Procedural Sedation

David Mazer, MD, FRCPC
Outline

• Definition of procedural sedation
• Goals of therapy
• Review drug options
• Choice of sedation techniques

• Disclosures: Honoraria +/- research support
  - NovoNordisk, Bayer, AstraZeneca, Cubist, Hospira, Oxygen Biotherapeutics, Medicines Company
What is Procedural Sedation

• "a technique of administering sedatives or dissociative agents with or without analgesics to induce a state that allows the patient to tolerate unpleasant procedures while maintaining cardiorespiratory function.

• Procedural sedation and analgesia is intended to result in a depressed level of consciousness that allows the patient to maintain oxygenation and airway control independently."
Goals of procedural sedation

• Alleviate anxiety
• Relieve pain
• Provide amnesia
• Facilitate ventilation
• Facilitate patient management
• Rapid onset and recovery
• Modulate stress responses
  – Tachycardia
  – Hypertension
# Levels of Sedation

<table>
<thead>
<tr>
<th>Neurologic Responsiveness</th>
<th>Minimal Sedation (Anxiolysis)</th>
<th>Moderate Sedation/ Analgesia (Conscious Sedation)</th>
<th>Deep Sedation/ Analgesia</th>
<th>General Anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal response to verbal stimulation</td>
<td>Purposeful response to verbal or tactile stimulation</td>
<td>Purposeful response after repeated or painful stimulation</td>
<td>Unarousable, even with painful stimulus</td>
</tr>
<tr>
<td>Airway</td>
<td>Unaffected</td>
<td>No intervention required</td>
<td>Intervention may be required</td>
<td>Intervention often required</td>
</tr>
<tr>
<td>Spontaneous Ventilation</td>
<td>Unaffected</td>
<td>Adequate</td>
<td>May be inadequate</td>
<td>Frequently inadequate</td>
</tr>
<tr>
<td>Cardiovascular Function</td>
<td>Unaffected</td>
<td>Usually maintained</td>
<td>Usually maintained</td>
<td>May be impaired</td>
</tr>
</tbody>
</table>

ASA Practice Guidelines Anesthesiology 2002; 96:1004–17
Difference Between Procedural Sedation and General Anesthesia

- Loss of consciousness and ability to respond purposefully = General Anesthesia
- The provider must be prepared and qualified to convert to general anesthesia when necessary.

ASA committee on Monitored Anesthesia Care, 2008
Difference Between Procedural Sedation and General Anesthesia

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ASA committee on Monitored Anesthesia Care, 2008
Injury and Liability Associated with Monitored Anesthesia Care

**Graph:**
- **MAC**
- **Regional**
- **General**

% of claims in anesthesia group

- **Death/Perm Brain Damage**
- **Permanent Disabling**
- **Temp/Nondisabling**

* P<.025 MAC versus Regional

Bhananker S, Anesthesiology 2006
Characteristics of an Ideal Agent for Procedural Sedation

- Sedation associated with appropriate arousability
- Predictable (short) onset and offset
- Wide therapeutic window
- Analgesia
- Hemodynamic stability
- Anxiolysis
- No respiratory depression
- No shivering
- No nausea and vomiting
- No bowel effects
Components of and Drugs for Procedural Sedation

- Sedation
  - Amnesia
  - Hypnosis
  - Anxiolysis

- Analgesia
  - Benzodiazepines
  - Propofol
  - Inhaled Anesthetics
  - Antipsychotics
  - Opioids
    - Ketamine
    - α₂ agonists
### Benzodiazepines

- **GABA agonists**
- **midazolam, lorazepam and diazepam**

<table>
<thead>
<tr>
<th>Potential Advantages</th>
<th>Potential Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Sedation, amnesia and anxiolysis</td>
<td>- Antegrade amnesia</td>
</tr>
<tr>
<td>- Rapid onset (IV)</td>
<td>- Respiratory suppression</td>
</tr>
<tr>
<td>- Availability, familiarity</td>
<td>- Active metabolites</td>
</tr>
<tr>
<td></td>
<td>- Recovery time</td>
</tr>
<tr>
<td></td>
<td>- Paradoxical excitation</td>
</tr>
<tr>
<td></td>
<td>- Drug interactions</td>
</tr>
</tbody>
</table>
Propofol

- Rapid onset and offset
- Titratable
- Anxiolytic and anticonvulsant
- Phenolic compound, GABA effects
- (fospropofol - phosphate-ester water soluble prodrug of propofol)

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<tr>
<th>Potential Advantages</th>
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<tbody>
<tr>
<td>Rapid onset and offset</td>
<td>No analgesic properties</td>
</tr>
<tr>
<td>Titratable</td>
<td>General anesthetic in higher doses</td>
</tr>
<tr>
<td>Anxiolytic and anticonvulsant</td>
<td>Potential respiratory depression</td>
</tr>
<tr>
<td></td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td>Cost</td>
</tr>
<tr>
<td></td>
<td>Lipid emulsion</td>
</tr>
<tr>
<td></td>
<td>- Infection</td>
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<td></td>
<td>- Pain on injection</td>
</tr>
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<td></td>
<td>- Increased triglycerides</td>
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<td></td>
<td>- Propofol infusion syndrome</td>
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## Opioids/Narcotics

