Challenges and Advances in Intubation: Rapid Sequence Intubation

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DEFINITION/OVERVIEW

Rapid sequence intubation (RSI) is a process whereby pharmacologic agents, specifically a sedative (eg, induction agent) and a neuromuscular blocking agent are administered in rapid succession to facilitate endotracheal intubation.1

RSI in the emergency department (ED) usually is conducted under less than optimal conditions and should be differentiated from rapid sequence induction (also often abbreviated RSI) as practiced by anesthesiologists in a more controlled environment in the operating room to induce anesthesia in patients requiring intubation.2–6 RSI used to secure a definitive airway in the ED frequently involves uncooperative, nonfasted, unstable, critically ill patients. In anesthesia, the goal of rapid sequence induction is to induce anesthesia while using a rapid sequence approach to decrease the possibility of aspiration. With emergency RSI, the goal is to facilitate intubation with the additional benefit of decreasing the risk of aspiration.

Although there are no randomized, controlled trials documenting the benefits of RSI,7 and there is controversy regarding various steps in RSI in adult and pediatric patients,8–13 RSI has become standard of care in emergency medicine airway management14–17 and has been advocated in the airway management of intensive care unit or critically ill patients.18 RSI has also been used in the prehospital care setting.14,19,20

KEYWORDS

• Intubation • Rapid sequence intubation • Endotracheal intubation

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although the results have been mixed, especially in trauma patients (most notably in traumatic brain injury patients), such that an expert panel found that “the existing literature regarding paramedic RSI was inconclusive.” Furthermore, training and experience “affect performance” and that a successful “paramedic RSI program is dependent on particular emergency medical services (EMS) and trauma system characteristics.”

ADVANTAGES AND DISADVANTAGES OF RAPID SEQUENCE INTUBATION

The purpose of RSI is to make emergent intubation easier and safer, thereby increasing the success rate of intubation and decreasing the complications of intubation. The rationale behind RSI is to prevent aspiration and its potential problems, including aspiration pneumonia, and to counteract the increase in systemic arterial blood pressure, heart rate, plasma catecholamine release, intracranial pressure (ICP), and intraocular pressure (IOP) that occurs with endotracheal intubation. Blunting the rise in ICP may be critical in patients with impaired cerebral autoregulation from central nervous system illness/injury. Similarly, avoiding an increase in IOP may be desirable in the patient with glaucoma or an acute eye injury. RSI eliminates the normal protective airway reflexes (such as coughing, gagging, increased secretions, and laryngospasm) that can make intubation more difficult. Use of RSI may limit cervical spine movement, thus, allowing for better control of the cervical spine during intubation with less potential for injury. RSI decreases the trauma to the airway that occurs with intubation. RSI should also decrease or eliminate the discomfort that occurs with intubation and the patient’s recall of the intubation.

Disadvantages of RSI are (1) the potential for side effects or complications related to the drugs administered for RSI, (2) prolonged intubation leading to hypoxia, and (3) “emergent” or a “crash” airway resulting in a cricothyroidotomy or other “emergent” airway procedure.

RAPID SEQUENCE INTUBATION: THE PROCEDURE

RSI generally consists of seven steps: (1) preparation, (2) preoxygenation, (3) pretreatment, (4) paralysis with induction, (5) protection and positioning, (6) placement of the tube in the trachea, and (7) postintubation management. These seven steps can be modified when appropriate to fit the clinical situation. The mnemonic “SOAPME” is one way to remember the essential equipment needed for intubation: Suction, Oxygen, Airway, Pharmacology, Monitoring, Equipment. For the airway, include the ET tubes, laryngoscopes, blades, stylets, and BVM. For pharmacology, select, draw up, and label the appropriate medications (sedative, neuromuscular blocker, ancillary drugs) based on the history, physical
examination, and equipment available. Monitoring should include pulse oximetry and cardiac monitoring at a minimum; also preferably with capnography.\textsuperscript{24}

Assembling adequate personnel needed to assist in the procedure and assigning their roles is also a key component of the preparation phase. Patient assessment should be done at this time. A focused history and physical examination should be done to identify any condition, illnesses, or injuries that may negatively affect airway procedures/manipulations, medication administration, BVM ventilation, intubation, RSI, or rescue airway procedures.

The preparation step is used to “MAP” (Monitor, Assemble, Patient assessment) out a treatment plan for intubation using RSI and a backup contingency plan in case of a failed intubation (can’t ventilate, can’t intubate scenario).\textsuperscript{25}

**Step 2—Preoxygenation**

Preoxygenation should be occurring during the preparation step. The purpose of pre-oxygenation is to replace the nitrogen in the patient’s functional residual capacity (FRC) with oxygen or “nitrogen wash-out oxygen wash-in.” “Denitrogenation” can be accomplished in 3 to 5 minutes by having the patient breathe 100% oxygen via a tight-fitting facemask or, if time is an issue, with four vital capacity breaths. Depending on circumstances, as long a period of preoxygenation as possible, (up to 5 minutes) should be administered. Ideally, positive pressure ventilation should be avoided during the preoxygenation step because of a risk for gastric insufflation and possible regurgitation. Because effective ventilation by the patient is not feasible in many ED patients, BVM ventilation may be necessary in apneic patients or patients with ineffective spontaneous breathing. In these instances, use of the Sellick procedure with gentle cricoid pressure should be applied in an attempt to limit gastric distention and avoid aspiration during BVM ventilation.

In the preoxygenation phase, replacing the nitrogen reservoir in the lungs with oxygen allows 3 to 5 minutes of apnea without significant hypoxemia in the normoxic adult.\textsuperscript{26} One caveat to remember is that certain patients have a lesser FRC (eg, infants and children and patients with an elevated diaphragm, specifically obese adults or pregnant patients). These patients will become hypoxic in a shorter time, eg, a normal child or an obese adult may start to desaturate within 2 minutes, while a normal adult may tolerate up to 5 minutes of apnea before they become significantly hypoxic.\textsuperscript{26}

**Step 3—Pretreatment**

Ancillary medications are administered during the pretreatment step to mitigate the negative physiologic responses to intubation. For maximal efficacy, the pretreatment drugs should precede the induction agent by 3 minutes, although this is not always possible. The pretreatment phase and preoxygenation phase can (and usually) do occur simultaneously during most instances of RSI in the ED. Medications and their usual dosages that may be given during the pretreatment phase are lidocaine 1.5 mg/kg, fentanyl 2–3 mcg/kg, and atropine 0.02 mg/kg (minimum 0.1 mg, maximum 0.5 mg). The clinical indications for these drugs are (1) for patients with elevated ICP and impaired autoregulation: administer lidocaine and fentanyl, (2) patients with major vessel dissection or rupture or those with significant ischemic heart disease give fentanyl, (3) adults with significant reactive airway disease, premedicate with lidocaine, and (4) atropine is indicated for pediatric patients \( \leq 10 \) years old and in patients with significant bradycardia if succinylcholine is given. One caveat to remember is to give fentanyl with caution to any patient in shock (whether compensated or uncompensated) who is dependent on sympathetic drive because of a potential decrease in blood pressure with fentanyl administration.
In patients who are receiving succinylcholine as their induction agent and who are at risk for increased ICP, one tenth of the normal paralyzing dose of a nondepolarizing (ND) neuromuscular blocking agent (NMB) can be given 3 minutes before receiving succinylcholine. The purpose of the defasciculating dose of the ND-NMB is to prevent the fasciculations (and therefore, the increase in ICP) that occurs with succinylcholine. For example, the dose would be 10% of the paralyzing dose of rocuronium (10% of 0.6 mg/kg = 0.06 mg/kg). The mnemonic “LOAD” has been used to indicate the pretreatment drugs for RSI: L = lidocaine, O = opioid (specifically, fentanyl), A = atropine, and D = defasciculation.27

