Cutting Edge Procedural Sedation

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Propofol for Procedural Sedation
- The model of sedation outside of the OR
  - Effectiveness, duration of action and safety have led to the wide adoption of this drug for procedural sedation.
  - It is used by a variety of specialties in a variety of locations for procedural sedation
  - Has begun to accumulate sufficient data to develop consistent approaches

Moderate or Deep Sedation?
- Controversy exists about the levels of sedation that can be achieved using propofol, and what the optimal level of sedation is.
  - Likely that moderate sedation is as effective and more safe than deep, but it is difficult to predictably induce deep sedation in clinical practice.
  - Generally considered deep sedation since this level is frequently achieved even when moderate sedation is the goal of the procedure.

Propofol - Pros
- Safety
  - Propofol has been studied and shown to be safe for procedural sedation relative to multiple other agents,
    - Opioids
    - Benzodiazepines
    - Etomidate
    - Methohexital
    - Benzodiazepine opioid combinations

Amnesia
- Propofol has been shown to reliably induce amnesia in both moderate and deep sedation
  - This includes a 2-3 retrograde amnesia when moderate or deep sedation is reached
  - makes the agent ideal for brief painful procedures that require patient compliance
  - Most recall associated with painful interventions near the end of the procedure
  - Associated with the level of awareness 2 minutes after the painful event

Duration
- Propofol results in rapid recovery after the conclusion of the procedure and can be customized to a variety of procedures.
  - Has been described for procedures as brief as 4 minutes and lasting much longer
### Propofol - Cons

- **Respiratory Depression**
  - Moderate and deep sedation with propofol can progress to the level of general anesthesia under normal use, and can result in respiratory depression at a variety of doses.
  - The occurrence of respiratory depression, hypoxia, and serious adverse events have not been quantified for different environments and different procedures.
  - Requires interactive monitoring by a dedicated provider.

### Moderate vs. Deep Sedation

- It is difficult to exactly control the level of sedation achieved with propofol, and excursions into levels of sedation deeper than intended occur frequently.
- Physicians who are not experienced in airway management or facilities unprepared for airway management are likely to experience more severe adverse events from propofol sedation than areas equipped for such adverse events.

### Limitations - Pain

- Propofol does not act as an analgesic, despite its amnestic properties.
  - The effect of untreated unperceived pain is not well understood for brief procedures.
  - There is adequate evidence to show the deleterious effects of untreated pain during general anesthesia.
  - The extent to which this applies to brief procedures is unknown.

### Limitations - Pain

- Given the increased risk of respiratory depression that has been shown with adding opioids to propofol, the best approach remains controversial.
  - Studies adding opioids to propofol for sedation have not shown benefit and have generally demonstrated increased risk.
  - Current research using low dose ketamine has attempted to addressed this issue.

### Procedural Pain

- Pain control throughout the experience of an injury is important to the patient’s outcome.
  - The surgical stress response.
  - Pre-emptive analgesia.
  - The significance of brief procedural pain that a patient cannot later recall is difficult to determine.

### The surgical stress response

- Inflammatory, metabolic, and endocrine changes associated with surgical stress, extrapolated to general pain (16,17).
- Associated with a variety of undesirable effects:
  - Vegetative symptoms
  - Immunosuppression
  - Increased energy expenditure for a given workload
  - Gastrointestinal dysfunction
  - Decreased vital capacity.
The surgical stress response

• Related to the total amount of pain experienced
• Decreased with the use of opioids (18)
• Benzodiazepines, etomidate, and clonidine have been shown to do this as well (19)
• General anesthetics not effective in blunting this effect (20-23)

Pre-emptive analgesia

• Pain perceived after a tissue injury can be modified by an analgesic administered before the noxious stimulus (24-29)
• Painful stimuli, especially repeated stimuli, modify the transmission of pain signals at the dorsal root ganglion
  – This is a cumulative effect related to the duration and intensity of pain
  – Limiting the reception of pain signals can disrupt this effect

Pre-emptive analgesia

• This is usually shown in animal models
• This has been shown with opioids and NMDA receptor antagonists
• The effect is more difficult to interpret with local anesthetics
• It is likely that treating pain aggressively may cause this effect

Duration of Sedation Outside of the Operating Room

• It has been suggested that the incidence of adverse events increases with the duration of sedation
• The length of the procedure should be a consideration in decided where to perform a procedure
• Longer procedures using deep sedation should be performed in the operating room.

Duration and Risk

• It is likely that adverse events increase with the time of sedation,
  • There have been studies showing an increase risk and the same risk between longer and shorter procedures.
• The amount of time that makes a procedure high risk is not known
  • Likely a variable assessment that weighs all of the factors involved with procedural risk

Everything you need to know about pain.

