REVIEW ARTICLE

Rapid sequence intubation: a practical approach for the pediatrician in the emergency room

Sequência rápida de intubação: uma abordagem prática para o pediatra em situações de urgência

Karina Camargos Martins[1], Adrianne Mary Leão Sette e Oliveira[2], Alexandre Rodrigues Ferreira[3]

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ABSTRACT

Intubation is one of the key procedures in emergency situations in Pediatrics. Rapid sequence intubation, which comprises the simultaneous or sequential administration of inducing agents (sedatives and analgesics) and neuromuscular relaxants, is not a common practice among pediatricians, despite many studies showing that it greatly improves intubating conditions and even reduces complications in the procedure. This article presents an update of the main available drugs as well as the indicated uses in airway management in the ICC.

Key words: Endotracheal Intubation; Intubation; Emergency Medicine; Airway Management; Children.

RESUMO

A intubação é, na Pediatria, um dos principais procedimentos realizados em situações de urgência. E sua sequência rápida – que compreende a administração sequencial ou simultânea de um agente indutor (analgésico e sedativo) e um relaxante neuromuscular – é prática pouco comum entre os pediatras. No entanto, muitos estudos têm mostrado que a mesma melhora muito as condições de intubação, reduzindo complicações do procedimento em si. Esse artigo se propõe a apresentar uma atualização das principais medicações disponíveis bem como as indicações de uso de cada uma nas situações de intubação na sala de urgência e CTI.

Palavras-chave: *Intubação Intratraqueal; Intubação; Medicina de Emergência; Manuseio das Vias Aéreas; Criança.*

[1] Horizontal Care Physician at the Pediatrics ICU at the University Hospital of the Federal University of Minas Gerais (UFMG). Belo Horizonte, MG – Brazil.
[2] Physician. Coordinator of the Pediatrics ICU at the University Hospital of the Federal University of Minas Gerais. Belo Horizonte, MG – Brazil.
[3] Physician. Associate Professor of the Department of Pediatrics at the Federal University of Minas Gerais School of Medicine. Medical Coordinator of the Functional Pediatrics Unit of the University Hospital of the Federal University of Minas Gerais. Belo Horizonte, MG – Brazil.

INTRODUCTION

Airway maintenance is a priority in patient care at the emergency sector. The objective is to ensure that ventilation and oxygenation are in accordance with patients' demand. Tracheal intubation (TI) is often the definitive procedure to reach that purpose.

Rapid sequence intubation (RSI) means the sequential or nearly simultaneous administration of an inducing agent (analgesic and sedative) and a paralyzing dose of a neuromuscular blocking agent.[1-3] It is precisely indicated in "full stomach" situations[4]. However, given the need to facilitate TI conditions and produce better visualization, RSI has been indicated as a standard procedure for TI in emergency settings.[3]

Ideal conditions for intubation are defined as complete mandible relaxation, open and immobile vocal cords, absence of coughing, resistance or of diaphragm movement in response to intubation.[2,3] To reach these ideal conditions, four objectives must be achieved with this technique: analgesia, amnesia or unconsciousness, muscle relaxa-

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Institution:
University Hospital of the Federal University of Minas Gerais – Functional Pediatrics Unit
Belo Horizonte, MG – Brazil

Corresponding Author:
Alexandre Rodrigues Ferreira.
E-mail: alexfer1403@gmail.com

tion, and reduction of autonomic reflexes generated by a nociceptive stimulus. Relative or absolute contraindications to RSI include lack of experience or training on the technique, and anticipation of a difficult airway. In those cases, there are safe alternatives to RSI and to unforeseen difficult intubation, such as the use of topic anesthesia and conscious sedation preserving spontaneous ventilation and the protective reflexes of the airway, or the use of supraglottic devices.

This article proposes to discuss mainly the medication used in RSI and its prescription according to clinical situation, with a focus on the emergency setting: intubation at emergency rooms and intensive care units. We will not focus on the elective situations of operating rooms and the neonatal period. This research attempts to approach the pediatric population, despite the several limitations this implies given the lack of studies on this age group. Therefore, many studies on adults will be quoted and used as references.