**Step 4—Paralysis with Induction**

Paralysis with induction is achieved by the rapid intravenous administration in quick succession of the induction agent and the NMB. The selection of a specific sedative depends on multiple factors: the clinical scenario, which includes patient factors (includes cardiorespiratory and neurologic status, allergies, comorbidity) and the clinician’s experience/training and institutional factors, as well as the characteristics of the sedative.28 Sedatives commonly used for induction during RSI are barbiturates (pentobarbital, thiopental, and methohexitol),29 opioids (fentanyl),1 dissociative anesthetics (ketamine),30 and nonbarbiturate sedatives (etomidate,31 propofol,32 and the benzodiazepines).21,33 The dosages and characteristics of these agents and are summarized in Table 1. One caveat to remember is that the induction dosages of these sedatives may be different (generally, slightly higher) than the dose used for sedation. For example, for etomidate the usual dose for procedural sedation is 0.2 mg/kg and for RSI is 0.3 mg/kg.31

**Step 5—Protection and Positioning**

Positioning of the head and neck is essential to achieve the best view of the glottic opening for conventional laryngoscopy by aligning the three axes: oral, pharyngeal, and laryngeal. This is achieved by extension and elevation of the neck to obtain the “sniffing the morning air” or the “sipping English tea” position, assuming there are no contraindications such as known or potential cervical spine injury.1

Protection refers to the use of maneuvers to prevent regurgitation of gastric contents with possible aspiration. This is achieved via the Sellick maneuver, which is the application of firm pressure on the cricoid cartilage to avoid passive regurgitation of gastric contents. The correct performance of the Sellick maneuver involves the use of the thumb and index or middle finger to apply firm downward pressure on the cricoid cartilage anteroposteriorly.

Several caveats regarding the proper technique need to be considered: location, timing, and amount of pressure. Cricoid pressure should be applied as soon as the patient starts to lose consciousness and should be maintained until the correct endotracheal position is verified. Pressure should be gentle but firm enough to compress the esophagus between the cricoid cartilage and the anterior surface of the vertebral body. The cricoid cartilage is opposite the C4–C5 vertebrae in an adult, and C3–C4 in an infant. Common mistakes include premature release of cricoid pressure, which puts the patient at risk for aspiration, especially if accidental esophageal intubation occurred; misplaced position (avoid applying pressure over the thyroid cartilage or entire larynx which may impede passage of the tube); and incorrect amount of cricoid pressure. The applied pressure should be graded and inversely related to the size of the patient with less force in smaller patients. One recommendation in smaller patients is placing the other hand under the neck to avoid changing the neck position while applying cricoid pressure (with the opposite hand), to avoid malpositioning the neck. This
is assuming there are no contraindications such as cervical spine injury. Should vomiting occur, cricoid pressure should be released immediately because of possible esophageal rupture, although there are no data to substantiate this possible complication, and neuromuscular blockade eliminates the possibility of active vomiting.

**Step 6—Placement of the Endotracheal Tube in the Trachea**

When the jaw becomes flaccid from the paralytics, it is time to begin intubation by standard methods. ET tube placement should be confirmed by the usual techniques.

**Step 7—Postintubation Management**

After ET tube placement and confirmation, the ET tube must be secured. A chest radiograph is done not only to check for proper ET tube placement but also to evaluate the pulmonary status and to monitor for any complications of the intubation and RSI. Continued sedation and analgesia, sometimes with paralysis as well as cardiopulmonary monitoring, is indicated as long as the patient requires advanced airway support.

**PHARMACOLOGY: SEDATIVE AGENTS FOR RAPID SEQUENCE INTUBATION**

According to the National Emergency Airway Registry (NEAR) study, the most frequently used induction agents were etomidate (69%), midazolam (16%), fentanyl (6%), and ketamine (3%).\(^3\)\(^4\) Considering just pediatric patients using the NEAR registry,\(^6\) etomidate was the most commonly used induction agent but was used in less than half the patients (only 42% compared with 69% for all patients),\(^3\)\(^4\) followed by thiopental (22%), midazolam (18%), and ketamine (7%).\(^6\)

**Etomidate**

Etomidate, the most commonly used sedative for RSI in adults, can also be administered for pediatric RSI.\(^3\)\(^1\) The usual dose is 0.3 mg/kg or 20 mg in a 70-kg adult. It often is used in trauma patients with known or potential bleeding, hypovolemic patients, and patients with limited cardiac reserve, because it does not have significant cardiovascular effects. Etomidate also decreases ICP and the cerebral metabolic rate, which suggests that it may have a neuroprotective effect. These features are why some clinicians consider it the sedative of choice in a patient who has multiple trauma with both a head injury and hemorrhage or shock.

Etomidate does inhibit 11-β-hydroxylase, an enzyme necessary for adrenal steroid production.\(^3\)\(^5\) Transient adrenal suppression has been noted after a single dose of etomidate, although this is probably not clinically significant.\(^3\)\(^6\) Some data indicate that etomidate has a negative impact on patient outcome in critically ill patients with sepsis and septic shock.\(^3\)\(^7\)–\(^3\)\(^9\) This has led to the suggestion that a corticosteroid be coadministered when etomidate is given for RSI.\(^3\)\(^8\) Although either dexamethasone (0.1 mg/kg) or hydrocortisone (1–2 mg/kg) may be given, dexamethasone often is chosen because it does not interfere with the adrenocorticotropic hormone (ACTH) stimulation test, which may be needed to later test for adrenal insufficiency. In any case, infusions of etomidate for continued postintubation sedation are contraindicated.\(^3\)\(^9\)

Myoclonus is another side effect of etomidate that may interfere with intubation if a paralytic is not used,\(^4\)\(^0\) although this is not the situation with RSI in which a sedative and paralytic generally are coadministered in quick succession.

