Rapid sequence induction/intubation controversies

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Abstract

Backgrounds: Since its first definition and publication on 1970, Rapid Sequence Induction / Intubation (RSI) technique has been accepted globally as the “standard” for doing rapid intubation after induction of anesthesia for patients with high risk of aspiration, especially in emergency situation. However, this technique is not so much a “standard” as there are numerous variations on its practice based on national surveys. Anesthesia providers have their own opinions on the practice of RSI components which need to be discussed to assess their advantages and disadvantages, while there has been no review article which discussed these controversies in the last ten years.

Objectives: To review the technique differences within RSI protocols.

Methods: Online databases were searched, including MEDLINE and COCHRANE for each step in the original RSI protocol using keywords such as: “rapid sequence induction” or “rapid sequence intubation” or “RSI” and “controversies” or “head position” or “cricoid pressure” or “neuromuscular blocking agent” or “NMBA” or positive pressure ventilation” or “PPV”; and so on. Articles were then sorted out based on relevancy.

Results and conclusion: Supported by new evidence, RSI practices may differ in: the positioning of patient, choices of induction agent, application of cricoid pressure, choices of neuromuscular blocking agent, and the use of positive pressure ventilation. A more updated and standardized guideline should be established by referring and evaluating to these controversies.

Keywords
Rapid sequence induction, rapid sequence intubation, intubation, emergency

Introduction

First defined in written protocol and published in 1970, rapid sequence induction/intubation (RSI) technique was aimed to avoid regurgitation, vomiting, or aspiration while performing rapid tracheal intubation on patients with suspected full stomach during induction of general anesthesia or cardiopulmonary resuscitation. In their publication, the authors reported the use of RSI on 80 patients with suspected full stomach and recorded no event of regurgitation. Since the original publication, the technique has received acceptance globally as the standard procedure to perform rapid intubation on patients with high risk of aspiration. However, the practice of RSI in fact varies widely between anesthesia providers. Many components of the original RSI technique are indeed a matter of debate; therefore, this review aims to highlight and discuss these variations of practice to support the establishment of a more standardized protocol in the near future.

Head-up position controversy

In the original publication, patients undergoing RSI was positioned in a semi-sitting, V position, with their head being elevated 30° to prevent regurgitation, while their feet elevated to avoid hypotension. In practice, a recent national survey study reported that 76% of respondents performed RSI while applying 20°–25° head elevation, and 11% of respondents applied 45° head elevation. Since the original publication, the technique has received acceptance globally as the standard procedure to perform rapid intubation on patients with high risk of aspiration. However, this technique is not so much a “standard” as there are numerous variations on its practice based on national surveys. Anesthesia providers have their own opinions on the practice of RSI components which need to be discussed to assess their advantages and disadvantages, while there has been no review article which discussed these controversies in the last ten years.

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Theoretically, 30° head-up position is expected to place larynx in a position higher than lower esophageal sphincter (LES) to such a distance which is capable of preventing regurgitation materials to fall into the tracheobronchial tree in case of regurgitation. In addition, head up positions (11°–44°, inclined position, and =45°, upright position) have been reported to have higher first pass rate success compared with supine position.6 Head elevation 20°–35° has also been associated with improving functional residual capacity (FRC) in normal, pregnant, and obese patients, therefore improving pre-oxygenation and prolonging the time duration between apnea and desaturation clinically.7 Meanwhile, the opposition of this theory argues that aspiration cannot be avoided nevertheless if patient vomits because gastric content will fall into the larynx due to gravity; therefore, many studies have been done to observe the use of head-down and supine positioning instead during RSI.5

During head-down position, carina is positioned higher than the larynx; therefore, the position is expected to distance regurgitation materials from the trachea.9 A recent study using mannequin able to regurgitate demonstrated that –15° head-down position combined with full cervical spine extension (Sellick position) was able to significantly reduce aspiration events; however, visualization of the vocal cord was more difficult in this position and thus longer time was needed to intubate.9

Supporters of the supine position argue that intubation is made possible the fastest in this position and that it is safe enough as long as cricoid pressure is applied with the right technique.10 Another recent national survey (National Emergency Airway Registry—NEAR) also reported that majority (96.2%) of healthcare professionals at the Emergency Department performed intubation in supine position; only 5.8% performed intubation in head-up position which was most likely done to patients with suspected difficult airway or obesity.11 They also concluded that both supine and head-up positions had similar first pass rate.11

There has been no study that directly compares the incidence of regurgitation or aspiration while performing RSI using the three different positionings, but generally head-up and supine positions are more commonly used. Current literature revealed controversial results and further studies are required to determine the absolute best position for RSI.