INDICATION AND PREPARATION FOR TRACHEAL INTUBATION (TI)

The main indications for TI in pediatric emergency settings are: treatment of shock and/or respiratory failure, and situations that lead to altered consciousness. The most common etiologies of respiratory failure may be didactically divided into: upper airway obstruction, lower airway obstruction, parenchymal diseases and breathing control (neurological issues that do not guarantee either airway protection or ventilation itself).[5]

RAPID SEQUENCE INTUBATION

A safe and effective RSI requires compliance to a specific sequence of steps that starts with a review of the patient's history and is followed by an adequate preparation of the equipment, personnel and medication. Subsequent steps are preoxygenation, pre-medication, (sedative) medication, neuromuscular blocking, observation, and post-intubation monitoring.[1-3]

Brief anamnesis and physical examination

To obtain the necessary information for a safe procedure, the SAMPLE history mnemonic can be used: signs and symptoms, allergies, medications, past medical history, last oral intake, and events leading up to the need for intubation.[5]

Before the TI procedure a clinical examination must always be conducted in order to estimate the potential risk of difficult intubation. Whenever possible, laryngeal masks or other supraglottic devices must be available for the cases when the procedure is not successful and ventilation is difficult.[3,6,7]

Preparation and monitoring

Preparation must always be initiated by checking and defining the necessary material for a successful procedure: operational O_2 source with humidifier, oxygen supply system (preferably high-flow with non-rebreather mask) for prior patient hyperoxygenation, vacuum source with suction probe connection, tested ventilation unit adequately sized for the child (producing adequate pressure and with a non defective reservoir), mask appropriate for the age group connected to the ventilation unit, appropriate and tested laryngoscope, tracheal tube (TT) in three sizes (one adequate for the age group, one smaller, and one larger), tube guide, and previously planned and prescribed medication. In addition, one must not forget two reliable calibrous access ways, cardiorespiratory monitoring, and a team prepared for the procedure.[3]

Several formulas may be employed to calculate the correct size of the tracheal tube for a given pediatric age group. For children over two years of age, the size (internal diameter in milliliters) may be calculated using the formula: uncuffed TT (tracheal tube) size (ID in mm) = (age in years/4) + 4, infants up to 1 year of age: 3.5, toddlers between 1 and 2 years: 4. TT (tracheal tube) cuffed size (ID in mm) = age (years)/4 + 3.5, infants up to 1 year of age: 3, toddlers between 1 and 2 years: 3.5 tube. Physicians should be aware that in case the cuffed tube is used, inflation pressure in the *cuff* must be between 20 and 25 cm H_2O. Formulae may also be used for estimating the depth of tube insertion. This insertion distance (depth) in centimeters (from the distal end of the tube to the alveolar ridge) for children over two years of age may be approximated by adding 12 to half the patient's age: insertion depth (cm) = age (years)/2 + 12. Alternatively, the insertion distance (in centimeters) from the distal end of the tube to the lip may be estimated by multiplying the internal diameter of the selected tube by three.[5]

All patients must be continuously monitored before, during, and after the RSI, with constant assessment of oxygenation (O_2 saturation), ventilation (capnography, if available), circulation (heart rate and ECG), and temperature. However, the most important aspect is the continuous supervision of the clinical aspects during every step of the RSI.

Preoxygenation

The first step – preoxygenation – may be completed with the use of oxygen at 100% from a mask with a nonrebreathing reservoir for 3-5 min.[2,3] The objective is to denitrogenate the patient, allowing for more time without desaturation so that the physician may perform the procedure without the risk of hypoxia. Children often tolerate less time until desaturation than adults, both due to the lower reserves and to the increased use of oxygen per kilogram.

Pre-medication

Part of the current RSI medication is made up of agents used to attenuate the adverse respiratory, cerebral, cardiovascular, and intraocular effects of laryngoscopy procedures. They are known as pre-medication, and the main ones are atropine, lidocaine, and opioids[1,2,3]. The choice depends on each child's clinical condition.