**Barbiturates**

Thiopental is the most commonly used barbiturate for pediatric RSI\(^6\) and may be the most commonly used barbiturate for anesthesia induction.\(^4\)\(^1\) However, it used is less
<table>
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<tr>
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<th>Precautions, Contraindication</th>
<th>Reversal Agent</th>
<th>Comment</th>
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<tr>
<td>Etomidate</td>
<td>0.3 (usual 70 kg Adult dose = 100 mg)</td>
<td>Induction agent (sedative). Often used in hypovolemic, hemorrhagic patients, and in trauma patients, especially if head injury and hemorrhage</td>
<td>Can cause myoclonic movements</td>
<td>Adrenal insufficiency. Use with caution if in septic shock and sepsis and consider giving corticosteroid</td>
<td>-</td>
<td>Myoclonic movements may make intubation difficult if NMB not given</td>
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<tr>
<td>Barbiturates, Thiopental</td>
<td>3–4</td>
<td>Induction agent (sedative). Used in patients with ↑ ICP if hemodynamically stable</td>
<td>Negative CV effects. Use low doses cautiously if CV disease, shock, hypovolemia</td>
<td>Porphyria</td>
<td>-</td>
<td>Avoid intra-arterial injection (can cause gangrene). Avoid extravasation; causes tissue necrosis</td>
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<tr>
<td>Barbiturate, Methohexital</td>
<td>1–1.5</td>
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<td>Use with cause in asthmatics or if hypotensive</td>
<td>-</td>
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<td>Induction agent</td>
<td>Sympathomimetic effects</td>
<td>Consider alternatives</td>
<td>Use with atropine if age ≤ 10 years or significant bradycardia</td>
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<td>Ketamine 0.5–2.0 (↓ dose if used with benzodiazepine or thiopental)</td>
<td>↑ ICP, ↑ IOP, ↑ BP, ↑ HR</td>
<td>if ↑ ICP, ↑ IOP may cause emergence reaction</td>
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<td><strong>Benzodiazepine, Midazolam 0.5–1.5</strong></td>
<td><strong>Respiratory depression, apnea, paradoxical agitation</strong></td>
<td><strong>Minimal CV effects unless hypovolemic</strong></td>
<td><strong>Flumazenil</strong>&lt;br&gt;Dose varies widely, ↓ dose if given with opioids, in elderly, renal failure, liver disease, significant CV disease</td>
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<tr>
<td><strong>Propofol 1–2.5 (↓ dose with age)</strong></td>
<td><strong>Hypotension, hypoxia, apnea, bradycardia. Use cautiously if volume depletion, hypotension, CV disease</strong></td>
<td><strong>Allergy to egg, soybean oil, EDTA</strong></td>
<td><strong>-</strong>&lt;br&gt;Ultra short acting. Negative CV effects limits its use in man ED-RSI patients</td>
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*Abbreviation: CV, cardiovascular.*
commonly than etomidate for ED RSI, at least partly because many ED RSI patients are hemodynamically unstable. Thiopental decreases both cerebral blood flow and the metabolic demands of the brain, which makes it an ideal sedative agent in patients with known increased ICP or patients with head injury who are hemodynamically stable. Thiopental has negative cardiovascular effects: myocardial depression and peripheral vasodilatation. Thus, hypotension with associated hypoperfusion can occur in patients who are hypovolemic or have myocardial depression. Generally, when hypotension occurs, there is a compensatory baroreceptor mediated reflex tachycardia. Unfortunately, patients who are hypovolemic or in shock or who are already tachycardic may not be capable of further compensatory heart rate increases and can experience a drop in blood pressure with thiopental administration. Similarly, patients with preexisting cardiovascular disease may also experience hypotension when given thiopental. The conclusion is to avoid using thiopental, if possible, in patients with underlying cardiovascular disease, hypovolemia, or shock or limit thiopental to small frequent doses (1–3 mg/kg) while carefully monitoring blood pressure.29

Thiopental has some respiratory side effects. It has a dose- and rate-related (eg, high dose, rapid administration) respiratory depression of the central nervous system (CNS) that can cause apnea, especially in head injured or hypovolemic patients. With “light” anesthesia, several untoward effects may occur, especially during airway manipulation: catecholamine release causing systemic or intracranial hypertension, laryngospasm, cough, and bronchospasm, especially in asthmatic patients.41 To mitigate or avoid these negative effects, it has been recommended to coadminister an analgesic (such as fentanyl) especially in head-injured patients.27

Tissue necrosis can occur with intraarterial injection or extravasation, so it is critical that thiopental be given intravenously as a dilute solution while being careful to avoid any tissue infiltration.29,41

**Ketamine**

Ketamine, a dissociative anesthetic, exerts its effects by interrupting the connection between the thalamo-neocortical tracts and the limbic system. Unlike all the other sedatives, it has an additional advantage in that it also has analgesic properties.

Ketamine’s sympathomimetic effects, acting via a centrally mediated mechanism, cause an increase in heart rate, blood pressure, and cardiac output. This makes ketamine an excellent sedative in patients who are hypotensive, especially if secondary to shock, hemorrhage, dehydration, pericarditis, or tamponade. However, these sympathomimetic effects are undesirable in patients who already have significant hypertension or tachycardia.30

Ketamine also causes an increase in ICP by both an increase in systemic blood pressure and cerebral vasodilatation and, therefore, is contraindicated in patients with ICP, an intracerebral hemorrhage, an intracranial mass, or head trauma; although a recent study has challenged this contraindication.42 This French study compared the cerebral hemodynamics of ketamine combined with midazolam and found no significant difference in ICP or cerebral perfusion pressure when compared with midazolam-sufentanil.42

It has previously been thought that young age (eg, <6 months) was a contraindication to the use of ketamine. However, a recent study indicates that ketamine is safe and effective even in neonates.43

Ketamine is probably the sedative of choice for asthmatic patients for many reasons. Ketamine, through the release of endogenous catecholamines, relieves bronchospasm by dilating bronchial smooth muscle and stimulating the pulmonary β receptors. Ketamine increases tracheobronchial/oropharyngeal secretions. This
may have a positive effect by decreasing mucus plugging in some cases. The excess secretions may, however, interfere with visualization of the airway during laryngoscopy. Fortunately, pretreatment with atropine (preferred for RSI) or glycopyrrolate (preferred for sedation) prevents excess secretions. The dose of atropine for RSI is 0.01 to 0.02 mg/kg intravenously with a minimum of 0.1 mg and a maximum of 0.5 to 1.0 mg. Glycopyrrolate is the antimuscarinic drug of choice for procedural sedation because it has a greater antisialagogue effect and fewer side effects (less tachycardia, fewer dysrhythmias, and no CNS side effects). In addition, atropine crosses the blood–brain barrier (glycopyrrolate does not so it has no CNS side effects) and may increase the incidence of emergence reactions. Although the routine use of atropine has been questioned, the consensus is that it is still useful in selected patients. Atropine is used for RSI because it causes an increase in heart rate, which is desirable when offsetting the bradycardic effects of succinylcholine during RSI.

Ketamine has respiratory/cardiovascular stability and maintains airway reflexes. As with all sedatives, rare instances of apnea and laryngospasm have been reported. Ketamine, an analog of phencyclidine (PCP), is associated with an occasional emergence reaction, so its use should probably be avoided in psychotic patients. Small doses of midazolam have been given for the treatment of emergence reactions. Traditional teaching is that coadministration of a benzodiazepin (eg, midazolam) with ketamine will prevent emergence reactions. This teaching has been challenged recently by several studies that reported the prophylactic administration of benzodiazepine did not decrease the incidence of emergence reactions but actually increased the risk of respiratory depression and prolonged recovery, while paradoxically increasing the incidence of emergence reactions in a subset of patients.

