

POST-INTUBATION ANALGESIA AND SEDATION

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Intubated patients experience pain and anxiety

- Mechanical ventilation, endotracheal tube
- Blood draws, positioning, suctioning
- Surgical procedures, dressing changes
- Awareness during neuromuscular blockade
- Invasive catheters
- Loss of control



Unrelieved pain and anxiety cause adverse effects

- Self-injury and removal of life-sustaining devices
- Increased endogenous catecholamines
- Sleep deprivation, anxiety, and delirium
- Impaired post-ICU psychological recovery
- Emotional and posttraumatic effects
- Ventilator dyssynchrony
- Immunosuppression

Treating pain and anxiety improves outcomes

- Use of pain and sedation scales in critically ill patients allows:
 - ▣ precise dosing
 - ▣ reduced medication side effects
 - ▣ reduced ICU and hospital length of stay
 - ▣ shorter duration of mechanical ventilation
- Analgesics should be provided first, then anxiolysis

- If you were intubated, how much lorazepam or midazolam, and fentanyl would you want per hour?



Intubated ED patients receive inadequate analgesia and sedation

- Retrospective study, tertiary ED
- 50% received no analgesia, 30% received no anxiolytic
- Of patients receiving postintubation vecuronium, 96% received either no or inadequate anxiolysis or analgesia
- Overall, 3 of 4 patients received no or inadequate analgesia and an equivalent number received no or inadequate anxiolysis

Analgesia: opioids

- Bind CNS and peripheral tissue receptors
 - Mu-1 receptors: analgesia
 - Mu-2 receptors: respiratory depression, vomiting, constipation, and euphoria
 - Kappa receptor: sedation, miosis, and spinal analgesia

Analgesia: opioids

- Provide mild anxiolysis, but no amnesia
- Help palliate coughing and subjective sense of dyspnea
- Little cardiovascular effect in euvolemic patients
 - ▣ In hypovolemic patients with reduced cardiac output, decreased venous return, reduced sympathetic tone, and reduction in heart rate can result in hypotension.

Morphine

- Poorly lipid soluble
- Slow onset (5-10 min)
- T_{1/2} 4 hrs
- Not preferred in hepatic or renal insufficiency
 - ▣ Resultant hepatic glucuronide metabolite is 20x more active than morphine
 - ▣ Eliminated renally

Remifentanil

- Highly lipophilic
- Rapid onset (seconds)
- $T_{1/2} = 3.2$ min
- Metabolized by widespread esterases to clinically inactive metabolites
- Relatively new drug; ICU use only
- Risk hyperalgesia and consequences of very abrupt withdrawal of analgesia

Fentanyl

- Highly lipophilic
- Rapid onset (1 min)
- $T_{1/2} = 1 \text{ hr}$
- Large volume of distribution into tissues
 - ▣ Risk of accumulation
- Good choice in renal insufficiency
 - ▣ Hepatic metabolism creates inactive metabolites which are renally excreted

Sedation

- Provide analgesia first
- Supplement with sedation
- Exception: during use of neuromuscular blocking agents
 - ▣ Deep sedation (amnesia) is required to avoid an awake but paralyzed patient.

Benzodiazepines

- Work on the neuroinhibitory γ -aminobutyric acid (GABA) receptor
- Anxiolytic, sedative, and hypnotic effects at increasing doses
- Antiepileptic properties

Benzodiazepines

- Two most common: midazolam and lorazepam
- Both lipophilic, although midazolam is more so in plasma (thus, more rapid onset (<1 min) than lorazepam)
- Hepatically metabolized via the CYP450 enzyme
- Lorazepam preferred in renal failure due to inactive metabolites, whereas midazolam metabolites are active
- Both generally safe and effective short-term sedatives
- ICU considerations
 - ▣ Accumulation in adipose tissues, propylene glycol toxicity from lorazepam vehicle, delirium

Sedation

- Worse outcomes with benzodiazepines compared to propofol or dexmedetomidine
 - ▣ Delirium, oversedation, delayed extubation, and longer time to discharge

Propofol

- Unclear mechanism; GABAergic and direct effects on the brain
- Powerful anxiolytic and amnestic
 - ▣ Provides no analgesia
- Lipophilic; onset in seconds to minutes
- Rapid (minutes) redistribution to peripheral tissues and a large volume of distribution

Propofol

- Preferred in traumatic brain injury
 - ▣ May decrease cerebral oxygen consumption
 - ▣ May reduces intracranial pressure
 - ▣ Antiepileptic
 - ▣ Allows for serial neurologic assessments due to rapidity of action, ease of titration, and lack of active metabolites
- Can cause hypotension, particular if in under volume-resuscitated patients
- ICU considerations
 - ▣ Hypertriglyceridemia, propofol infusion syndrome

