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PREMEDICATION DURING RAPID SEQUENCE INTUBATION: A Necessity or Waste of Valuable Time?

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INTRODUCTION

Every day, thousands of patients who present to emergency departments (EDs) require tracheal intubation for optimal care. Most acute intubations are performed using rapid sequence intubation (RSI), with the administration of an intravenous sedative followed by a paralytic agent, to obtain the best chance for successful intubation. Premedication with various agents prior to RSI when certain conditions are present is recommended by experts in acute airway management, as well as by many authors of major emergency medicine textbooks and advanced airway instructional courses. This premedication is touted as a way to limit physiologic responses to intubation that may adversely affect the patient. Despite expert opinions in favor of premedication, a paucity of data in the literature supports these practices. This fact, combined with the chaos, anxiety, and confusion often associated with securing a critical airway, can cause the physician performing RSI to question whether the administration of additional medications is truly essential or simply an unnecessary and burdensome measure.

The central nervous, respiratory, endocrine, and cardiovascular systems all respond in various ways to laryngoscopy and tracheal intubation (LTI), and many of these responses can be harmful. See Table 1. LTI stimulates the sympathetic nervous system which causes release of catecholamines and an increase in mean arterial pressure, heart rate, myocardial and cerebral oxygen consumption, cerebral blood flow, intraocular pressure (IOP), and intracranial pressure (ICP). Laryngospasm, bronchospasm, cough, and dysrhythmias can also result. In children, LTI will often lead to a paradoxical bradycardia due to stimulation of the vagus nerve. These physiologic responses are worsened by prolonged and aggressive LTI attempts, as well as by stimulation of the carina with the endotracheal tube. In theory, these responses could adversely affect patients

Table 1. Physiologic responses increased by laryngoscopy and intubation

-
- Blood pressure
 - Pulse
 - Cerebral oxygen demand
 - Myocardial oxygen demand
 - Cerebral blood flow
 - Intracranial pressure
 - Intraocular pressure
 - Laryngospasm
 - Bronchospasm
 - Cough
 - Dysrhythmia
-

with such conditions as myocardial ischemia, aortic dissection or aneurysm, head trauma, ocular trauma, traumatic bleeding, asthma, and chronic obstructive pulmonary disease (COPD). See Table 2.

Table 2. Conditions for which pre-medication may be beneficial

-
- Myocardial ischemia
 - Aortic dissection
 - Aortic aneurysm
 - Head trauma
 - Ocular Trauma
 - Traumatic bleeding
 - Asthma
 - Chronic obstructive pulmonary disease
-

“LOAD”: Premedication To Prevent Potentially Harmful Physiologic Responses

Efforts to premedicate for RSI and prevent detrimental responses to LTI center on the use of four medications or classes of medications. The mnemonic “LOAD” may be used to recall the pre-medication cocktail consisting of lidocaine, opiates (largely fentanyl), atropine, and defasciculating neuromuscular blocking agents. These agents are believed to hold the best hope for preventing adverse physiologic responses to LTI. Recommendations are to administer pre-medications three minutes prior to intubation. See Table 3.

Table 3. Medications used in premedication during rapid sequence intubation

Medication	Dose
Lidocaine	1.5 mg/kg intravenously
Fentanyl	3 mcg/kg intravenously
Atropine	0.02 mg/kg intravenously (minimum dose 0.1 mg, maximum dose 1 mg)
Rocuronium	0.06 mg/kg intravenously
Vecuronium	0.01 mg/kg intravenously

Available data show that these agents are used much more frequently in the United States (US) than in the United Kingdom (UK). Interestingly, this difference in practice pattern prompted much of the research done in this area. A survey of US emergency medicine residency program directors done in 1995 illustrated that of the programs that responded, 87% used lidocaine, 81% used defasciculation, and 49% used fentanyl when performing RSI in adults with elevated ICP.¹ In a UK review of 60 emergency intubations, of which only 26% were performed by emergency physicians, no patients received lidocaine or defasciculation.² This variation in practice patterns exemplifies the lack of consensus opinion and evidential support.