**Benzodiazepines**

Midazolam is the most commonly used benzodiazepine for RSI and ED sedation primarily because it has a rapid onset and short duration. Other advantages of midazolam versus diazepam include fewer adverse effects, better amnesia, and greater potency.

All of the benzodiazepines, including midazolam, diazepam, and lorazepam, have sedative, hypnotic, amnestic, anxiolytic, muscle relaxant, and anticonvulsant properties. Benzodiazepines bind to a specific benzodiazepine receptor site on the GABA (gamma-aminobutyric acid) receptor. GABA is an inhibitory neurotransmitter. This opens a chloride channel causing hyperpolarization of the neuronal cell membrane, thereby blocking neuronal depolarization or activation.

The antagonist, flumazenil, can reverse the effects of the benzodiazepines. Advantages of the benzodiazepines include minimal cardiovascular effects (unless the patient is hypovolemic), can be used in patients with coronary artery disease, positive nitroglycerin-like effect in patients with heart failure (decreases the increased ventricular filling pressure), and seizure treatment. The main disadvantage of the benzodiazepines is that they can cause respiratory depression and apnea. Other uncommon side effects are paradoxical agitation, vomiting, coughing, and hiccups.

The benzodiazepine dosage for RSI and sedation varies widely and should be decreased when given along with opioids, in the elderly, patients with renal failure, or severe hepatic disease, or significant heart disease.

**Propofol**

Propofol is an ultra–short-acting sedative hypnotic agent. It has no analgesic effects, and its amnestic effects are variable. The advantages of propofol are its very quick...
onset and short duration. It also has antiemetic properties, can be used in malignant hypothermia patients, and the dosage is unchanged for patients with renal or liver disease, although higher doses may be needed in pediatric patients and lower doses in geriatric patients.32 Side effects include hypotension, bradycardia, hypoxia and apnea,32 so it should be administered slowly. Propofol also has negative cardiovascular effects so it should be used with caution in patients with volume depletion, hypotension, or cardiovascular disease.32 Because of these side effects/complications its use as a sedative for RSI is limited in many ED patients.38

PATHOPHYSIOLOGY

A discussion of the anatomy and physiology of the neuromuscular junction is valuable in understanding how the neuromuscular blockers work.

Anatomy

The neuromuscular or myoneural junction is the junction between the nerve fiber ending or nerve terminal, the muscle fiber including the muscle fiber membrane or sarcolemma, and the interposed synaptic cleft (synaptic space). The motor end plate refers to the complex of branching nerve terminals that invaginate into (but actually lie outside) the sarcolemma. (Fig. 1) Subneural clefts are folds of the muscle cell (myocyte) membrane, which markedly increase the surface area at which the synaptic neurotransmitter Ach can act (Fig. 2). A single terminal branch of the nerve axon lies in the synaptic gutter or synaptic trough, which is an invagination of the sarcolemma (see Figs. 1 and 2). Structures found in the nerve terminal include synaptic vesicles containing the neurotransmitter Ach, the dense bar areas (Ach from the vesicles is released into the synaptic cleft through the neural membrane adjacent to the dense bars), voltage gated calcium channels (which are protein particles that penetrate the neural membrane), and mitochondria (which supply the adenosine triphosphate [ATP]-that acts as the energy source for the synthesis of Ach) (Fig. 3).

The nicotinic receptor, a protein particle located on the postsynaptic myocyte membrane has two parts: a binding component and an ionophore component. The binding component projects outward from the postsynaptic myocyte membrane into the synaptic space where it binds the neurotransmitter Ach. The ionosphere component extends through the postsynaptic neural membrane to the interior of the postsynaptic membrane. The ionosphere may serve as an ion channel that permits the movement of ions (in this case primarily sodium ions, as well as other ions) through the membrane (Fig. 4).

Fig. 1. Motor end plate of the neuromuscular junction. (Courtesy of Sharon E. Mace, MD, and Dave Schumick of the Cleveland Clinic Center for Medical Art and Photography, Cleveland, OH; with permission.)
Neurotransmitter: Acetylcholine

Acetylcholine (Ach), the neurotransmitter at cholinergic synapses, is released from the ending of preganglionic and postganglionic parasympathetic nerves and preganglionic sympathetic nerves. Ach is synthesized from choline and acetic acid in the nerve and packaged in vesicles. With nerve stimulation, the impulse reaches the nerve ending causing the Ach vesicles to travel to the nerve surface and rupture, thereby releasing Ach into the synaptic space (synaptic cleft). Exocytosis is the process whereby the Ach containing vesicles fuse with the nerve terminal membrane and release their Ach. When the action potential depolarizes the presynaptic membranes, the calcium ion channels open, increasing the neural membrane permeability to calcium, allowing calcium ions to stream into the presynaptic nerve ending. The calcium ions bind with “release sites” that are unique protein molecules on the inner surface of the presynaptic neural membranes. The coupling of the calcium ion to the specific protein molecule opens the release sites, which permits the vesicles to release the neurotransmitter Ach into the synaptic space (Fig. 5).

Ach then diffuses across the synaptic cleft to the motor endplate. Attachment of Ach to the nicotinic receptors on the skeletal muscle leads to a conformational change in the nicotinic receptor. This altered protein molecule on the nicotinic skeletal muscle receptor increases the permeability of the skeletal myocyte cell to various ions (sodium, potassium, chloride, and calcium) with an influx of sodium into the skeletal myocyte (see Fig. 4). This produces a large positive potential charge within the skeletal

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**Fig. 2.** Neuromuscular junction shows nerve axon terminal in synaptic trough, the sarcolemma with subneural clefts, and the interposed synaptic space. (Courtesy of Sharon E. Mace, MD, and Dave Schumick of the Cleveland Clinic Center for Medical Art and Photography, Cleveland, OH; with permission.)

**Neurotransmitter: Acetylcholine**

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**Fig. 3.** Structures in the neuromuscular junction. (Courtesy of Sharon E. Mace, MD, and Dave Schumick of the Cleveland Clinic Center for Medical Art and Photography, Cleveland, OH; with permission.)
myocyte, referred to as the “end plate potential.” The end plate potential creates an action potential that travels along the skeletal myocyte membrane causing muscle contraction (Fig. 6).

The release of Ach from the nicotinic receptor on the skeletal myocyte ends depolarization. Ach can either diffuse back into the nerve ending or be broken down by the acetylcholinesterase enzyme into choline and acetic acid (see Fig. 5). Under normal circumstances, large amounts of the enzyme acetylcholinesterase are found in the synaptic space.
The Flow of Ions and the Action Potential

Physiologically, an abrupt increase of greater than 20 to 30 millivolts causes further opening of additional sodium channels, allowing for an action potential in the skeletal muscle fiber membrane. A weak local end plate potential, less than 20 to 30 millivolts, will be insufficient to cause an action potential in the skeletal muscle fiber membrane. This is what happens with various drugs or toxins. For example, the drug curare competes with Ach for the nicotinic receptor sites on the skeletal muscle, which results in blocking the action of Ach in opening the sodium ion channels. The botulinum toxin prevents depolarization by decreasing the amount of Ach released by the nerve terminals. The flow of ions is important, because decreasing the resting membrane potential voltage to a less negative value increases neural excitability leading to depolarization when the threshold (about 50 millivolts in skeletal muscle) is reached, whereas conversely increasing the resting membrane potential to a more negative number makes the neuron less excitable (see Fig. 6).