- NMDA
- Opioids
- Substance P
- Glutamate
- Alpha 2
- Mu
What is my target

The fundamental question is:
- Which target will get my patient to the right level of sedation for the right amount of time with the least adverse events?

Pain Control

- Establish adequate pain control prior to beginning procedure
  - Morphine 0.1 mg/kg followed by 0.05 mg/kg q 0-15
  - Fentanyl 1.5 ug/kg followed by 0.75 ug/kg q 5
- The half life of pain medications is much longer than short acting anesthetics and they should be bolused separately

Ketamine Analgesia

- Low dose Ketamine
  - Likely enhances the effect of opioids
  - May decrease the amount of opioids needed to treat pain with a resulting decrease in the adverse events typically associated with opioids but without the agitation reported with typical ketamine dissociative doses
  - Has also been show to decrease the amount of opioids needed after procedures when combined with other agents for sedation and analgesia during the procedure

Ketamine Sedation

- Dissociative anesthetic
- Analgesic and Amnestic Qualities
- Can be given IM or IV
- Not associated with hypotension
- Usually not associated with respiratory depression

IM Ketamine

- Generally provides sedation for 15 to 20 minutes, return to baseline mental status at 30 to 60 minutes
- Can be given 1-4 mg/kg IM

Ketamine

- 1 mg/kg
  - Lumbar puncture, splinting, burn dressing, complex laceration repair age > 7
- 2 mg/kg
  - Oral laceration repair age > 7, I and D abscess
- 3 mg/kg
  - Complex laceration repair age 1-7
- 4 mg/kg
  - Oral laceration repair age > 7
IV Ketamine

- 1 mg/kg usually sufficient to induce dissociative state
- Onset 1 to 2 minutes
- Length of sedation 8-12 minutes
- Has a higher rate of respiratory depression than reported for IM ketamine (miner 2008)

Ketamine - Pros

- Analgesia
- Low incidence of adverse respiratory events
  - Respiratory depression after fast IV bolus is more pronounced than propofol
  - Longer duration than other sedatives without associated increase in risks
  - Ketamine risks manifest at the induction and recovery phases

Ketamine - Cons

- Hypersalivation
  - atropine 0.01 mg/kg (min dose 0.1 max 0.3)
- Laryngospasm
- Hypoventilation
- Emergence Phenomenon
  - midazolam 0.1 mg/kg (max 4 mg) may not be necessary
    (Walthen et. al.)

Ketofol

- Combinations of ketamine and propofol
- Theoretical benefits
  - Fast onset without respiratory depression
  - Analgesia without respiratory effects of supplemental opioids
  - Antiemetic effects of propofol
  - Amnestic effects complimentary

Ketofol - Theoretical Risks

- All the risks without a high enough dose reached to manifest amnesia or adequate sedation
- New adverse events not associated with either drug alone

Ketofol

- Optimal ratio of ketamine has not been established
  - Ranges from 1:3 to 4:1 reported
- Comparative clinical trials have been done
  - Appears there may be an improvement in blood pressure and a small decrease in respiratory depression with ketofol
  - Time of sedation and time to return to baseline mental status appears somewhat longer the higher the ketamine dose
Ketofol - Cons
- Higher rates of nausea, psychomimetic side effects, and delayed discharge over propofol alone
- Seems to have less adverse effects when give with smaller ratios of ketamine (4:1, Daabiss et al, Miner et al.)
- Satisfaction is lower in ketofol than propofol alone (60% vs 95%)

Ketofol - Pros
- Data is sufficient to support its use as safe, but lacking to support its use over either agent alone
- Many of the studies have been with larger doses than are typical for the ED
  - Propofol 1.5mg/kg plus ketamine 0.5 mg/kg has the best data around it
  - Lower doses typical of ED use un likely to have worse adverse events

Ketofol 1:1 vs 4:1 vs Propofol
- Just published study from HCMC
- None of the agents were associated with recall or perceived pain
- Propofol had the shortest recovery time
- 4:1 had the least adverse events
- 1:1 had the longest recovery time

Conclusion
- Limitations
  - The effect of unperceived pain of brief duration is unknown
  - Treating this theoretical pain is associated with a measurable increase in procedural risk
  - The inflection point of safety versus duration of procedure is not well defined
  - We haven't defined when a procedure requires too much sedation to be done out of the OR

Conclusions
- Ketamine, ketofol, and propofol have strong roles in EM practice
  - Propofol has the best data supporting its use for brief procedures
  - Ketofol 4:1 likely offers a benefit in longer procedures or in procedures with more need for deeper sedation
  - Ketamine is likely safer in patients at risk for hemodynamic compromise

What's next?
- Studies of longer procedures with ketofol vs propofol vs ketamine
- Ketamine vs etomidate in ASA 3 patients
- Moderate vs deep target sedation level with each agents