**Induction agent controversy**

Based on the original publication, thiopental was used as the induction agent for RSI with satisfying results.1 However, based on a national survey in the United Kingdom, the most commonly used induction agent for RSI in practice nowadays is in fact propofol, with as many as 64% of respondents opted to use it.4

Ideally, the most suitable induction agent for RSI is an agent with fast onset and predictable pattern in achieving loss of consciousness (LOC) and avoiding awareness, capable of improving quality of intubation condition, has minimal hemodynamic effects, and capable of blunting the sympathetic response toward laryngoscopy and tracheal intubation.3 Thiopental, as used in the original protocol of RSI, has potentially fatal hemodynamic side effect as reported by a study comparing the use of thiopental, fentanyl, and midazolam as induction agents for RSI, where 93% of the subjects in the thiopental group was successfully intubated within 2 min of muscle paralysis but experienced an average of 38 mmHg fall of systolic blood pressure.12 Therefore, many research has been done to find the most optimal induction agent for RSI instead of thiopental.

Based on hemodynamic stability and minimal side effects, midazolam and the combination of ketamine–midazolam were concluded to be better than thiopental or ketamine.13 Etomidate, due to its minimal respiratory and cardiovascular side effects compared with propofol, midazolam, and ketamine, is considered the drug of choice when even the slightest hemodynamic change cannot be tolerated.14 Etomidate also has protective effects on the brain, therefore also made the drug of choice for head-injured patients.14 However, it was reported to cause adnenocortical suppression, therefore not indicated in septic patients.15,16 Ketamine has been proposed as an alternative for critically septic patients instead.16 On the other hand, when comparing induction agents based on the intubation condition produced and neuromuscular blocking agent (NMBa) used, propofol was reported to be superior compared with etomidate17 and thiopental18 when rocuronium 0.6 mg/kg was used.

The variety of induction agents used for RSI is therefore accounted to the clinical scenario faced, the patient’s condition, and NMBa used.

**Cricoid pressure controversy**

The original publication of RSI stated that cricoid pressure (CP) was to be applied right after sedation was injected or at the onset of LOC.1 CP was first described by Sellick in 1961, where using cadaver he showed that applying pressure toward cricoid cartilage backward against the cervical vertebra could occlude the esophagus, therefore preventing regurgitation into the pharynx.19

In contrast, however, reports showed that fatal regurgitation and aspiration had occurred even when CP was applied.20,21 In defense of CP, incorrect application technique of CP, mistiming of the application, and/or lack of force given during application have been accused as the reasons for failure to prevent regurgitation.22,23 In his original publication, Sellick did not mention the exact amount of force needed to apply CP optimally19; however, a study recommended the application of 10 N (1 kg) of force toward conscious patient and gradually increased to 30 N (3 kg) at the time of LOC.24

Nevertheless, several studies still argued that even when applied correctly, CP increased aspiration risk instead of
reducing it because its application of 20 N force decreased LES tone from 24 to 15 mmHg, and further decreased LES tone to 12 mmHg when 40 N of force was applied.\textsuperscript{25} Complication of CP should also be considered, which include esophageal rupture,\textsuperscript{26} cricoid cartilage fracture,\textsuperscript{27} and difficulty in laryngoscopy visualization.\textsuperscript{28}

Radiography studies also play a role in the CP debate. A study using computed tomographic (CT) scans reported that nearly half the subjects studied had lateral displacement of the esophagus, meaning the esophagus was actually not in line with the cricoid cartilage.\textsuperscript{29} The authors then did another study using magnetic resonance imaging (MRI) to compare the anatomy of subjects before and after CP application.\textsuperscript{30} They revealed that 52.6\% of subjects had lateral displacement of the esophagus before CP was applied, and 90.5\% after CP was applied.\textsuperscript{30} Another study using MRI, however, concluded that the anatomical position of esophagus was not entirely relevant because in fact it was the hypopharynx that was directly located beneath the cricoid cartilage.\textsuperscript{31} The study also revealed that CP application reduced the anteroposterior diameter of hypopharynx up to 35\%; therefore, the technique was still deemed relevant to prevent aspiration.\textsuperscript{31}