NEUROMUSCULAR BLOCKERS

Definition

Neuromuscular blocking agents (NMBs) are substances that paralyze skeletal muscles by blocking nerve impulse transmission at the neuromuscular or myoneural (muscle-nerve) junction.

There are several critical factors to remember with RSI. First, a sedative is coadministered with the NMB. Patients given an NMB may be aware of their environment, including painful stimuli, even though they are unable to respond. Failure to sedate the patient allows the possibility of negative physiologic responses to airway manipulation such as increased ICP, hypertension, and tachycardia. In addition, the patient may be aware of and remember the intubation, which is considered inhumane. Concomitant sedative use limits or helps avoid these adverse physiologic responses to airway manipulation and may even result in a better view of the airway during laryngoscopy.

However, whenever an NMB is used, the physician must be prepared for a difficult or failed airway with the possibility that a surgical airway may be necessary if the patient cannot be oxygenated or ventilated adequately with a bag-valve mask or extraglottic device. Assessment of the airway, especially if there is the potential for a difficult or failed airway, should be done before administering an NMB.
NMBs are depolarizing or nondepolarizing. Depolarizing agents mimic the action of Ach. They cause a sustained depolarization of the neuromuscular junction, which prevents muscle contraction. Nondepolarizing agents work by competitive inhibition to block Ach’s action at the neuromuscular junction to prevent depolarization.

According to the NEAR registry, the most frequently used NMBs were succinylcholine (82%), rocuronium (12%), and vecuronium (5%).34 For pediatric patients only, succinylcholine (90%) was also the most commonly used NMB, with vecuronium used in 7%, and rocuronium in 2%.6

**Pharmacology**

All NMBs are structurally similar to the neurotransmitter Ach. Ach and all NMBs are quaternary ammonium compounds; the positive charges of these compounds at the nitrogen atom account for their attraction to the cholinergic nicotinic (ionotropic) receptors at the neuromuscular junction and at other nicotinic receptor sites throughout the body. This nonspecific action at sites throughout the body, eg, nicotinic (ganglionic) and muscarinic autonomic sites, not just at the neuromuscular junction, helps explain some of their side effects.

**DEPOLARIZING NEUROMUSCULAR BLOCKING AGENTS**

**Succinylcholine**

Succinylcholine (Sch) is the only depolarizing agent currently available in the United States, has been used in innumerable patients since its introduction as an NMB in 1952, and is the most commonly used NMB for ED RSI.6,34

Sch is the prototype of the depolarizing agents. Because its chemical structure (eg, quaternary ammonium compound) is similar to that of Ach, it binds to the acetylcholine receptor (AchR) on the motor end plate and depolarizes the postjunctional neuromuscular membrane, resulting in continuous stimulation of the motor end plate AchRs. The neuromuscular block/motor paralysis is terminated when the NMB (eg, Sch) unbinds from the AchR and diffuses back into the circulation where it is hydrolyzed by plasma cholinesterase. Plasma cholinesterase (also referred to as “pseudocholinesterase” or “butyrylcholinesterase”) rapidly hydrolyses Sch to succinylmonocholine (a very weak NMB) and choline. Sch’s short duration of action is caused by the rapid hydrolysis by plasma cholinesterase both before Sch reaches and after Sch leaves the neuromuscular junction, because there is minimal if any pseudocholinesterase at the neuromuscular junction. Some Ach may diffuse back into the nerve terminal, although the majority of Ach is hydrolyzed by plasma cholinesterase. Muscle contraction will not re-occur until the neuromuscular junction returns to the resting state and then is depolarized again. Transient fasciculations (caused by initial depolarization) are followed by blockade of neuromuscular transmission with motor paralysis when Sch is given.

The major advantages of Sch are its rapid onset with complete motor paralysis occurring within 45 to 60 seconds and short duration of action lasting only 6 to 10 minutes when given in the recommended 1.5-mg/kg intravenous dose.

**Dosing of Succinylcholine**

There are some “pearls” regarding Sch dosing. Use the total body weight (not the lean weight) even in the morbidly obese or pregnant patient. Do not underdose the drug. It is preferable to overestimate rather than underestimate the dose because an insufficient dose may make it difficult to intubate if the patient is not adequately paralyzed. Thus, the preferred dose is 1.5 mg/kg (or about 100 mg in a 70-kg adult)1 (some experts suggest 1.5 to 2.0 mg/kg in an adult)47 and not 1 mg/kg as stated in some
The recommended Sch dose in infants (including neonates) is 2 mg/kg based on their higher volume of distribution, and some even recommend up to 3 mg/kg in newborns. Administer Sch as a rapid bolus followed by a 20 to 30 cc saline flush to avoid incomplete paralysis. Sch has been given intramuscularly in a 3- to 4-mg/kg dose in a rare life-threatening situation in which there is inability to obtain venous access.

Repeat doses or prolonged use of Sch is to be avoided for several reasons. Repeat dosing or prolonged use of Sch potentiates its effects at the sympathetic ganglia and vagal effects. The negative muscarinic effects from vagal stimulation may lead to bradycardia and hypotension even at recommended doses. This is one reason some experts recommend atropine pretreatment in infants/small children, anyone with significant bradycardia, and those receiving multiple doses of Sch. Desensitization blockage, whereby the neuromuscular membrane returns to the resting state and becomes resistant to further depolarization with Sch can also occur with repeat doses of Sch.

In patients with myasthenia gravis, there is a functional decrease in AchRs at the neuromuscular junction secondary to an antibody-mediated autoimmune destruction of the AchRs. Sch can be used in patients with myasthenia gravis, although the dose is increased to 2 mg/kg to reach and activate the remaining AchRs unaffected by the disease.

Be careful to check the expiration date on the drug vial, especially if the drug is not refrigerated, because Sch degrades gradually at room temperature. Refrigeration lowers the drug’s degradation rate so that it maintains 90% activity for up to 90 days.

**Succinylcholine Contraindications**

The absolute contraindications to Sch are (1) a history of malignant hyperthermia in the patient or family and (2) patients at high risk of severe hyperkalemia.

**Malignant Hypothermia**

Malignant hyperthermia is a rare genetic myopathic disorder precipitated by multiple drugs, especially certain inhalational anesthetics (such as halothane, sevoflurane, desflurane, isoflurane) and Sch. It is thought to be caused by an abnormal ryanodine receptor causing marked leakage of calcium from the sarcoplasmic reticulum of skeletal muscle cells resulting in extremely high intracellular calcium levels.

