multidose succinylcholine



LOAD – Defasiculating NMB Dose

- Indication
 - Prevention of fasciculations, myalgias associated with depolarizing NMBs
 - Prevention of ICP elevation
- Depolarizing (SCh) vs. Non-depolarizing (Roc)





Stollings JL, et al. Ann Pharmacother 2014; 48(1):62-76 Images: pharmacology.blogspot.com ©2017 MFMER | slide-32

What do we know?

- 94% incidence of fasciculations from succinylcholine; 51% incidence of myalgias
- Defasciculating dose decreased myalgia at 24hr by 36-75%
- Its complicated, and serious adverse events occur
 - Voice changes, diplopia, potential med errors

10% dose of non-depolarizing NMB not recommended in any patient prior to depolarizing NMB in RSI



Schreiber JU, et al. Anesthesiology 2005;(103):877-84

Self-Assessment Question #3

Which of the following is an indication for atropine prior to intubation in pediatric patients?

- A. Septic Shock
- B. Prior to first dose of succinylcholine in a 12yo
- C. Ventricular tachycardia
- D. Prevention of ICP elevations with intubation



Conclusion

- RSI causes a RSRL; unknown if temporary hemodynamic changes influence outcomes
- Limited evidence for premedication in RSI; atropine and fentanyl look most promising
- Commit dosing to memory; quick recall may be required in emergent scenarios





Questions & Discussion roy.david@mayo.edu