Preparation for Premedication
Recommendations for Premedication in Rapid Sequence Intubation

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PGY2 Emergency Medicine Pharmacy Resident

Pharmacy Grand Rounds
January 17th, 2017
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
7 P’s of RSI

- Preparation
  - Pre-oxygenation
  - Premedication
  - Paralysis
  - Protection
  - Placement
  - Post-intubation

- 0 min
- -10 min -5 min -3 min +1 min +2 min

Mace, SE. *Emerg Med Clin N Am* 2008, 24(4)
Why do we premedicate? – RSRL

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

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
Pathophysiologica lresponse

<table>
<thead>
<tr>
<th>Physiologic Variable</th>
<th>RSRL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial pressure (ICP)</td>
<td>Increase (5 mmHg)</td>
</tr>
<tr>
<td>Mean airway pressure</td>
<td>Increase</td>
</tr>
<tr>
<td>Bronchospasm/Laryngospasm</td>
<td>Increase</td>
</tr>
<tr>
<td>Mean arterial pressure (MAP)</td>
<td>Increase (20-25 mmHg)</td>
</tr>
<tr>
<td>Heart rate (HR)</td>
<td>Increase/Decrease (30 BPM)</td>
</tr>
</tbody>
</table>

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

Image: Basow DS (Ed), UpToDate, Waltham, MA 2013. Accessed January 11, 2017
<table>
<thead>
<tr>
<th>Physiologic Variable</th>
<th>Airway Pressure</th>
<th>Spasm</th>
<th>ICP</th>
<th>HR</th>
<th>MAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSRL Response</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Populations at Risk</td>
<td>Asthma COPD</td>
<td>Ocular Trauma Cranial Trauma</td>
<td>Myocardial ischemia Aortic dissection/aneurysm Trauma/Bleeding Pediatrics</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **A** “Asthma”
- **B** “Brains and babies”
- **C** “Cardiac”

**Physiologic Variables:**
- **Airway Pressure:** Increase
- **Spasm:** Increase
- **ICP:** Increase (5 mm Hg)
- **HR:** Decrease/Increase (30 BPM)
- **MAP:** Increase (25 mm Hg)

**Populations at Risk:**
- Asthma
- COPD
- Ocular Trauma Cranial Trauma
- Myocardial ischemia
- Aortic dissection/aneurysm
- Trauma/Bleeding Pediatrics

**Abbreviations:**
- HR: Heart rate
- MAP: Mean arterial pressure
- ICP: Intracranial pressure

“The difficult emergency airway is far more likely to be the result of challenging physiology 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 |
| O | Opioids (fentanyl) | 2 – 5 mcg/kg |
| A | Atropine | 0.01 – 0.02 mg/kg |
| D | Defasciculating dose of NMB | 10% of intubation dose |

LOAD – Lidocaine

- 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

Intubation raises ICP?

- ICP increases during endotracheal intubation, suctioning in elective neurosurgical patients

![Graph showing ICP changes during laryngoscopy and intubation with lidocaine question.]

Bedford, RF. *Probl Anesth* 1988. 2(201)
## Lidocaine and ICP

<table>
<thead>
<tr>
<th>Design</th>
<th>Prospective, RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question</td>
<td>Does lidocaine blunt ICP increases associated with endotracheal intubation?</td>
</tr>
<tr>
<td>Intervention</td>
<td>Lidocaine 1.5 mg/kg vs. placebo; 2 minutes prior to RSI</td>
</tr>
<tr>
<td>Population</td>
<td>20 patients w/ brain tumors, elective neurosurgical cases</td>
</tr>
<tr>
<td>Results</td>
<td>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]</td>
</tr>
<tr>
<td>Conclusion</td>
<td>Lidocaine 1.5 mg/kg given 2 minutes prior to intubation blunts intubation-related ICP elevations more significantly than placebo</td>
</tr>
</tbody>
</table>

Bedford, RF. *Probl Anesth* 1988. 2(201)
Lidocaine dosing

**What dose?**

- Coughing (%)
  - Lidocaine dose (mg/kg)
    - 0.5: 70%
    - 1.0: 60%
    - 1.5: 20%
    - 2.0: 0%

**When to give it?**

- Coughing (%)
  - Time after lidocaine (2mg/kg) administration, minutes
    - 1: 13%
    - 3: 13%
    - 5: 13%
    - 7: 20%
    - 10: 40%
    - 15: 67%

Is lidocaine safe?

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

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

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

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can RSI increase ICP?</td>
<td>CONFIRMED</td>
</tr>
<tr>
<td>Can lidocaine attenuate ICP rise?</td>
<td>PLAUSIBLE</td>
</tr>
<tr>
<td>Is it safe?</td>
<td>PLAUSIBLE</td>
</tr>
<tr>
<td>Does it improve outcomes?</td>
<td>BUSTED</td>
</tr>
<tr>
<td>Use in pediatrics?</td>
<td>BUSTED</td>
</tr>
</tbody>
</table>

“No evidence in acute head injury that lidocaine before RSI reduces ICP or improves neurological outcomes”

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”

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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

HR

MAP

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)

### How often do we use it?

<table>
<thead>
<tr>
<th>Design</th>
<th>Retrospective Chart Review</th>
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</thead>
<tbody>
<tr>
<td><strong>Question</strong></td>
<td>How often are neuroprotective agents used in the ED in RSI patients w/ neurological injury?</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>RSI patients intubated for neurological indication (stroke, TBI)</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>77 patients RSI for neuro indication</td>
</tr>
<tr>
<td></td>
<td>- 74% (57) had indication for neuroprotective premeds</td>
</tr>
<tr>
<td></td>
<td>- Lidocaine: 84.2%</td>
</tr>
<tr>
<td></td>
<td>- Fentanyl: 33.3%</td>
</tr>
<tr>
<td><strong>Conclusion</strong></td>
<td>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</td>
</tr>
</tbody>
</table>

Fentanyl Recommendations

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

<table>
<thead>
<tr>
<th>Indications</th>
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<tbody>
<tr>
<td>With ↑ ICP (TBI, meningitis, stroke)</td>
</tr>
<tr>
<td>With CAD or aortic dissection</td>
</tr>
<tr>
<td><strong>Without</strong> hemodynamic instability (sepsis)</td>
</tr>
</tbody>
</table>

- Not recommended in children
- **Do not delay** intubation for fentanyl administration

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
LOAD – Atropine

- 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

Clinical studies have focused on HR variation, not progression from stable to unstable bradycardia.
Atropine recommendations

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

<table>
<thead>
<tr>
<th><em>Per SCCM:</em></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to intubation; critically ill neonates</td>
<td></td>
</tr>
<tr>
<td>≤ 5 y.o w/ first succinylcholine dose</td>
<td></td>
</tr>
<tr>
<td>&gt; 5 y.o w/ multidose succinylcholine</td>
<td></td>
</tr>
<tr>
<td>Prior to intubation; septic shock</td>
<td></td>
</tr>
<tr>
<td>If given multidose succinylcholine</td>
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</tbody>
</table>


SCCM: Society of Critical Care Medicine
LOAD – Defasiculating NMB Dose

• Indication
  • Prevention of fasciculations, myalgias associated with depolarizing NMBs
  • Prevention of ICP elevation

• Depolarizing (SCh) vs. Non-depolarizing (Roc)

Images: pharmacology.blogspot.com
What do we know?

- 94% incidence of fasciculations from succinylcholine; 51% incidence of myalgias
- Defasciculating dose decreased myalgia at 24 hr by 36-75%
- It's 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

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