Symptoms generally begin within an hour of the drug or anesthetic administration but may be delayed for hours. The clinical presentation generally includes muscle rigidity (especially masseter stiffness), increased CO₂ production, acidosis, sympathetic hyperactivity with hyperthermia (up to 113°F), and sinus tachycardia. Complications that can occur include rhabdomyolysis, electrolyte abnormalities, dysrhythmias, hypotension/shock, disseminated intravascular coagulation, and death. With intensive medical therapy including dantrolene sodium, the mortality rate has decreased from 70% to less than 10%. Thus, any history of malignant hyperthermia in the patient or any family member is an absolute contraindication to Sch. Unfortunately, with RSI in the ED, a history is often not available.

**Hyperkalemia**

Even in “normal” patients, Sch may increase the serum potassium up to 0.5 mEq/L because of depolarization of the myocytes (skeletal muscle cells). Generally, the rise has no clinical significance except in patients with a predisposition to hyperkalemia, such as a patient with rhabdomyolysis or patients with chronic skeletal muscle disease in whom there is “up-regulation” from increased sensitization of extrajunctional AchR.
in muscle. Such susceptibility is not present immediately after the onset of neuromuscular disease or after a traumatic injury but can develop within 4 to 5 days and last indefinitely.

Hyperkalemia can occur whenever there is massive tissue destruction or severe muscular wasting. The extrajunctional AchR sensitization becomes clinically significant 4 to 5 days after injury or illness onset, so the risk of life-threatening hyperkalemia does not start until days (usually 3–5 days) after the injury or illness onset. This is important because Sch can be used in the acute trauma patient, the acute stroke or head injured patient, or a patient with neuromuscular disease, immediately after their injury or disease onset. Patients with extensive muscle wasting from denervating neuromuscular diseases include patients with a spinal cord injury, multiple sclerosis, motor neuron injury, stroke, and muscular dystrophies, eg, Duchene muscular dystrophy or Becker muscular dystrophy.

With rhabdomyolysis, the destruction of myocytes secondary to tissue injury releases potassium from the cells causing the serum potassium level to increase. The second mechanism, up-regulation, causes hyperkalemia because the abnormal up-regulated AchRs have low conductance and prolonged ion channel opening times that lead to an increase in potassium. Up-regulation usually occurs within 3 to 5 days and lasts indefinitely, even years (3 or more years) after an acute injury or a progressive disease. Giving defasciculating doses of nonpolarizing NMBAs does not affect the hyperkalemic response. The hyperkalemic response to Sch has also been reported in patients in the intensive care unit with life-threatening infections, especially if there is disuse atrophy and chemical denervation of the Ach receptors. Sch also should not be used in patients with myopathies, including Duchene muscular dystrophy, because the Sch interacts with the unstable muscle membrane of the myopathic cells causing rhabdomyolysis and hyperkalemia.

Although the longstanding tenet has been to avoid Sch in patients in chronic renal failure who have normokalemia, there is no supportive evidence for this. In reality, most patients with renal failure undergo successful RSI with Sch without any untoward cardiovascular events. However, Sch is not recommended for patients with known hyperkalemia because of concern that even the “usual” potassium increase of 0.5 mEq/L may precipitate fatal dysrhythmias in a patient with existing significant hyperkalemia and acidosis. Thus, Sch should be avoided in patients with ECG changes of hyperkalemia.

**Bradycardia**

Bradycardia after Sch administration most frequently occurs in infants and children because of the vagal predominance of their autonomic nervous system but can also occur in patients of any age with repeated Sch doses. Pretreatment with atropine, 0.02 mg/kg, minimizes or eliminates this bradycardia response.

**Prolonged Neuromuscular Blockade**

Any factor that inhibits the breakdown of Sch will prolong neuromuscular blockade and paralysis. An abnormal form or a decrease in pseudocholinesterase (either acquired or congenital) leads to prolonged paralysis from delayed degradation of Sch. Various genetic variants of pseudocholinesterase exist including one disorder with defective pseudocholinesterase in which individuals receiving Sch remain paralyzed for up to 6 to 8 hours after a single dose of Sch. Decreased pseudocholinesterase levels can also occur secondary to various acquired disorders: liver disease, renal failure, anemia, pregnancy, chronic cocaine use, increased age, connective tissue disease, various malignancies, and organophosphate poisoning. However, this finding has little
clinical significance because even large decreases in pseudocholinesterase activity cause small increments in the duration of neuromuscular paralysis after Sch administration because baseline pseudocholinesterase levels are quite high.

**Increased Intracranial Pressure**

The effect of Sch on ICP has been debated with various studies noting conflicting results. Some researches have noted small increases in ICP (range, 5–10 mm Hg), whereas other studies have shown no increase. More importantly, there has been no evidence of neurologic deterioration secondary to the transient ICP increase associated with Sch. Pretreatment with a nondepolarizing NMB prevents the increase in ICP, although the additional time and steps associated with such pretreatment may be impractical and time consuming in an airway emergency, and the suggested pretreatment dose of a nondepolarizing NMB may, by itself, cause some paralysis.

The extensive experience with Sch in the clinical setting of patients with acute intracerebral pathology documenting its safety and efficacy coupled with the dangers of a failed airway with secondary cerebral insult from hypoxia obviates against these theoretical, small, and likely clinically insignificant transient increases in ICP with Sch.

**Increased Intraocular Pressure**

Sch can increase the IOP by 6 to 8 mm Hg. Sch has been used safely and effectively in patients with penetrating eye injuries during RSI anesthesia. Some experts have recommended the use of Sch even in patients with an open globe injury if there is a need for emergent securing of the airway, citing the greater risk from allowing the negative side effects of an uncontrolled intubation (including hypoxia and coughing or vomiting, which also likely results in a greater increase in IOP).

**Trismus**

Masseter muscle spasm (trismus) occurs in 0.001% to 0.1% of patients after Sch administration. It has been associated with malignant hyperthermia. However, it may occur in isolation. Management includes giving a standard dose of a ND-NMB, although a cricothyrotomy has been necessary in rare cases.

**Fasciculations**

Fasciculations are involuntary, unsynchronized muscle contractions. They are caused by the depolarization of Ach receptors. This, in turn, initiates an action potential, which is propagated to all of the muscles supplied by the nerve. Fasciculations have various negative effects: myalgias, increased creatinine kinase, myoglobinemia, increased catecholamines (with secondary increased blood pressure and heart rate), and increased cardiac output (increased oxygen consumption and increased carbon dioxide production). The transient small increases in cerebral blood flow and ICP that occur with Sch may be caused by fasciculations. Defasciculation can be accomplished by pretreatment with lidocaine at 1.5 mg/kg or 10% of the intubating dose of a nondepolarizing NMB.