TI is a noxious stimulus and laryngoscopy induces several physiological changes in children, the most frequent being marked vagal response and bradycardia with repercussions. Before birth and during the first 3-6 months of life, an autonomic imbalance can be observed due to dense vagal innervation of the sinoatrial node and poor sympathetic innervation of the ventricles and conduction system[8]. The vagal response may happen both by hypoxia and by laryngoscopy, in addition to certain medications that induce bradycardia. In cases considered reflexive, such as hypoxia, and in laryngoscopy, what can be seen is that there is peripheral vasoconstriction simultaneous to bradycardia, and the effects are compensated in the systemic pressure. However, in the cases of vagomimetic bradycardia such as those induced by drugs, this vasopressor response generally does not happen, with devastating effects. As an example, succinylcholine can induce severe bradycardia and asystole regardless of the disease or concomitant use of other medication.[8]

Given all that has been discussed up to this point, use atropine is always recommended as pre-medication for children under the age of one year, from 1-5 years when using succinylcholine, and above that age if a second dose of succinylcholine is used.[2,3,5,8] The use of atropine as pre-medication has also been currently recommended for septic shock, considering the potentially devastating effects bradycardia could have in such conditions, especially if followed by vasoplegia.[8,9] The recommended dose is 0.02 mg/kg, bearing in mind that the minimum dose is 0.1 mg, and that the maximum dose is 0.5 mg. Doses lower than the minimum may induce paradoxical bradycardia.

Lidocaine may also be used in this phase and is mainly prescribed in cases of head trauma or when intracranial hypertension is suspected. Its exact mechanism of action is not yet clear, but it is probably related to the suppression of coughing, depression of brain metabolism, and membrane stabilization.[1,10,11]

Opioids have traditionally been excluded from RSI, which included the use of only one sedative (Thiopental, at the time) and a muscle relaxant (succinylcholine).[12,13] However, in recent years, opioids have been added to the arsenal of drugs used in rapid sequence intubation. The most frequently used and most easily available at emergency centers is fentanyl, a powerful analgesic with mild sedative effects. It also decreases the hypertensive response to intubation, a reaction more significant in adults.[1,14] It may cause chest tightness, which seems to occur more commonly with high doses and fast injection.

Table 1 - Materials for intubation

Ventilation / Oxygenation	Tube Preparation	Laryngoscopy	Drugs	Verification and Fixation
Oxygen source; Non-rebreather Mask; Tested ventilation unit; Silicon masks for ventilation; Oropharyngeal and Nasopharyngeal cannulae.	2.5 to 5.0 tubes, non cuffed; 5 to 8 tubes, cuffed; Guide wire; 10 or 20ml syringe; Personal Protection Equipment: apron, hood, mask and gloves.	Straight blades: 00.0 and 1; Curved blades: 2, 3 and 4. Padding for head positioning; Suction probes and assembled and checked suction device.	Syringes / Needles; Lidocaine without vasoconstrictor; Atropine; Anesthetics / Sedatives / Relaxants.	Stethoscope; Wrist oximeter; Adhesive tape and/or wire; Capnograph, if available.

Extra care must be taken when drugs are used in hemodynamically unstable conditions, since there are negative hypotensive and inotropic effects, mainly when associated to benzodiazepines; lower doses must be considered in these cases.[3,15]

Induction agents: sedatives

The choice of induction agent must be made according to the clinical setting. There is no ideal medication for all circumstances, but preference must be given to those with most benefits and minimal side effects. The ideal medication must have a rapid and predictable onset of action to produce loss of consciousness and improve intubation conditions in cases of inadequate paralysis.[12] The main properties of each agent must therefore be well known.

