SI Pharmacology

her Brand, MD
Introduction

Sedatives

Paralytics

Adjunctive medication
Why RSI?

Predictions?

Who should do RSI?

What are the dangers?

What are the alternatives?
Ongoing sedation
Intubation
Paralytic
Induction

Rapid Sequence Induction

"
SI - Contraindications

Uncorrectable hypoxia
Difficult airway on exam
Profound instability
SI - Considerations

- Awareness
- Hemodynamics
- Ease of intubation
- Physiologic effects
- Adverse reactions
SI Pharmacology

Induction & Sedation

Paralytics
Induction/Sedation

- Render unconsciousness
- Reduce response to laryngoscopy
- Reduce metabolic demand
agents

Etomidate

Propofol

Benzodiazepines

Opiates

Ketamine

Barbiturates
tomidate

Unique anesthetic

Rapid acting

Hemodynamically stable
tomidate

mg/cc

0 and 40 cc vials

Abbojet (?availability)

in USA 1 year half life

Pregnancy Risk “C”
Commonly used
Predictable & seemingly safe
Falling into disfavor
Good: Hemodynamic stability
Bad: Adrenal suppression
Adrenal suppression:

- Sepsis
- Trauma
- ? any significant stressor
Single-Dose Etomidate for Rapid Sequence Intubation May Impact Outcome After Severe Injury

Keir J. Warner, BS, Joseph Caschieri, MD, Gregory J. Jurkovich, MD, and Eileen M. Budger, MD

Etomidate is an induction agent used for the rapid-sequence intubation (RSI) of trauma patients because of its favorable hemodynamic and respiratory effects. However, recent studies have shown etomidate to be associated with increased postintubation inflammation, potentially influencing outcomes for severely injured patients. We attempted to determine if etomidate may alter the occurrence of acute respiratory distress syndrome (ARDS) in injury victims.

We analyzed data collected prospectively from a blinded trial of patients undergoing RSI at two trauma centers. Patients were randomized to whether they did or did not receive etomidate for preintubation sedation. The incidence of ARDS was compared between the two groups by Fisher's exact test. Logistic regression was used to adjust for the influence of other known risk factors for ARDS.

Over a 1-year period, 50 trauma patients underwent RSI of which 45 received etomidate (90%). There were no significant differences in demographic, physiological, and injury severity scores, or use of preintubation analgesia between the groups. After adjusting for physiology, injury, and trauma factors, etomidate was associated with ARDS (OR 3.0, 95% CI 1.46–12.4)

Thus, Single-dose etomidate for RSI in severely injured patients may be associated with increased ARDS and multiple organ dysfunction syndrome, in part, because of an effect on the inflammatory response. Further research is needed to determine whether etomidate, used for emergent intubation in severely injured patients, was associated with development of post-traumatic ARDS.

PATIENTS AND METHODS

Study Design
End point => ARDS

40% in etomidate vs. 20% in others

- $p = .02$  OR $= 3.86 \ [1.24-12$

Longer stay $p = .02$

Fewer Days on Vent $p = .04$
tomidate

What to expect

Very rapid take down
last 3-5 min

Be ready with second sedative

n/v common if used without paralytic

Appropriate role??
Agents

- Etomidate
- Propofol
- Benzodiazepines
- Opiates
- Ketamine
- Barbiturates
Propofol

- Not a common EMS drug
- Frequently used in OR’s, ICU’s & ER’s
- Can cause hypotension
  - Particularly in volume depletion
- Excellent sedative and induction agent
Propofol

Milk of Anesthesia

Mechanism of Action Unclear

“hypnotic”

Michael Jackson

Role in EMS
Propofol

deal uses

Seizures

Adgitated delerium

Eclampsia

Isolated TBI and Head Bleeds
Anesthetics

- Etomidate
- Propofol

Benzodiazepines

- Opiates
- Ketamine
- Barbiturates
enzodiazepines

Diazepam (Valium)
Lorazepam (Ativan)
Midazolam (Versed)
...and others
benzodiazepines

Receptor mediated

GABA receptor
Midazolam

Uses:
- Anti-convulsant
- Sedation and hypnosis
- Anxiolysis
- Antegrade amnesia
- Muscle Relaxation
Most suited for critically ill

IV, IM, IN, etc

Rapid predictable onset

(not fast enough for Induction)

Sedation (45 min - 1 hr)
Lidazolam

Water soluble

One compartment model

Highly protein bound

$T_{1/2} = 3-6 \text{ hrs}$

Metabolized by liver
Midazolam

Provides safe sedation

Doses for sedation:

- 0.1 - 0.2 mg/kg

Very frequently underdosed

NOT a good induction agent

ONLY provides sedation/amnesia

No analgesia
lidazolam / Fentanyl

Frequently combined
dangerous in hypovolemic pts
Causes Hypotension

VERY DANGEROUS IN HEAD INJURED PATIENTS!!!!!!
THERE ARE BETTER OPTIONS
the Equation:

\[ \text{cbf} = \text{map} - \text{icp} \]
Agents

- Etomidate
- Propofol
- Benzodiazepines
- Opiates
- Ketamine
- Barbiturates
Opiates

Morphine
Opium
Hydromorphone
Fentanyl
Sufentanyl
Opiates

Very important class

Pain medication

Anesthetic

Antitussives, antidepressants
Opiates

- Discovered" in 1552
- Popularized in 1804
- Heroin in 1900
- Criminalized in 1914