**NONDEPOLARIZING NEUROMUSCULAR BLOCKING AGENTS**

Nondepolarizing (ND) NMBs competitively block Ach transmission at the postjunctional cholinergic nicotinic receptors. Unlike Sch, which causes a conformational change in the AchR receptor resulting in depolarization of the neuromuscular junction, the nondepolarizing NMB prevents Ach from access to the nicotinic receptor, thereby preventing muscle contraction. Fasciculations do not occur with the ND-NMBs.
Some ultra short ND NMBs are undergoing research, but they are not yet clinically available. Currently, the only ultra short NMB available in the United States is the depolarizing NMB, Sch. However, doubling the dose of rocuronium from 0.6 mg/kg to 1.2 mg/kg shortens the onset of complete neuromuscular blockade from about 1.5 minutes (mean, 89 seconds) to 1 minute (mean, 55 seconds). If Sch cannot be used and intubation in less than 90 seconds is needed, then the higher doses of the ND-NMB can be used. The high dose regimen for RSI is preferred over the “priming technique,” whereby a small subparalyzing dose of the ND-NMB (eg, 10% of the intubating dose) is given 2 to 4 minutes before the second large dose for tracheal intubation for several reasons: intubating conditions are less optimal than with Sch, priming has risks (including aspiration), and there are side effects.

**Indications for Nondepolarizing Neuromuscular Blocking Agents**

The ND-NMBs are used: 1) for muscle relaxation if Sch is contraindicated or unavailable, 2) to maintain postintubation paralysis (remember that repeated doses of Sch should be avoided, if possible), and 3) as a pretreatment agent to lessen or eliminate the fasciculations and their side effects (eg, myalgias and increased IOP, ICP, intragastric pressure [IGP]) associated with Sch use.

The contraindication for the use of ND-NMBs is the same as for a depolarizing NMB, inability to secure the airway with the possibility of a difficult or failed airway.

**Specific Nondepolarizing Neuromuscular Blocking Agents**

The medical use of ND-NMBs originated from the use of curare as the poison in the arrows of South American Indians. Some of the ND-NMBs, such as d-tubocurarine, were originally isolated from various naturally occurring sources, especially various plants growing in several jungle regions throughout the world. Most ND-NMBs are classified according to chemical class: steroids (aminosteroids), benzylisoquinolinium, or others; or according to onset or duration of action: ultra short acting, short acting, intermediate, or long acting. The clinical duration (in minutes) for the NMB are ultra short acting, less than 10, short acting, 10 to 20; intermediate, 20 to 50; and long acting, greater than 50. Currently, there are no clinically approved ultra–short-acting ND-NMB blockers, although several ND-NMBs are being developed and tested. Short-acting ND-NMBs include rapacuronium and mivacurium; intermediate acting include vecuronium, rocuronium, atracurium, and cisatracurium; and long-acting include pancuronium, pipecuronium, d-tubocurarine, metacurine, doxacurium, alcuronium, and gallamine. The doses and classes of some of the commonly used ND-NMBs are given in Table 2. The older NMBs such as tubocurarine have a higher incidence of hypotension and cardiovascular side effects secondary to histamine release than the newer NMBs (for example, rocuronium, vecuronium, and cisatracurium), which are preferred.

**Nondepolarizing Versus Depolarizing Agent for Rapid Sequence Intubation**

Sch is still the most commonly used NMB in ED-RSI and is the drug of choice for RSI in the ED and anesthesia. Of the ND-NMBs, rocuronium (0.6–1.2 mg/kg dose) is the most commonly used paralytic agents for RSI because of its rapid onset and short duration with vecuronium (0.15 mg/kg/dose) as a second choice. Sch’s advantages include rapid onset and offset (eg, short duration of action), profound depth of neuromuscular blockade, and better intubating conditions.

Comparative trials of Sch with rocuronium found that Sch (1 mg/kg) resulted in superior intubation conditions when compared with rocuronium (0.6 mg/kg). However, a low dose of rocuronium was used. Another recent study also noted...
similar results with Sch (1 mg/kg) providing superior intubation conditions when compared with rocuronium (again, a lower dose 0.6 mg/kg was used) with no difference in the incidence of adverse airway effects.\textsuperscript{53} A Cochrane meta-analysis concluded “succinylcholine created superior intubation conditions to rocuronium when comparing both excellent and clinically acceptable intubating conditions.”\textsuperscript{54}

**Use of Nondepolarizing Neuromuscular Blocking Agents as Pretreatment**

The ND-NMBs in a dose that is approximately 10\% of the intubating dose can be used as a pretreatment for Sch to prevent fasciculations and their side effects. Rocuronium is the most commonly used ND-NMB because of its rapid onset, and it can be given 1.5 to 3 minutes before the induction of anesthesia.

In clinical practice, the ND-NMB is generally administered 2 minutes before giving the intubating dose of Sch. Although defasciculation is achieved, there are several confounding issues to consider. Giving ND-NMB increases the muscle’s resistance to Sch’s action such that increasing the Sch dose by 50\% is recommended. Use of a ND-NMB may result in less favorable conditions for tracheal intubation and slow the onset of Sch. Perhaps, more importantly, for the emergent intubation in the ED is the extra time (about 2 or more minutes) added to the procedure before intubation occurs. Some clinicians also use fasciculations as a clue to when neuromuscular blockade has occurred, and conditions are ready for ET tube placement. Use of a defasciculating dose of ND-NMB adds another drug to RSI (with the additional risk of possible side effects/complications and drug errors), another step, and additional time to the process.\textsuperscript{21} Timing or the use of a small subparalyzing dose of a ND-NMB has several problems as well. There is a danger of aspiration, difficulty swallowing, and uncomfortable visual disturbances for the patient with partial neuromuscular block.\textsuperscript{50}

A drug familiar to emergency medicine, lidocaine, can be used as an alternative to ND-NMB for priming before Sch administration. Lidocaine is effective in minimizing or preventing the fasciculations with their side effects that occur after Sch administration. The dose is 1.5 mg/kg of lidocaine.

**The Future of Rapid-Sequence Intubation**

There is a new reversal agent, sugammadex, which is anticipated to be clinically available (eg, approved by the US Food and Drug Administration) in the near future.\textsuperscript{55–57} Some experts anticipate that the availability of a reversal agent for the ND-NMB will expand the use of nondepolarizing NMBs, specifically rocuronium (in a 1.2 mg/kg dose) for RSI,\textsuperscript{57} and overall greatly decrease the use of Sch.\textsuperscript{58} There is also a newer sedative, dexmedetomidine, which has been used in the operating room, but there are no data available regarding its use for RSI in the ED.\textsuperscript{59} Esmolol has also been used as a preinduction agent for RSI. It most often is used for neurosurgical patients with an increase intracranial pressure and is synergistic with fentanyl. Currently, there are limited data regarding its use for RSI in the ED.