Etomidate

Etiomidate is an induction agent rarely used in Pediatrics. It is a hypnotic barbituric that has a fast onset of action (30-60 seconds), peak action within a minute, and short half-life (10-15 minutes), with an induction dose of 0.2 to 0.4 mg/kg.[3,5] It practically has no effect on blood pressure, and was considered ideal until very recently for situations with risk of hypotension.[1] Etomidate has a brain protection effect because it reduces blood flow brain and brain use of O_2 and is recommended as the sedative of choice in situations of traumatic brain injury (TBI), particularly in hypotension.[2,3] It has no analgesic effects and may reduce the seizure threshold in patients with the risk of convulsive seizures, such as epileptic patients.[1,2]

Several current studies have shown that single doses of this medication can interfere in the production of cortisol and have, for this reason, been contraindicated for sepsis and septic shock.[9,16]

Ketamine

Ketamine is a dissociative agent whose pharmacology is different from other analgesics and sedatives.[17] It causes dose-dependent depression of the CNS characterized by deep amnesia and analgesia associated to slow nystagmus, eye movement, and electroencephalographic dissociation between the corticothalamic and limbic systems. It is characterized by a powerful analgesic effect (the single sedative described in this article with analgesic properties), sedation and amnesia, while it maintains cardiovascular stability and preserves spontaneous respiration and the protective reflexes of the airways, as well as having bronchodilator properties.[2,3,5,17]

Differently from most agents, it is not titratable, with dissociative effects shown with 1.5-2 mg/kg venous (IV) and 3 or 4 mg/kg intramuscular (IM) doses.[17] Once the dissociative effects are reached, administration of additional doses does not improve or deepen sedation, as is the case with opioids, sedatives, and inhalational agents, but it increases the action time. In addition, it has been described that the amount of ketamine does not have relevant effects on the integrity of the airway and respiration, and the highest risk of respiratory depression is associated to the rapid infusion of the medication in a time bracket that must be between 30-60 seconds.[17]

Despite a laryngospasm-inducing effect that has been described in several conditions, including asthma, there are no contraindications in this clinical setting for intubation with this agent provided that a neuromuscular blocker is used.[17] In fact, many articles on the subject consider ketamine the agent of choice in bronchospasm situations.[1-3]

There are many questions about the possibility of increased intracranial pressure with the use of ketamine.[18] The practical *guideline* for the use of ketamine in the emergency department[17] has removed Traumatic Brain Injury from the list of relative contraindications. However, it has maintained masses, CNS abnormalities and hydrocephaly as diagnoses that require careful use (relative contraindications). In regard to the use of alternative agents, it would be prudent to use the latter if the patient conditions so allow, especially if the patient shows barriers to the flow of cerebrospinal fluid.[17] In case of ICH and hemodynamic instability, one must weigh the risks versus the benefits of the use of ketamine. Hypersalivation and dysphoric and psychometric effects are not usual during RSI.

Still according to the *guideline*,[17] other relative contraindications of ketamine are porphyria, glaucoma, ocular injury, and known or suspected cardiovascular disease (angina pectoris, heart failure, hypertension or risk factors for coronary heart disease). It should be used with caution in cases of ongoing pulmonary disease or other situations that may induce laryngospasms (keeping in mind that the contraindication ceases to exist with the use of muscle relaxants). The *guideline* mentions as absolute contraindications to the use of

ketamine age below three months and psychiatric disorders, bearing in mind that this guideline is intended to be the rule not only for TI, but for sedation in general. It is therefore considered that, in the case of age, the concern is airway obstruction, laryngospasm and apnea, which can be precipitated by ketamine. In RSI and with the use of muscle relaxants such effects would seem less important. Ketamine has also been advocated for due to its minimal cardiovascular effects and the potential of adrenal suppression of other agents with blood pressure preservation effects (etomidate) as the drug of choice in pediatric septic shock.[9]

Midazolam

Despite its very frequent use, midazolam is considered a suboptimal agent for intubation, both for not producing proper sedation and for producing non-ideal sedation conditions.[2] It has sedative, hypnotic, amnesiac, anxiolytic, muscle relaxant and anticonvulsant effects.