C. 1910
Opiates

Receptor mediated drugs"
Opiates

delta - receptors
peripheral neurons
analgesia
antidepressant
dependancy
opiates

Kappa receptors

brain

spinal cord

sedation

miosis

dysphoria
Opiates

Mu - Receptors

- brain
- spinal cord
- peripheral neurons
- intestinal tract
- analgesia
- dependance
- euphoria
Nociceptin - Receptor

Brain
spinal cord
anxiety
depression
appetite
tolerance
Entanyl

Sublimaze

Very Lipophilic

First pass effect in lungs
Entanyl

Blood pressure may decline

Hemodynamically stable Agent

Dangerous in combination w/ Benzodiazepines

TBI, Volume depleted, etoh

THE EQUATION
Fentanyl

- Pain: 0.5 - 1.5 mcg/kg
- Can cause apnea in some people
- Sedation: 5-7 mcg/kg
- Anesthesia: 10-40 mcg/kg
Can be used for sedation

Not rapid enough for RSI

Large role in pain

Caution with other sedative

Except ketamine
Agents

- Etomidate
- Propofol
- Benzodiazepines
- Opiates
- Ketamine
- Barbiturates
etamine

Class: Phencyclidine
Conger: Ketamine

Developed in Mid 60's
Used in Vietnam
Popular in 70's
Sometimes sold as Ecstasy
"special K"
etamine

MDA Receptor Antagonist (dissociates brain form inal cord) Hallucinogenic Dissociative esthesia Binds to μ receptors (higher ses) hyperdynamic effects
Ketamine

How does it work?

- Separates the mid-brain from the cortex
- Disorganizes the brain
- Lower brain controls vital functions and is stimulated by Ketamine => excitation
- Occupies opiate receptor
Pharmacokinetics:

- IV/PO/IM
- Lipid soluble (two compartments)
- Hepatic Metabolism
- 3 hour half life (20-40min duration of action)
- Two compartment model
- Hepatic clearance
Etamine

Induction:
- 2-4 mg/kg IV (quickly)
- 4 mg/kg IM

Sedation
- 2mg/kg IV (slowly) or IM
etamine

Dosing: Pain adjunct

0.1 mg/kg IV increments to effect
etamine

Physiologic effects

- Increased CBF out of proportion to CNS metabolic needs
- Sympathetic tone
- Respiratory drive is reduced but ventilation persists (descriptions of apnea at higher does)
- Betsy’s case
etamine

Physiologic Effects

- Smooth muscle relaxant => bronchodilatation
- ↓ peak pressures
- ↑ HR, MAP, Contractility, ↓ MVO2 (1st dose)

Subsequent doses do not further ↑ sympathetic tone
etamine

Advantages

No hypotension
Continues to ventilate (usually)
Can combine benzo’s or opiates (dose sparing)
Anesthesia, Sedation and/or analgesia
IM/IV/PO/PR
etamine

Emergence Reaction

- Vivid dreams (stronger w/ PCP)
- More common in adults
- Benzo’s reduce frequency and severity

Hypersalivation / Laryngospasm

Resp sedation in higher doses (rapidly given)
etamine - cautions

Caution with Cardiac disease

Caution with Psychiatrically Ill

Pregnancy

Early in pregnancy can increase uterine pressures and cause contractions

Does not have FDA pregnancy classification

Laryngospasm
etamine - ideal uses

Induction for trauma or sepsis

Post intubation Sedation

Smooother transition from induction to sedation

Head Injury – particularly multi-trauma

Procedural sedation

Acute bronchospasm

Pain out of control

Agitated delirium (maybe)
sedatives

Etomidate

Propofol

Benzodiazepines

Opiates

Ketamine

Barbiturates
arterurates

Pentobarbitol
Thiopental
Methohexitol
arbiturates

Lipid soluble

Open chloride channels

Can produce “flat eeg”

(propofol, etomidate)
Prone to cause hypotension

Limited or No EMS role
SI Pharmacology

Induction & Sedation

Paralytics
Neuromuscular Blockers

- Succinyl Choline
- Rocuronium
- Vecuronium
- Atracurium
The poison arrow
South american hunters
Sir Walter Raleigh
Very important to science
Artificial ventilation
neuromuscular Blockers

Blocks the neuromuscular junction

at the muscle cell itself

Acetycholine is the transmitter

Acetylcholinesterase breaks down Ach

·Neostigmine & Organophosphates
Neuromuscular Junction
Buccinylcholine

Sux for short

Depolarizing agent

- Causes stimulation at the ACh receptor
- 2 phase action
  - Stimulation
  - Relaxation

Very fast onset
succinylcholine

Dose: 1 - 1.5 mg/kg

Onset 30 seconds

Push quickly, precede with anesthetic
ACETYLCHOLINE

ADVERSE REACTIONS

Hyperkalemia (K
neuromuscular disease
Paralysed
subacute burns
Rhabdomyolysis
Acute Kidney Injury
Auccinylcholine

Advantages:

- Fast onset
- Short duration of action

Disadvantages:

- Risk of hyperkalemia and death
Non-Depolarizing Agents

Rocuronium
Vecuronium
Atracurium
Ocuronium

Fastest of the ndpa’s
5 second onset
0.5 - 1.5 mg/kg (higher for RSI)
tubating conditions in 60 sec
sux is faster
Pharmacokinetics

Two Compartment Model

Hepatic metabolism

Biliary and renal clearance

20-40 min duration 1st dose

20 min (0.5mg/kg) subsequent dose
Cautions:

- Pregnancy Category C
- Liver and renal disease
ecuronium

-4 min onset

epatic/renal/hoffman

0 min with typical dose
Tracurium

Similar to Vecuronium

Hoffman
Questions? Comments?