Dexmedetomidine

- Central α_2 agonist
 - ▣ Similar to clonidine, but more specific for the receptor
- Lipophilic
- New sedative and analgesic without respiratory depression; provides lighter sedation
- Side effects
 - ▣ Bradycardia and hypotension
 - ▣ Can be mitigated by avoiding a loading dose and initiating a slow infusion rate
- ICU use

Ketamine

- Unique analgesic and anesthetic agent
- Phencyclidine derivative, produces a “dissociative” state
- Prevents bronchoconstriction induced by histamines
- Directly relaxes bronchial smooth muscle
- Multifactorial mechanism of action; acts centrally and increases catecholamine levels
- Lowers airway resistance, increases lung compliance, increases airway secretions
- Increase oxygenation, decreases hypercarbia
- Rapidly acting; plasma T $\frac{1}{2}$ 7-11 minutes, tissue T $\frac{1}{2}$ 2-3 hours
- Metabolized hepatically to active metabolites

Ketamine

- Due to sympathomimetic effects, contraindicated in hypertension, cardiovascular disease, high intracranial pressure (controversial), preeclampsia, glaucoma, and history of psychosis
- Other side effects: lowering of the seizure threshold, altered mood, delirium, laryngospasm, and aspiration
- Has been used for RSI and sedation in severe, decompensating asthmatics refractory to maximal medical therapies
- Infusion rate: 1 mg/kg/hr IV
- May need to treat hypersalivation with adjunctive atropine or glycopyrrolate

Recommendations



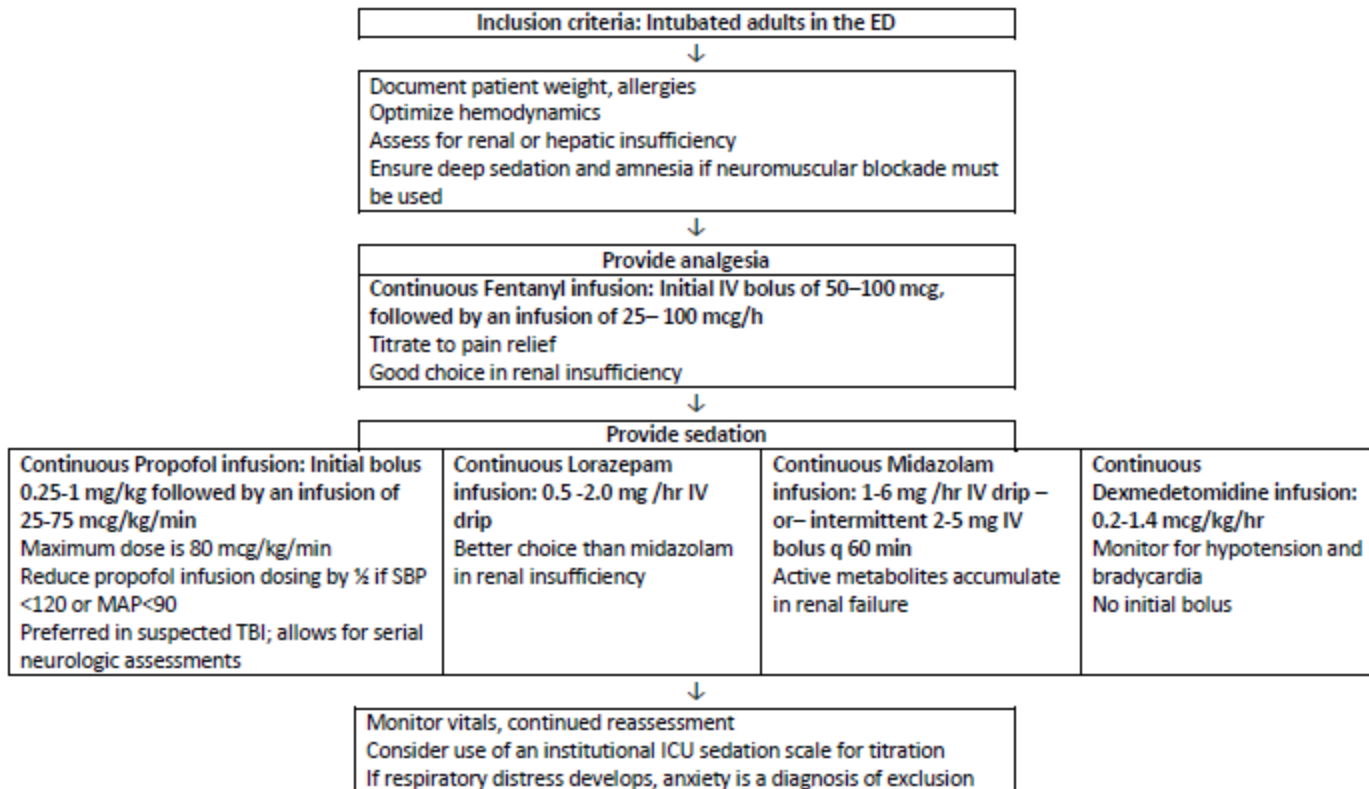
Analgesia

- Continuous Fentanyl infusion
 - ▣ Initial IV bolus of 50–100 mcg, followed by an infusion of 25–100 mcg/h
- Consider using an established sedation scale to monitor patient comfort (e.g. RASS)