It must be used with caution in conditions of hemodynamic instability due to its negative and vasodilator inotropic effects, especially if associated with opioids.[3]

Thiopental

This is a thiobarbituric with fast onset of action (30 seconds) and short half-life. It reduces O_2 consumption, cerebral blood flow and intracranial pressure.[1,3] However, it is associated with hypotension due to effects in myocardial contractility, vascular resistance and venous return.[1,3] Therefore, it must not be used in patients with hemodynamic instability[1,3]. Thiopental may cause laryngospasm, hypersalivation, and bronchospasm.[1]

The most classical use of this drug as an inducing agent is in normotensive patients, normovolemic patients with status epilepticus or ICH and patients with seizures.[1-3]

Propofol

Propofol is a liposoluble agent that induces hypnosis in the arm-brain circulation time.[1] It has a short half-life and duration of action, anticonvulsant and antiemetic properties, and provides the best conditions for intubation without the use of muscle relaxants.[1,2,12] Propofol also reduces intracranial pressure and brain metabolism. It has a tendency to lower blood pressure and must be used with caution in patients with risk of hypotension, especially considering that hypotension reduction leads to a reduction in cerebral perfusion.[1-3]

Neuromuscular blocking

It is common to avoid the use of neuromuscular blocking in the pediatric practice of intubation.[19] Nevertheless, to reach acceptable conditions for intubation, many times high doses of opioids and sedatives are used and present a high risk of hypotension and bradycardia. Studies show that intubation conditions become much better with the use of neuromuscular blocking, with higher success rates and reduction of airway trauma during the procedure.[2,3,19-25] Neuromuscular blocking must always be used as a part of RSI, except under conditions that predict difficult airways or when there are no alternative conditions to approach the "no intubation, no ventilation" situation.

In addition to reducing laryngeal trauma, optimal intubation conditions may reduce morbidity for patients during the procedure (deoxygenation and its consequences) by facilitating it.

Neuromuscular blocking drugs are divided into two classes based on their mechanism of action at the neuromuscular junction: a) depolarizing agents, and b) nondepolarising agents. Both induce motor paralysis by preventing acetylcholine stimulus on the nicotinic receptors, thereby interrupting neuromuscular transmission. Succinylcholine and rocuronium are the most appropriate NMBs for RSI.

Depolarizing: succinylcholine

Depolarizing neuromuscular blockers, whose only representative for clinical use is succinylcholine, operate as acetylcholine receptor agonists in a biphasic manner: first it opens the sodium channels of the cellular membrane, resulting in a brief depolarization which can be clinically observed, such as muscle fasciculation. It then prevents the binding of acetylcholine to its receptors, where it binds and promotes a complete block.[1,3]

Succinylcholine has a fast onset of action (one minute) and short duration time (5-15 minutes) and ventilation may return in 9-10 minutes.[1] Dosing is controversial, with references mentioning mainly the faster metabolism of children under three years of age

and advocating higher doses for this age group.[3,20] The dose is 3 mg/kg for infants under one year of age and 2 mg/kg for the other age groups.

Despite the emergence of new agents and given all of the above mentioned properties, succinylcholine remains the relaxant of choice in most intubation procedures in emergency settings.[1,2,20]

Succinylcholine must be avoided after the first 24 hours in patients with burns and after 72 hours in patients with acute denervation syndromes or polytrauma. In these cases, muscle nicotinic receptors *upregulate*, leading to an exaggerated hyperkalemic response, particularly in cases of rhabdomyolysis.[1-3] It causes an increase in serum potassium of up to 0.5 mEq/L.[3] Succinylcholine causes masseter muscle rigidity in 0.3 to 1% of pediatric patients. Such condition, if severe, can be an early sign of malignant hyperthermia.

Another relative contraindication includes patients with intracranial or intraocular pressure; there is much controversy on the matter.[1,2] The risks versus benefits of its use must always be measured, considering that there is no conclusive evidence for this contraindication.

Succinylcholine may induce arrhythmias, the most frequent of them being bradyarrhythmias, which justifies the use of atropine as pre-medication in children.[2,3,5]

Nondepolarising

Nondepolarizing neuromuscular blocks are competitive antagonists of acetylcholine receptors and are an alternative to succinylcholine. They are also called steroidal relaxants.