Another study compared the effect of CP application toward aspiration risks in patients prone to microaspiration (gastroesophageal reflux disease, obesity, and diabetes mellitus) undergoing elective endotracheal intubation.\textsuperscript{32} They reported that there was no evidence of difference between the group of patients given CP and the group of patients who were not.\textsuperscript{32} It is important to note, however, that the study was observing aspiration risks in elective patients prone to microaspiration, not in emergency patients with actual full stomach. Meanwhile, meta-analysis and review studies concluded that current literatures showed unconvincing benefit of applying CP to prevent aspiration during RSI.\textsuperscript{33,34}

While there is a recent randomized controlled trial (RCT) showing similar rate of pulmonary aspiration with or without cricoid pressure, it failed to demonstrate the non-inferiority of the placebo.\textsuperscript{35} It did, however, concluded that CP increased difficulty of tracheal intubation, proven by longer intubation time and higher grade of Cormack and Lehane classification system in the CP group.\textsuperscript{35} Meanwhile, an RCT comparing aspiration syndrome between CP application with the ideal force (30–40 N) and the standard force (unmeasured) is still ongoing.\textsuperscript{36} Application of CP is therefore still a highly debatable topic although no longer routinely recommended.

**NMBA controversy**

Among patients with high risk of regurgitation or vomiting that leads to aspiration, the time period between anesthesia induction and tracheal intubation must be kept as minimum as possible. NMBA is given to facilitate the process of intubation by decreasing the risks of airway trauma and creating a good intubation condition.\textsuperscript{37} NMBA was also reported able to decrease prevalence of hypoxemia and complications related to emergency intubation (esophageal intubation, endobronchial intubation, dental trauma, traumatic intubation, and aspiration).\textsuperscript{38}

In the original protocol, NMBA used for RSI was succinylcholine chloride given intravenously with the dose of 100 mg/70 kg of body weight (BW).\textsuperscript{1} The suggested dose, equal to 1.43 mg/kg BW, actually far exceeded the effective dose of succinylcholine, which is less than 0.3 mg/kg BW.\textsuperscript{39} A prospective, randomized, double-blind study involving 200 patients compared the use of succinylcholine 0.3 mg/kg BW, 0.5 mg/kg BW, 1 mg/kg BW, and normal saline (control) to provide acceptable intubation conditions within 60 s.\textsuperscript{40} They concluded that the use of succinylcholine significantly produced more acceptable intubation condition compared with saline, but there was no significant differences between the groups of different succinylcholine doses (92\%, 94\%, and 98\% of patients achieved acceptable intubation condition after given 0.3, 0.5, 1 mg/kg BW of succinylcholine, respectively).\textsuperscript{40} Another experimental study comparing the use of succinylcholine 0.45, 0.6, and 1 mg/kg BW among patients requiring emergency intubation concluded that intubation was 100\% successful in all three groups.\textsuperscript{41} Increased dose of succinylcholine, however, was associated with faster onset, longer duration of action, as well as more obvious abdominal fasciculation.\textsuperscript{41} Similarly, a prospective, randomized, double-blind study involving 180 patients with a suspected difficult airway studied the effects of succinylcholine 0.3, 0.6, and 1 mg/kg BW for tracheal intubation reported that good and excellent intubation condition were achieved in 80\%, 91.7\%, and 93.3\% of patients given succinylcholine 0.3, 0.6, and 1 mg/kg BW, respectively. Therefore, succinylcholine 0.6 mg/kg BW produced similar intubation condition to 1 mg/kg BW; however, recovery of spontaneous respiration after succinylcholine 1 mg/kg BW was significantly longer.\textsuperscript{42}

Due to its rapid onset (~1 min) and recovery, succinylcholine is still the first drug of choice for RSI.\textsuperscript{43} Succinylcholine can also create a good intubation condition within 1 min, despite the depth of anesthesia.\textsuperscript{43} Compared with succinylcholine, other NMBA such as rocuronium requires certain depth of anesthesia to create a good intubation condition.\textsuperscript{43}

Unfortunately, succinylcholine has several potentially fatal side effects. Injection of succinylcholine produces uncontrolled muscle movement and fasciculation which increase intragastric pressure up to 40 cmH\textsubscript{2}O in adult patients, although this side effect can be minimized using non-depolarizing muscle relaxant defasciculating dose.\textsuperscript{43} Succinylcholine also causes increased tone of masseter muscle, reaching its maximum effect when fasciculation ceases; therefore, intubation can only be done 20–30 s afterward.\textsuperscript{43} But the most potentially fatal side effect of succinylcholine is acute hyperkalemia.\textsuperscript{44} Hyperkalemia is
more likely to be found among patients with muscle inflammation or trauma, thermal trauma, disse use atrophy, use of long-term muscle relaxant, upper or lower motor neuron defect, and severe infection. These patients experience an upregulation of nicotinic acetylcholine receptors in the muscle, injection of succinylcholine will depolarize them and cause the efflux of intracellular potassium to the plasma, causing hyperkalemia. Due to these side effects, another NMBA, rocuronium, is fastly studied and recommended to replace succinylcholine for RSI when succinylcholine is contraindicated or unavailable.

