**Introduction**

Rapid sequence intubation (RSI) is an essential procedure in emergency and critical care medicine for securing a definitive airway in unstable patients who are at risk for aspiration. It involves the rapid administration of sedative and paralytic medications to facilitate endotracheal intubation under controlled conditions.

The origins of RSI date back to 1961 when Dr. Brian Sellick first described the use of cricoid pressure during induction to minimize the risk of aspiration. Over the decades, RSI techniques evolved to incorporate pre-treatment agents, induction agents, and neuromuscular blockers to streamline the intubation process. Today, RSI is a core competency for emergency medicine physicians, intensivists, and anesthesia providers managing critically ill patients.

RSI holds particular importance in emergency medicine given the uncontrolled environments and high-acuity settings. Providers must act swiftly to secure airways in patients with acute respiratory failure, traumatic injuries, and other immediately life-threatening conditions. Expertise in RSI pharmacotherapy enables clinicians to induce rapid sedation, maintain hemodynamic stability, prevent aspiration, and create optimal intubating conditions.

**Understanding Rapid Sequence Intubation**

RSI involves the sequential administration of potent induction agents and neuromuscular blocking agents to rapidly secure a definitive airway while mitigating the risk of aspiration. It is defined by 3 critical steps performed in succession:

Pre-oxygenation with cricoid pressure

Administration of sedative-hypnotic and paralytic medications

Immediate laryngoscopy and intubation without ventilatory assistance

This is in contrast to standard intubation, where providers deliver ventilatory support between induction and intubation. The key differentiator is that RSI does not involve bag mask ventilation, which could inadvertently fill the stomach with air and increase the aspiration risk.

The "7 P's" provide a useful framework for conceptualizing RSI:

Preparation: Assemble equipment, assign roles, identify difficult airway characteristics

Preoxygenation: Denitrogenate lungs with 100% O2 for 3-5 minutes

Pretreatment: Administer lidocaine, opioids, vasopressors, atropine per clinical judgment

Paralysis: Give sedative-hypnotic and neuromuscular blocker for rapid sequence induction

Protection: Apply cricoid pressure to occlude esophagus

Pass the tube: Laryngoscopy and intubation immediately after fasciculations cease

Post intubation care: Confirm tube placement, secure airway, initiate mechanical ventilation

RSI is indicated when there is an immediate threat to the airway or a high risk of aspiration from gastric contents. This encompasses patients across the emergency medicine and critical care spectrum, including trauma, seizures, drug overdose, shock, sepsis, substance withdrawal, and primary respiratory drive depression.

**Indications for Intubation**

There are several key indications that warrant rapid sequence intubation:

* Failure to Oxygenate or Ventilate
  + Inability to maintain oxygen saturation >90% with supplemental oxygen or inadequate ventilation resulting in respiratory acidosis are leading indications to secure a definitive airway. This includes conditions like acute respiratory distress syndrome, severe pulmonary edema, airway burns, and status asthmaticus.

* Protection Against Aspiration
  + Patients who have not been fasted or have a pathologically full stomach are at risk for aspiration during intubation. This includes trauma patients, obstetric patients, bowel obstruction, alcohol intoxication, seizures, and advanced dementia. RSI allows intubation without positive pressure ventilation, which can push gastric contents into the airway.

* Emergent Procedures
  + RSI may be required to enable emergent procedures like neurosurgery, cesarean section, or damage control laparotomy. The controlled induction conditions protect the patient during the procedure.

**Case Study on RSI Indications**

* A 65-year-old male presents after a high-speed MVC. On evaluation, he has diffuse abdominal tenderness and an obvious degloved scalp laceration. Vital signs are blood pressure 78/40 mm Hg, heart rate 118 bpm, respiratory rate 28 breaths/min, and oxygen saturation 92% on non-rebreather mask. Focused assessment reveals muffled heart sounds, absent bowel sounds, and crepitus over the chest. Surgery is urgently preparing for a trauma laparotomy. However, the patient's mental status is rapidly declining and shock is worsening. To protect the airway from aspiration and enable urgent surgery, the decision is made to perform rapid sequence intubation. Cricoid pressure is applied and intravenous induction agents are administered for rapid anesthetization and neuromuscular blockade. The trachea is intubated without intermittent positive pressure ventilation to prevent insufflation of air into the stomach.

