Airway Series: Induction Medications

Introduction

1. Rapid sequence intubation (RSI) is a process whereby an induction agent and a neuromuscular blocking agent are given in rapid succession to facilitate endotracheal intubation
2. 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
3. Etomidate remains the most commonly used induction agent, however, it is not without its own pharmacologic considerations
4. The use of ketamine is continuing to rise especially due to its unique pharmacologic profile and its niche is becoming prevalent in situations where the risk of hypotension is significant

Pharmacology			
	Etomidate	**Ketamine**	**Propofol**
Dose	0.3 mg/kg IV	1-2 mg/kg	1.5-2 mg/kg
Administration	IV push	IV Push	IV push
Formulation	20 mg/ 10 ml vial	Prefilled 50 mg/5 ml Syringe	1000 mg/100 ml vial
PK/PD	Onset: ~20 seconds Duration: 4-10 minutes Metabolism: Hydrolysis of the ethylester side Renal Excretion: 75%	Onset: ~ IV 30 seconds IM 3-4 minutes Duration: 5-10 minutes Metabolism: N- demethylation Renal Excretion: 91%	Onset: ~10-50 seconds Duration: 3-10 minutes Metabolism: CYP2B6 Renal Excretion: 88%
Adverse Effects	Injection site pain, nausea, vomiting, myoclonus	Hypertension, tachycardia, emergency phenomenon	Hypotension, bradycardia
Drug Interactions	No major reactions	No major reactions	No major reactions
Compatibility	Incompatible with vitamin c and vecuronium	Incompatible with furosemide, insulin, phenytoin, and sodium bicarbonate	Incompatible with methylprednisolone, phenytoin, and metoclopramide
Comments	There is hypothetical concerns about adrenal insufficiency with a single dose. **Hemodynamically neutral**	Rapid IV push my cause apnea, Option for delayed sequence intubation. **Increase BP and HR**	Large dose rapid doses can cause large **drops in HR and BP. Option for increase ICP**

Drug	Hemodynamic Effect	Comments
Etomidate	↔ BP, ↔ CO, ↔ HR, ↓ cortisol , ↔ ICP	Prolonged inhibition of steroid synthesis in the critically ill; withdrawn from number of countries
Ketamine	↑BP, ↑ HR, ↑ CO, ↔ cortisol, ↑↓ ICP	↔ or ↑ CPP and ↔ ICP with standard anesthetic management
Propofol	↓ BP, ↔ HR,↓ CO, ↔ cortisol, ↓ ICP	Hemodynamic compromise marked in elderly, ASA 3 or more or hypovolemic patients with 'standard' induction dose

Comments by ED Physician Attendings

	Pros	Cons
Ketamine	Ketmaine has some bronchodilatory properties and can be useful if intubating for asthma angioedema, airway narrowing from anaphylaxis, infection or malignant processes are the typical examples	The dose should be greatly reduced in shock states- most notably hypovolemic shock as it is a direct myocardial depressant There are some case reports of cardiac arrest when full induction doses of ketamine are pushed in these patients. In those patients I will push 10mg at a time until dissociation occurs (usually around 0.2-0.3 mg/kg in my experience).
Etomidate	Most commonly used unless there circumstance where the patient will not be paralyzed such as difficult airways such as angioedema, airway narrowing from anaphylaxis, infection or malignant processes	Very short duration of action is important- 3 to 5 minutes Etomidate with rocuronium can be a recipe for paralysis without sedation unless you are right on top of providing post intubation sedation
Propofol	Due to vasodilatory and anti-epileptic properties, propofol is most useful in hypertensive head bleeds and patients with status epilepticus those with enough BP to work with but titrate 10 mg at a time	Hypotension and bradycardia should be noted, especially in trauma patients

Overview of Evidence			
Author, year	Design/ sample size	Intervention & Comparison	Outcome
Dietrich, 2018	Retrospective review/ n=83	Propofol vs Non-propofol (etomidate or midazolam)	↑ **post-intubation hypotension** with propofol OR 3.64 (95% CI 1.16-13.24) **Similar rates of hypotension** were seen among patients who received ≤2 mg/kg and those receiving >2 mg/kg No significant differences between groups in **hospital length of stay or mortality**
Lyons, 2015	Cohort study/ n=261	Etomidate+ Succinylcholine (Group 1) vs Fentanyl+ ketamine+ rocuronium (Group 2)	Significantly better laryngeal views with fentanyl/ketamine/rocuronium group **100% first attempt intubation** with fentanyl/ketamine/rocuronium group ↑ **post-intubation MAP+ HR** with etomidate + succinylcholine
Bruder, 2015	Cochrane Review	Etomidate Midazolam Propofol Ketamine	There was **no difference** in mortality, hospital LOS, duration of ventilation, and duration of vasopressors Etomidate associated with ↑ **ACTH and ↓ in cortisol level**
Tekwani K, 2010	RCT/ n=122	Etomidate 0.3 mg/kg vs midazolam 0.1 mg/kg	**No significant differences** in median hospital LOS (9.5 vs 7.3 days), ICU LOS (4.2 vs 3.1 days), In-hospital mortality (26% vs 43%) or ventilator days
Jabre P, 2009	RCT/ n=469	Etomidate 0.3 mg/kg vs Ketamine 2 mg/kg	**No difference in intubating condition**, SOFA score, 28 day mortality, Vent free days, vasopressor support, or GCS
White, 1982	RCT/ n= 80	Ketamine1.5 mg/kg Thiopental 4 mg/kg Midazolam 0.3 mg/kg Midazolam 0.15 mg/kg + ketamine 0.75 mg/kg	Thiopental ↓ MAP by 11%, ketamine increased MAP by 10%, while neither midazolam nor the midazolam-ketamine combination significantly changed MAP Midazolam effectively attenuated both the cardiostimulatory responses and unpleasant emergence reactions associated with ketamine

References

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