Rocuronium, however, has its own limitations. For one, the use of rocuronium to produce good intubation condition is dependent on the choice of induction agent. Propofol and etomidate with fentanyl pre-medication were reported to produce the best intubation condition when rocuronium was used. The optimum dose of rocuronium for RSI itself is a matter of debate. Rocuronium 0.6 mg/kgBW with propofol as the induction agent was reported to be suitable as an alternative NMBA for RSI when succinylcholine is contraindicated. Meanwhile, another study showed that the use of higher dose of rocuronium (1.2 mg/kgBW) produced faster onset (55 s), which was similar to the average of succinylcholine onset (50 s). One of succinylcholine’s characteristics is its short duration of action, which is uniquely valuable for RSI. Short duration of action means rapid recovery of spontaneous respiration, which gives succinylcholine superiority in “cannot intubate, cannot oxygenate” situations. Rocuronium, a non-depolarizing muscle relaxants, instead can even cause post-operative residual curarization which may lead to, among other things, respiratory insufficiency. However, studies have suggested that this limitation might be able to be redeemed by using sugammadex, a selective relaxant binding agent, which can reverse rocuronium’s neuromuscular blocking actions selectively.

A number of studies comparing the use of succinylcholine and rocuronium as NMBA for RSI have been published. A systematic review study concluded that there was no difference in intubation condition between the two drugs when propofol was used as the induction agent. An RCT study also reported that there was no difference between the group receiving succinylcholine and the group receiving rocuronium in the incidence and severity of desaturation, quality of intubation condition, and incidence of failure to intubate among patients undergoing RSI in the intensive care unit. A more recent systematic review concluded that succinylcholine was superior to rocuronium in creating a good intubation condition, but because the levels of bias and heterogeneity were high, the level of evidence from that conclusion was only moderate.

In general, succinylcholine is still the first choice of NMBA for RSI. However, rocuronium has been widely accepted as a suitable alternative to succinylcholine when it is contraindicated or unavailable.

The ban of using positive pressure ventilation (PPV) controversy

The original protocol of RSI advised to avoid using PPV. Allowing the use of PPV is feared to cause gastric inflation which may lead to pulmonary aspiration. The supporters of this theory argue that pre-oxygenation should be enough to provide adequate oxygen reserve while intubation is attempted, because the window period between LOC and intubation has always been aimed to be as short as possible.

On the other hand, some argue that providing ventilation just before attempting intubation is essential to prevent desaturation, especially in groups of patients with high oxygen consumption or low FRC who cannot optimally take advantage of pre-oxygenation, thus some RSI providers still apply ventilation during RSI. Ventilation just before intubation is also deemed necessary when NMBA used is not succinylcholine, because the onset and duration of action will be longer.

Gentle mask ventilation (inspiratory pressure < 20 cmH₂O) is suggested to be acceptable before intubation. Indeed even without application of CP, providing bag-mask ventilation with inspiratory pressure < 15 cmH₂O did not cause gastric inflation. With the help of CP, gastric inflation was not found when airway pressure was up to 45 cmH₂O.

Up to date, there has been no study published comparing the incidence of regurgitation or aspiration in patients who received PPV and those who did not right before intubation during RSI. However, some have suggested that providing gentle mask ventilation might be considered especially for patients who are unable to receive optimal pre-oxygenation.

Conclusion

As a summary, head-up and supine positions are more commonly used than head-down position during RSI even though there has been no study comparing the effectiveness of the three directly; the choice of induction agent is adjusted based on the clinical scenario, patient’s condition, and NMBA used; application of CP is still widely used though no longer routinely recommended while the relevant studies are unavailable or still ongoing; the first choice of NMBA for RSI is still succinylcholine, while rocuronium is accepted as a suitable alternative; and finally providing PPV may be considered for patients with high risk of desaturation even after pre-oxygenation. Obviously, plenty still need to be done before establishing a more standardized protocol for RSI, preferably starting from evaluating these controversies using relevant studies.

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