**Pharmacotherapy**

A variety of pharmacologic agents may be utilized in the rapid sequence intubation procedure, each with unique therapeutic considerations:

**Pre-Treatment Medications**

* Atropine: Blocks vagal response to intubation (0.02 mg/kg IV)
* Lidocaine: Blunts increase in intracranial pressure (1.5 mg/kg IV)
* Fentanyl: Lessens sympathetic response to intubation (1-3 mcg/kg IV)
* Midazolam: Provides anxiolysis before intubation (0.05-0.1 mg/kg IV)

The benefit of these agents is controversial and they are infrequently used in modern RSI protocols given lack of proven impact on patient-oriented outcomes. However, judicious use based on clinical context may be reasonable.

**Induction Agents**

Propofol

* Dose: 1-2 mg/kg IV
* Ultra-short acting GABA agonist that provides rapid anesthesia
* Decreases cerebral oxygen consumption and intracranial pressure. In a study of 6 patients with head injuries, propofol decreased ICP by an average of 14 mm Hg.
* Hepatically metabolized to inactive glucuronides

Etomidate

* Dose: 0.3 mg/kg IV
* Imidazole-derivative that provides hemodynamic stability
* Minimally effects intracranial pressure and bronchial smooth muscle
* Primarily metabolized by ester hydrolysis in the liver and blood

Ketamine

* Dose: 1-2 mg/kg IV
* Dissociative anesthetic with analgesia and amnesia properties
* Causes sympathomimetic effects like hypertension and tachycardia
* Preserved respiratory drive unlike other induction agents
* Hepatically metabolized to active metabolite norketamine

Methohexital

* Dose: 1-1.5 mg/kg IV
* Ultra-short acting barbiturate with rapid onset of action
* Decreases cerebral oxygen consumption and intracranial pressure
* Dose-related myocardial depression and venodilation
* No active metabolites following hepatic metabolism

Midazolam

* Dose: 0.2-0.3 mg/kg IV
* Short-acting benzodiazepine that provides sedation and amnesia
* Hemodynamic effects include dose-related hypotension and bradycardia
* Delayed onset compared to other induction agents
* Hepatic hydroxylation to active metabolite 1-hydroxymidazolam

Choice of agent depends on clinical context such as hemodynamic status, intracranial pressure concerns, bronchospasm risk, and pregnancy status.

**Paralytic Agents**

Succinylcholine

* Dose: 1-1.5 mg/kg IV
* Depolarizing neuromuscular blocker with 30-45 second duration
* Duration of 3-6 minutes
* Rapid onset of action facilitating excellent intubating conditions
* Avoid in renal failure, neuromuscular disorders, burns, and trauma
* Metabolized by plasma cholinesterase; no active metabolites

Rocuronium

* Dose: 0.6-1.2 mg/kg IV
* Non-depolarizing neuromuscular blocker with onset in 1-2 minutes
* Duration of action 30-60 minutes (Some studies reporting up to 4 hours with dosing > 1mg/kg)
* Slower onset than succinylcholine with dosing < 1mg/kg, but fewer contraindications
* Dosing >1 mg/kg has similar onset( ~40 seconds) to succinylcholine
* Ideal for patients with hyperkalemia or neuromuscular disorders
* Hepatic metabolism and renal excretion of inactive metabolites

Vecuronium

* Dose: 0.08-0.10 mg/kg IV
* Non-depolarizing neuromuscular blocker with slower onset
* Intermediate duration of action 20-40 minutes
* Avoid in myasthenia gravis due to exaggerated neuromuscular blockade
* Undergoes hepatic metabolism and biliary excretion

Succinylcholine is preferred for most RSI due to its rapid onset. However, rocuronium is acceptable and vecuronium is a third-line option when optimal agents are unavailable.