LIDOCAINE

Lidocaine premedication is used to limit rises in intracranial pressure, intraocular pressure, bronchospasm, dysrhythmia, and cardiovascular responses, such as elevated heart rate and blood pressure. Regardless of the clinical indication or age of the patient, it is given at a dose of 1.5 mg/kg intravenously three minutes before intubation. It has never been shown to produce an adverse effect.³

Despite its history of safety, little evidence supports premedication with lidocaine to prevent rises in ICP when performing RSI. In 2001, Robinson and Clancy published an evidence-based medicine review that addressed whether pretreatment with intravenous lidocaine leads to an improved neurological outcome in patients with head injury undergoing RSI. They found no direct evidence that answered their query. However, six studies did partially address their question. These particular studies were performed in patients with intracranial pressure monitors in place in an intensive care unit (ICU) or operating room (OR). None of the studies involved ED patients. They were limited in size, with the largest involving only 22 patients. All either used intubation in the OR with induction medications not commonly used in the ED or endotracheal suctioning in the ICU as the noxious stimulus. Again, none used RSI in the ED. None of the studies focused on long-term outcomes of clinical importance, such as improved disability or reduced mortality. No studies were found that examined the use of lidocaine in children.^{4,5}

Intraocular pressure is raised by a number of factors often present during RSI, including succinylcholine, LTI, and patient movements such as coughing, gagging, crying, or combative behavior. One study showed that premedication with lidocaine given at 2 mg/kg significantly attenuated the rise in IOP associated with intubation, but the importance of this rise in IOP, which averaged 5.5 mmHg, is unclear.⁴ No reports of vitreous extrusion following RSI with succinylcholine have ever been reported.⁶

Substantiation for the use of lidocaine to reduce bronchospasm in response to LTI is also minimal and conflicting. One study showed a reduction in bronchospasm when patients were exposed to inhaled histamine rather than LTI.⁷ The only study that examined bronchospasm in LTI showed no benefit to premedication with lidocaine.⁸ Once again, no long-term outcomes were examined in either study, and minimal pediatric data were collected.

Lidocaine has also been used to limit the hemodynamic responses to LTI. In 1994, Lev and Rosen performed a review of the literature and found that eight of 25 studies showed suppression of tachycardia and hypertension; seven showed suppression of tachycardia only, and 10 showed no benefit. Fentanyl, another agent used to limit this response, has shown a more consistent ability to limit hemodynamic surges from LTI.^{3,9-12}

Several studies have demonstrated that lidocaine can prevent dysrhythmias and electrocardiographic (ECG) changes induced by LTI. The most common dysrhythmias and ECG changes included premature atrial and ventricular contractions, ST-segment depression, and T-wave inversions. All of these are usually transient and of questionable clinical significance. No studies demonstrated adverse long-term

outcomes associated with the occurrence of these transient reactions to LTI.³

Overall, compelling evidence exists advocating the safety of lidocaine when used in premedication prior to RSI, but little or conflicting evidence suggests it has a definite and important clinical effect in preventing hemodynamic surges, bronchospasm, rises in intracranial pressure, or dysrhythmias induced by LTI.

OPIOIDS (FENTANYL)

Although fentanyl is poor at preventing the tachycardia from LTI, its status as the most effective agent to reduce the hypertension associated with LTI has been documented in multiple studies with LTI in the OR.⁹⁻¹² The typical dose is 3 mcg/kg of fentanyl intravenously three minutes prior to intubation. It is usually advocated for patients in whom hypertension can be particularly dangerous, such as those with elevated ICP, intracranial hemorrhage or cerebral aneurysm, ischemic heart disease, and aortic aneurysm or dissection. No studies examined long-term benefits associated with its use.

Fentanyl is a powerful agent that must be dispensed appropriately. It should be the last premedication agent prescribed, as it has the potential to cause hypotension, and should be administered within a 30- to 60-second timeframe. Doses greater than 5 mcg/kg have been associated with hypotension in 11 to 45 percent of patients.¹⁰ Consequently, caution must be used when it is given to patients with hypotension or hypovolemia. Muscular rigidity associated with fentanyl is associated with rapidly administered doses greater than 500 mcg. Adhering to slow administration and doses of 3 mcg/kg should prevent these complications.

Esmolol is another agent sometimes used to blunt the hemodynamic response to LTI.¹³ Although effective in reducing the occurrence of both hypertension and tachycardia (unlike fentanyl), it has an increased incidence of adverse effects, such as negative inotropy and bronchoconstriction, when compared with fentanyl. Its clinical use, therefore, is limited.