**MODIFICATION OF RAPID-SEQUENCE INTUBATION**

“Facilitated intubation” refers to the use of a sedative only (without a paralytic) to pharmacologically assist with intubation. Facilitated intubation, also referred to as “pharmacologically assisted intubation,” has been recommended by some clinicians in specific circumstances because it does not involve neuromuscular blockade. Some advocate the avoidance of a neuromuscular paralysis and the use of sedation alone (“facilitated intubation”) in clinical scenarios in which a difficult airway is anticipated.\textsuperscript{21}
<table>
<thead>
<tr>
<th>Drug (Pretreatment Drugs)</th>
<th>Dose (IV) (mg/kg)* for Intubation</th>
<th>Indication</th>
<th>Side Effects</th>
<th>Precautions Contraindications</th>
<th>Reversal Agent</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine*</td>
<td>1.5</td>
<td>† ICP, adults with reactive airway disease</td>
<td>May cause hypotension</td>
<td>Allergy</td>
<td></td>
<td>Often used with fentanyl for † ICP</td>
</tr>
<tr>
<td>Fentanyl* (an opioid)</td>
<td>2–3 mcg/kg</td>
<td>† ICP, major vessel dissection/rupture, CAD</td>
<td>May cause hypotension</td>
<td>Avoid bolus injection to avoid chest wall/masseter rigidity, bradycardia; Allergy</td>
<td>Naloxone, Naltrexone</td>
<td>Often used with lidocaine for † ICP</td>
</tr>
<tr>
<td>Atropine</td>
<td>0.02 Minimum 0.1 mg Maximum 0.5 mg</td>
<td>Pediatric patients ≤ 10 yrs, Patients with significant bradycardia</td>
<td>May cause tachycardia, hypertension</td>
<td>Avoid if patient has significant tachycardia or hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rocuronium (Defasculating dose of ND-NMB)*</td>
<td>0.06 (1/10&lt;sup&gt;th&lt;/sup&gt; of paralyzing dose)</td>
<td>† ICP † IOP</td>
<td>May cause incomplete paralysis</td>
<td>Avoid doses &gt;0.06 (may cause paralysis), Allergy</td>
<td>Sugammadex (not yet available)*</td>
<td></td>
</tr>
</tbody>
</table>
### Neuromuscular Blocking Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose (Adult/Infant/Newborn)</th>
<th>Mechanism of Action</th>
<th>Contraindications</th>
<th>Reversal Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Succinylcholine</td>
<td>Adult 1.5 (some recommend 2 in adults); ↑ dose to 2 myasthenia gravis patients, Infants 2, Newborns 3, Avoid repeat doses/ prolonged use</td>
<td>Depolarizing neuromuscular blocker, Short acting</td>
<td>Bradycardia in children (pretreat with atropine) use with caution if ↑ ICP/IOP/IGP, patients with pseudocholinesterase inhibitors</td>
<td>Contraindication: malignant hyperthermia, patients with known severe hyperkalemia, nonacute (&gt;4–5 days) burn patients or neuromuscular disease patients (may cause hyperkalemia), Allergy</td>
</tr>
</tbody>
</table>
| Rocuronium | 0.6–1.0, 1.2 high dose | Nondepolarizing neuromuscular block, Intermediate acting | High dose, 1.2 mg/kg has a shortened onset but long duration | Allergy | Blocks acetylcholine from binding to receptors, Sugammadex, (not yet available)

(continued on next page)
### Table 2 (continued)

<table>
<thead>
<tr>
<th>Drug (Neuromuscular Blocking Agents)</th>
<th>Dose (IV) (mg/kg)* for Intubation</th>
<th>Indication</th>
<th>Side Effects</th>
<th>Precautions Contraindications</th>
<th>Reversal Agent</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vecuronium&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.1</td>
<td>Nondepolarizing neuromuscular blocker, Intermediate acting</td>
<td>Onset 2.5–3 min. Duration, 20–40 min.</td>
<td>Allergy</td>
<td>Blocks acetylcholine from binding to receptors, Sugammadex, (not yet available)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Slow onset, Long duration</td>
</tr>
<tr>
<td>Pancuronium&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.1</td>
<td>Nondepolarizing neuromuscular blocker, Long acting</td>
<td>Onset 2–3 min, Duration 60–100 min.</td>
<td>Allergy</td>
<td>Blocks acetylcholine from binding to receptors, Sugammadex (not yet available)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Slow onset, Long duration</td>
</tr>
</tbody>
</table>

Note: Doses are in mg/kg except for fentanyl, which is in mcg/kg; doses for intubation are generally higher than for procedural sedation. Not all the available drugs are listed, but the more commonly used drugs are given.

**Abbreviations:** ICP, intracranial pressure; IOP, intraocular pressure; IGP, intragastric pressure; CAD, coronary artery disease; CV, cardiovascular; ND, nondepolarizing; NMB, neuromuscular blocker; BP, blood pressure; HR, heart rate.

<sup>a</sup> Coadministration of lidocaine and fentanyl may have a synergistic effect.

<sup>b</sup> Lidocaine also prevents fasciculations with succinylcholine so a defasciculating dose of ND-NMB may be unnecessary if lidocaine is given.

<sup>c</sup> Sugammadex is a new reversal agent, anticipated to be available in the near future, which can reverse the ND-NMBs.

<sup>d</sup> The ND-NMBs that have a longer duration (specifically, vecuronium and pancuronium) are not commonly used for RSI in the ED because of their long duration.
For facilitated intubation, the most common sedative used has been etomidate, although midazolam has also been used. Proponents of facilitated intubation suggest that there may be clinical scenarios in which paralysis is not an option. A study in the prehospital air medical setting, using 0.3 mg/kg of etomidate as their sedative without any NMB reported an 89% rate of successful intubation, difficult intubation in 16%, and episodes of clenched jaws and orofacial muscle spasm. A later study from the same investigators (an air medical transport service) prospectively compared facilitated intubation using etomidate versus RSI using etomidate and succinylcholine. The results were: 63% (15 of 24) of the facilitated intubation (etomidate only) group received additional medications versus 4% (1 of 25) in the RSI group, and laryngoscopic conditions using several scoring systems was significantly more difficult for the facilitated intubation (etomidate only) versus RSI. The conclusion was that facilitated intubation (etomidate only) had a decreased rate of success when compared with RSI (etomidate + succinylcholine). A prehospital study of facilitated intubation using midazolam alone noted a successful intubation rate of only 62.5%, which is less than the usual success rate for prehospital RSI. When comparing successful rates of intubation, based on these studies, RSI has higher success rates than facilitated intubation.

For ED intubations, the results of the NEAR studies confirm the superiority of RSI over facilitated intubation. The successful intubation rate for first attempt was RSI = 85%, and sedative only (no NMB) = 76%. The successful rate for first intubation was RSI = 91%, and sedative only (no NMB) = 88%. For pediatric patients, the first attempt intubation success rates were RSI, 78%; sedative only, 44%; and no medication. 47%.

SUMMARY

RSI is the process involving administration of a sedative (eg, induction agent) followed almost immediately by a NMB to facilitate endotracheal intubation. The procedure of RSI generally consists of seven steps: preparation, preoxygenation, pretreatment, paralysis with induction, protection and positioning, placement of the endotracheal tube, and post intubation management. The purpose of RSI is to make emergent intubation easier and safer, thereby increasing the success rate of intubation while decreasing the complications. Possible disadvantages are complications from the additional drugs, prolonged intubation with hypoxia, and precipitating an emergent or crash airway. Controversy has arisen regarding various steps in RSI; however, RSI remains the standard of care in emergency medicine airway management.

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