Rocuronium is one of the most used in the clinical practice. It derives from vecuronium and is the nondepolarizing neuromuscular relaxant with the fastest onset of action. It blocks the binding of acetylcholine to the nicotinic receptor. Rocuronium is the drug of choice when succinylcholine is contraindicated. In 0.6 mg/kg doses it has an onset of action of about 90 seconds and duration of 45 minutes in infants and 27 minutes in children; in higher doses, such as 1.2 mg/kg, the onset of action is 30 seconds and average duration is 53 minutes.[1] Intubation conditions are described as the same as with acetylcholine in some of the literature[24], but a review by Cochrane in 2008[25] comparing intubation conditions ranks succinylcholine as superior if lower doses are used, but shows no difference when 1.2 mg/kg doses of rocuronium are used, bearing in mind that with that dose the duration time increases.

Since neuromuscular junctions in young patients are insufficient, steroidal relaxants have a longer time of action with higher doses,[20] which extends even more the blocking time when they are used. In cases of presumed difficult airways, they must be avoided. Neuromuscular blocking induced by rocuronium may be completely antagonized by acetylcholinesterase inhibitors such as neostigmine.

CONCLUSION

Rapid sequence intubation must always be the method of choice for intubation in emergency situations. The steps must be remembered for a safe procedure and materials must always be checked before initiating the RSI. It is important that emergency room pediatricians know the drugs available to them as well as their indications and contraindications so that they are able to choose the best option according to the clinical scenario of each child. The use of muscle relaxants should not be disregarded, especially because they facilitate TI conditions and also cause less airway lesions and other complications.

Table 2 - Steps for endotracheal intubation of children and adolescents

Steps	Actions
Check materials	Check necessary equipment and connections; Calculate the doses for pre-medication, sedatives, and neuromuscular relaxants available at the facility; Arrange for cardiac arrest sheet to be filled out.
Monitor	Wrist oximetry and ECG.
Maintain Airways	Open airways and position head; Suction secretion; If possible pre-oxygenate with non-rebreather mask or other high flow device (ex. HOOD for infants); Ventilate with mask and ventilation unit connected to the oxygen source if necessary (ex. apnea before administering all medication); Check for chest expansion, auscultation, and saturation measures.

To be continued…

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Table 2 - Steps for endotracheal intubation of children and adolescents

Steps	Actions
Pre-medication	**Atropine** (indicated for children aged less than one year, for children aged 1-5 years when succinilcoline is administered, or for older children if a second dose of succinilcoline is administered). Also indicated for septic shock; Hemodinamically stable patient: administer **fentanil** as an analgesic (consider smaller doses if instability is noticed); Administer **lidocaine** for head trauma or increase in intracranial pressure.
Sedatives	**Normotensive patients:** midazolam or etomidate or propofol or thiopental or ketamine; **Hypotensive or hypovolemic patients:** etomidate or ketamine (if not available, use midazolam at lower dosage). Remember that the best choice for septic shock is ketamine; **Patients with head trauma or epileptic state:** normotensive: thiopental or midazolam or propofol or etomidate; hypotensive: etomidate or midazolam at low dosage; **Severe asthma patients:** preferably ketamine. Midazolam and the others are options.
Neuromuscular blocker	First choice: succinylcholine; Options: preferably rocuronium. Pancuronium and veruronium may also be used.
Intubation procedure	Position patient in supine position with up to 5 cm of head elevation with padding for older children and adults; for children below 3 years of age the padding must be used on the shoulders. The ideal position is that in which the auditory meatus is aligned with the sternum; Perform direct laryngoscopy: the right hand extends the head in cases of suspected spine trauma; Hold the laryngoscope with the left hand, push the tongue to the left and introduce the blade towards the medial line of the base of the tongue. The laryngoscope handle is twisted upwards and forward at a 45o angle. Suction the secretion from airways, if present. Introduce the tube between the vocal chords and if necessary use the guide wire; Ventilate with ventilation unit; The procedure should last 30 seconds at most, or less in cases of loss in saturation or heart rate.
Checking	Check if the tube position is adequate; inspection, auscultation, ventilation, elevation of heart rate and saturation measurement. If possible, x-ray; Attach the tube adequately and write on the medical record the tube number used, mark where it was attached and how the procedure happened; Supply the patient with respiratory support.

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