ATROPINE

Bradycardia is thought to arise when children are intubated due to stimulation of the vagus nerve by LTI. Succinylcholine may also cause a drop in heart rate. Most major pediatric emergency texts and airway courses recommend 0.02 mg/kg of intravenous atropine three minutes prior to intubation with succinylcholine to prevent this bradycardia in all children between 5 to 10 years of age. According to the literature, most studies that support its use were conducted in the OR and involved repeat dosing of succinylcholine, a practice that is rare and not recommended in the ED.

The largest study examining the use of atropine as a premedication was a retrospective review of 143 pediatric ED intubations. Sixty-eight patients in this study received atropine prior to intubation, while 75 received no premedication. Bradycardia was a rare event: only six patients developed the condition, three from each group. There was no statistically significant difference in the occurrence of bradycardia between children who did and did not receive atropine. There was, however, a statistically significant difference in rates of hypoxia. Twenty-eight percent of the atropine group versus 16% of the non-atropine group ($p = 0.046$) became hypoxic.¹⁴

These results suggest that atropine administration, although uniformly recommended, may not be necessary. Bradycardia is a relatively rare phenomenon, and atropine may not offer protection against its occurrence. This recommendation has never been subjected to randomized clinical trials in the ED, causing some to question the necessity of this step.¹

DEFASCICULATION MEDICATIONS

Some evidence demonstrates that the administration of succinylcholine raises ICP. Traditionally, premedication with a non-depolarizing neuromuscular blocking agent three minutes before RSI with succinylcholine was recommended in patients who might be adversely affected by a rise in ICP. Pretreatment agents commonly used are 0.06 mg/kg of rocuronium and 0.01 mg/kg of vecuronium administered intravenously.

Most of the evidence supporting the use of these agents comes from intubations in the OR. One study looked at 12 patients undergoing craniotomy for tumor excision: six received a pretreatment dose of metocurine, a non-depolarizing neuromuscular blocker, and six received a placebo prior to intubation with 1 mg/kg of intravenous succinylcholine. The placebo group experienced a rise in ICP of 11 to 23 mmHg, while the ICP did not rise in the metocurine group.¹⁶

Another study was done wherein 13 patients with brain tumors who were being mask ventilated were first administered succinylcholine, after which their ICP rose an average of 5 mmHg, with 5 patients rising 9 mmHg or greater. After the ICP measurements were recorded, the patients were intubated and stabilized until neuromuscular function returned to normal. They were subsequently given a full paralyzing dose of vecuronium, in contrast to a pretreatment dose, and were again given succinylcholine while already intubated. The pretreatment with a full paralyzing dose of vecuronium prevented the rise in ICP associated with the administration of succinylcholine. However, if the doses of vecuronium used in this study were applied to RSI, a

subsequent dose of succinylcholine would not be necessary, as the vecuronium alone would adequately paralyze the patient. In addition, the patients in this study had already been intubated prior to the vecuronium administration. Thus it was not a true premedication before intubation.¹⁷

While some evidence shows that defasciculation prevents rises in ICP associated with succinylcholine administration, the evidence is limited. In addition, pretreatment with defasciculating agents can rarely cause premature apnea before the physician is ready to intubate. If vecuronium is used, an additional step is needed, since reconstitution is required before its use.

As previously mentioned in the lidocaine subsection, the administration of succinylcholine has been associated with a rise in IOP of 3 to 8 mmHg.¹⁸ Defasciculation prior to the administration of succinylcholine in patients with penetrating ocular trauma has been recommended. However, there has never been a case report of vitreous extrusion in RSI with succinylcholine despite its extensive use. The clinical importance of these rises in IOP is unclear.⁶ In addition, patient movements such as coughing, gagging, or combative behaviors, have been associated with much higher elevations of IOP and are eliminated by the paralysis induced during RSI.¹⁸

SUMMARY

Although premedication when performing RSI is often recommended, data supporting the use of these agents are limited. Very few studies have been performed using acute intubations with RSI in the ED, and no improvement in outcomes has ever been demonstrated. When physicians performing RSI decide to include premedication in their regimen, a number of standard references can be found supporting their practice. Physicians who perform RSI with a simpler approach, electing not to utilize premedication, should also feel validated, as there is a lack of research demonstrating improved clinical outcomes associated with premedication in RSI. Randomized, placebo-controlled clinical trials addressing important outcomes, such as neurologic function or death, in patients undergoing RSI in the ED are needed to examine the utility of premedication during RSI.

The views expressed in this article are those of the author and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

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