Sedation

- Consider hemodynamics, renal or hepatic insufficiency
- Continuous infusions:
 - ▣ Propofol: initial bolus 0.25-1 mg/kg followed by an infusion of 25 – 75 mcg/kg/min
 - ▣ Lorazepam 0.5 –2.0 mg/hr IV drip
 - ▣ Midazolam 1-6 mg/hr IV drip or 2-5 mg IVP q 60 min
 - ▣ Dexmedetomidine infusion: 0.2-1.4 mcg/kg/hr

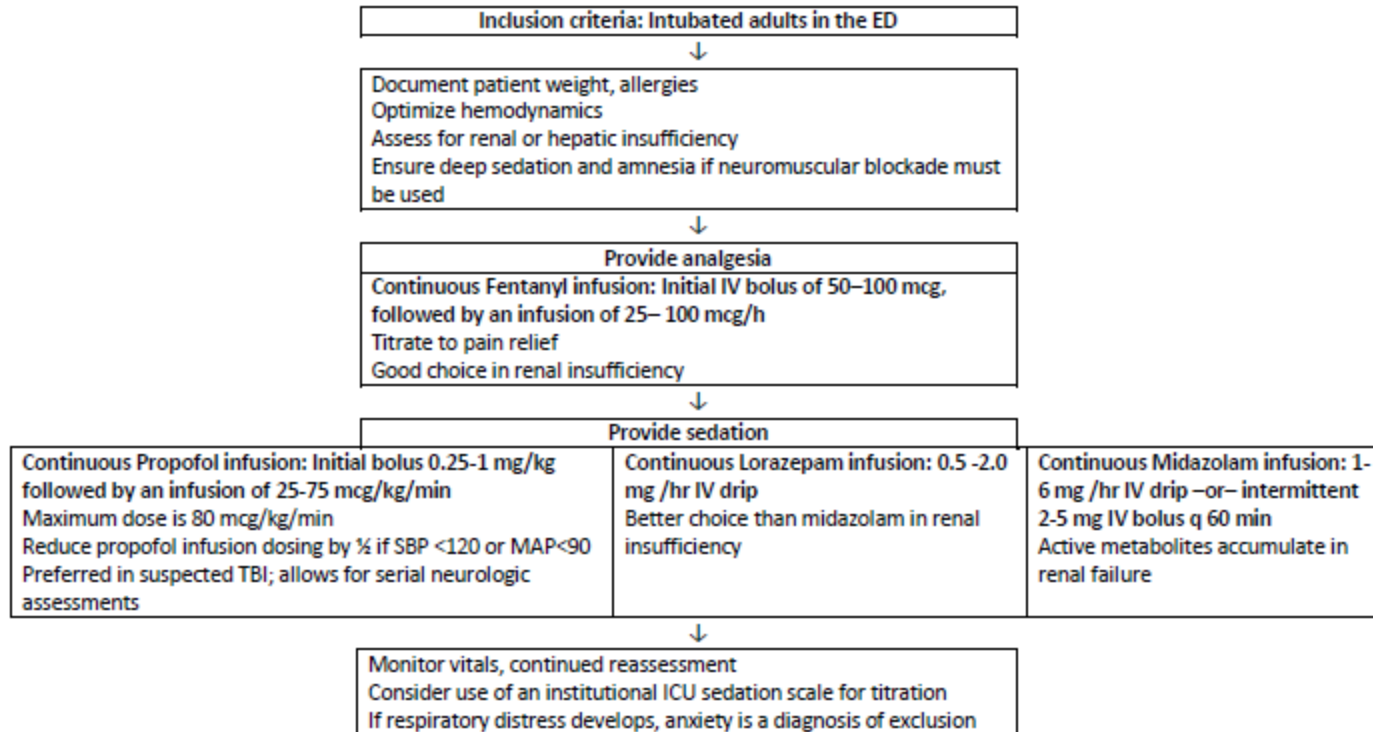
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This guideline was ratified by the emergency department faculty at Maine Medical Center in June 2012. It reflects our expert opinion and is not necessarily applicable to all institutions. It is intended to be a reference for clinicians caring for patients and is not intended to replace providers' clinical judgment.

Produced by Julie Pelletier, MD, and _____

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References

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