**Special Populations**

RSI requires special considerations in certain patient populations:

Pediatric Patients

* Use simplified weight-based dosing for induction agents and neuromuscular blockers
* Atropine pre-treatment often included due to vagal tone

Renal/Hepatic Impairment

* Avoid succinylcholine in renal failure due to hyperkalemia risk
* Reduce dose of renally eliminated drugs like rocuronium
* Increase induction dose interval in hepatic dysfunction

Pregnancy

* Propofol preferred induction agent due to safety profile
* Succinylcholine crosses the placenta rapidly

Obesity

* Use ideal or adjusted body weight to calculate induction doses
* Morbid obesity associated with reduced respiratory reserve

Neuromuscular Disorders

* Avoid succinylcholine in myasthenia gravis or denervating disorders
* Titrate non-depolarizing neuromuscular blockers carefully

**Key Evidence**

**Induction Agents**

A randomized controlled trial by Jabre et al. compared etomidate (n=328) to ketamine (n=327) for rapid sequence intubation in the emergency department. No difference was found in intubating conditions between the groups (median intubation difficulty score 1 [IQR 0-3] in both groups; p=0.70). However, adrenal insufficiency was significantly higher with etomidate (OR 6.7, 95% CI 3.5-12.7).

In a randomized controlled trial, Smischney et al. compared propofol (n=42) to ketofol (n=42) for induction during rapid sequence intubation. Propofol was more likely to cause a 20% reduction in systolic blood pressure than ketofol (48.8% vs 12%, p<0.001).

**Paralytics**

A multicenter randomized controlled trial by Marsch et al. compared succinylcholine (n=198) to rocuronium (n=203) for rapid sequence intubation in the ICU. No difference was found in oxygen desaturations between the groups (p=0.67).

A randomized controlled trial by Magorian et al. compared the onset times of rocuronium 0.6 mg/kg, rocuronium 0.9-1.2 mg/kg, vecuronium 0.1 mg/kg, and succinylcholine 1 mg/kg during rapid sequence induction. The onset times of rocuronium 0.9-1.2 mg/kg and succinylcholine were similar, while rocuronium 0.6 mg/kg and vecuronium had longer onset times.

**Clinical Scenarios**

A 68-year-old male with a history of coronary artery disease arrives in the emergency department with respiratory distress. He is tachypneic, using accessory muscles, and oxygen saturations are 85% on room air. Furosemide 40 mg IV is given without improvement. The decision is made to perform RSI using etomidate for induction given its neutral hemodynamic profile. Rocuronium 1 mg/kg is administered for neuromuscular blockade. Cricoid pressure is applied and the trachea is intubated just as fasciculations cease.

* This case highlights the importance of choosing an induction agent with minimal cardiac effects in patients with ischemic heart disease. The rapid onset neuromuscular blockade provided by rocuronium facilitated first pass intubation success.

Paramedics bring in a 35-year-old female who was found down after a suspected heroin overdose. She has pinpoint pupils and respiratory rate of 5 breaths/minute. 0.4 mg naloxone is administered IV without improvement in mental status or respiratory drive. Her oxygen saturation is 78% so the decision is made to perform rapid sequence intubation. Given her unknown substance use, ketamine is selected for induction. Succinylcholine 1.5 mg/kg IV is administered for neuromuscular blockade. Cricoid pressure is applied and the trachea is intubated once fasciculations have ceased.

* This case highlights the advantages of ketamine for induction in undifferentiated respiratory depression. Ketamine maintains respiratory drive and airway reflexes, while providing analgesia and sedation. Succinylcholine was the paralytic of choice given the rapid onset necessary in this critical hypoxic patient.

**Tips for Board Exam Questions**

When answering questions on RSI:

* Match the induction agent to the patient's hemodynamic status
* Avoid positive pressure ventilation between induction and intubation
* Confirm dosage ranges for pediatric patients are weight-based
* Monitor for post-intubation hypotension and treat accordingly

**Summary**

In summary, the key concepts for RSI pharmacotherapy include:

* RSI involves timed administration of sedative-hypnotic and neuromuscular blocking agents without positive pressure ventilation
* Clinical context including aspiration risk, respiratory failure, and hemodynamic status guide RSI use
* Propofol, etomidate, ketamine and methohexital allow rapid anesthetization based on clinical needs
* Succinylcholine provides the fastest neuromuscular blockade, while rocuronium is an acceptable alternative
* Avoid bag mask ventilation between induction and intubation to prevent insufflation of air
* individualize pharmacotherapy based on patient factors and adjust dosing in special populations

Expertise in RSI pharmacology enables clinicians to secure airways safely and effectively across emergency medicine and critical care settings. Ongoing application of evidence-based principles and practice guidelines ensures optimal patient outcomes.

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