



Pharmacy Friday Pearls

Brief pearls related to acute care pharmacology and evidence-based medicine

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Airway Series: Post-Intubation Sedation

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 immediate post intubation period in the ED is a critical time for continued patient stabilization.
3. While physical adjuncts like securing the tube, in line suctioning, and elevating the head of the bed are part of general post intubation management, post intubation analgesia and sedation is a key component to remember.
4. Depending on the paralytic used, clinicians can be eased into the assumption that the patient is tolerating the ventilator and not in need of sedation or analgesia
5. Administering analgesia and sedation is key to preventing patient awareness during paralysis and preventing PTSD

	Fentanyl (Sublimaze)	Propofol (Diprivan)	Midazolam (Versed)	Dexmedetomidine (Precedex)
Dose	Bolus: 0.35 to 1.5 mcg/kg IV every 0.5 to 1 hour Infusion: 25-300 mcg/hr	Bolus: Infusion: Titrate in 5-50 mcg/kg/min	Bolus: 0.5 to 4 mg Infusion: 1-10 mg/hr	Bolus: Not recommended Infusion: 0.1-1.4 mcg/kg/hr
Administration	IV Bolus + Infusion	IV Bolus + Infusion	IV Bolus + Infusion	IV Infusion
PK/PD	Onset: IV almost immediate Duration: 30- 60 min Metabolism: CYP3A4 Excretion: > 90% inactive metabolite renally eliminated	Onset: 10-40 sec Duration- 3-10 min Metabolism: Hepatic Phase II Excretion: Urine (~88% metabolites)	Onset: 3-5 min Duration: 30-80 min Metabolism: CYP3A4 (active metabolites) Excretion: 45% to 57% Renally eliminated (metabolites)	Onset: 15-30 min Duration: 4 hours Metabolism: Hepatic Phase II+ CYP2A6 Excretion:
Adverse Effects	Chest wall rigidity CNS depression	Hypotension, bradycardia, hypertriglyceridemia	Hypotension, respiratory depression	Hypotension, bradycardia
Drug Interactions	CYP 3A4 inhibitors, serotonergic agents	Bupivacaine, St. John's Wort	CYP 3A4 inhibitors, CNS depressants	CNS depressants and antihypertensive
Compatibility	Protonix	Calcium chloride, Nimbex, Cipro, gentamicin, phenytoin	Fosphenytoin, sodium bicarbonate, Zosyn, hydrocortisone	Protonix, phenytoin,

Comments per EM Physicians

Fentanyl	"I love fentanyl. short acting, quick action, has least hemodynamic effect of IV narcotics"
Propofol	"I'm a big propofol fan. It has reliable sedation, quick onset. The hypotension is not ideal but these are sick patients anyway so I'm ok with starting pressors or more fluid if they can tolerate it to keep up with adequate propofol dosing."
Dexmedetomidine	"I'm also a Precedex fan! It has same quick on, quick off. Bradycardia I've seen has been related to infusion rate, but we used to use it primarily as part of CIWA (GAWAS) protocol where I worked and it saved us many an intubation."
Midazolam	"Versed has an onset slower than I would like, especially if we have to bolus from the pump for acute agitation on the vent. Sometimes sedation is prolonged. In my practice it has less reliable in dose effects than propofol. I've seen people chew through a lot of versed without adequate sedation, but all of the side effects. I tend not to use it."

Overview of Evidence

Author, year	Design/ sample size	Intervention & Comparison	Outcome
Groetzing, 2018	Retrospective review/ n=91	Ketamine infusion 0.125 to 1.2 mg/kg/hr	63% of patients discontinue other sedatives or analgesic within 24 hours of initiating ketamine ↑ in the number of sedation scores at goal ↓ in agitation, defined as SAS >4, after the initiation of ketamine
Shehabi, 2018	Prospective Cohort/ n=703	Light Sedation vs Deep Sedation (using sedation intensity score)	Sedation intensity independently, in an ascending relationship, predicted increased risk of death, delirium, and delayed time to extubation
Fraser, 2013	Meta-Analysis/ n= 1,235 patients	Benzodiazepines Vs Non-benzodiazepines	Non-benzodiazepine sedatives associated with ↓ ICU LOS and ↓ Ventilator days
Amini, 2013	retrospective cohort study/ n=100	rocuronium-assisted RSI) + PharmD vs rocuronium-assisted RSI) - PharmD	PharmD associated with time to sedation 9 min vs 28 min PharmD associated with time to analgesia 21 min vs 44 min PharmD associated with sedation within 5 min 33% vs 11%
Watt, 2012	retrospective cohort study/ n=200	Succinylcholine 1.7 ± 0.7 mg/kg vs Rocuronium 1.3 ± 0.4 mg/kg	After intubation, 77.5% (n=155) of patients were initiated on a sedative infusion of propofol (n=148) or midazolam (n=7). Mean time to post intubation sedation was significantly greater with rocuronium compared to succinylcholine (27 min vs 15)
Shehabi (SPICE), 2012	Prospective Cohort/ n=251	Light Sedation vs Deep Sedation	4 hours after starting mechanical ventilation 76% of patients were deeply sedated RASS, -3 to -5 Early deep sedation was a significant independent predictor of death and time to extubation.
Jakob, 2012	RCT/ N=498	Dexmedetomidine 0.2-1.4 mcg/kg/hr Vs Midazolam 0.03-0.2 mg/kg/hr	Lighter sedation, fewer ventilation days
Strom, 2010	RCT/ n=140	No sedation (PRN morphine) vs Propofol or midazolam infusion + (PRN morphine)	No sedation group had ↓ ventilator free days, ↓ ICU and ↓ hospital LOS

References

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