- **opioid receptors**
- **Morphine, demerol, fentanyl, remifentanil**

### Potential Advantages
- Potent analgesia
- Some sedation
- Suppress cough
- Familiarity/experience
- Synthetic compounds
  - Short acting
  - Minimal cardiovascular effect

### Potential Disadvantages
- Respiratory depression
- Duration of action
- Bradycardia
- Dysphoria/rigidity
- Pruritus
- GI effects
- Tolerance/Addiction
Remifentanil - Ultiva™

- Opioid, pure μ agonist
  - Little binding at k, s, and d receptors
- Potency 1.2 x fentanyl
- Rapid onset of action (~1 min), and offset (within 5-10 min)
- Rapid response to titration
- Non-specific esterase metabolism
- Elimination unaffected by gender, age, weight, or renal/hepatic function
- Can be used for short or long procedures
Volatile Anesthetics (Isoflurane)

Potential Advantages

- Sedation, amnesia and anxiolysis
- Titratable, predictable
- Organ protection (preconditioning)
- Minimal metabolism
- Rapid predictable recovery

Potential Disadvantages

- Intubated patients
- Device dependent
- Environmental contamination
Ketamine

- NMDA receptor antagonist, Phencyclidine derivative (like PCP)
- Onset 1-3 minutes, duration 10-30 minutes

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<tr>
<td>Analgesic</td>
<td>Delirium, hallucinations (~10-20%)</td>
</tr>
<tr>
<td>Dissociative hypnotic, amnestic</td>
<td>Increases BP, HR, and ?ICP</td>
</tr>
<tr>
<td>Minimal respiratory depression</td>
<td>Increases airway secretions</td>
</tr>
<tr>
<td>IV or IM administration</td>
<td></td>
</tr>
<tr>
<td>Short duration</td>
<td></td>
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</table>
“Ketofol”

- Co-administration of ketamine and propofol (1:1 or 0.5:1)

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<th>Potential Disadvantages</th>
</tr>
</thead>
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<tr>
<td>Synergy</td>
<td>Little evidence of benefit over monotherapy</td>
</tr>
<tr>
<td>Lower doses of either drug</td>
<td>Different pharmacokinetics/half lives</td>
</tr>
<tr>
<td>Balanced side effects (respiratory depression, analgesia, emesis, agitation)</td>
<td></td>
</tr>
<tr>
<td>?higher satisfaction</td>
<td></td>
</tr>
</tbody>
</table>
Dexmedetomidine - Precedex™

- Potent $\alpha_2$ agonist in brain (locus ceruleus), brain stem, and spinal cord
- Rapid distribution ($t_{1/2\alpha}$ 6 minutes) and elimination ($t_{1/2\beta}$ 2 hours)

Potential Advantages

- Sedative, analgesic, and anxiolytic effects
- Cooperative sedation (arousable and oriented patient)
- No respiratory suppression
- Extubation possible during therapy
- Antishivering
- May reduce delirium

Potential Disadvantages

- May decrease HR and BP
- Vasoconstriction (↑BP) with rapid infusion or at high doses
- Potentiates effects of opioids, sedatives, and anesthetics
- Dry mouth
Patient Controlled Sedation (PCS)
Patient Maintained Sedation (PMS)

- Allows patient to control their own level of sedation
- Used to provide sedation for local or regional anesthesia
- PCS – patient initiated bolus dosing
- PMS – computer controlled infusion system
  - Maintain target blood concentrations
  - Allows patient adjustment of infusion rates
Factors influencing choice of agents for procedural sedation

- Agent specific characteristics (including side effects)
- Length and type of procedure
- Expected level of pain/discomfort
- Respiratory status (mechanical vs spontaneous ventilation)
- Knowledge and familiarity with technique
- Availability of drugs
- Cost
Which medications to avoid in people at risk of delirium: a systematic review

- **Drugs which increase delirium risk:**
  - Opioids (morphine, demerol) OR 2.5, 95% CI 1.2–5.2
    - Inverse dose relationship (?inadequate pain control increases delirium)
  - Benzodiazepines (OR 3.0, 95% CI 1.3–6.8)
    - Longer acting agents/higher doses associated with higher risk
  - ?Antihistamines (diphenhydramine) (OR 2.1, 95% CI 0.9–5.2)

- **Drugs with no or uncertain delirium risk:**
  - Neuroleptics (haloperidol) (OR 0.9, 95% CI 0.6–1.3)
    - Haloperidol prophylaxis reduced duration of delirium after hip surgery
    - Risperidone (cardiac surgery) 32
  - NSAIDs (OR 0.4, 95% CI 0.1–1.5)
  - Steroids (OR 0.5, 95% CI 0.2–1.7)
Which drugs or techniques might reduce the risk of delirium

Light vs Deep Propofol sedation for hip fracture with spinal anesthesia
- 19% vs 40% delirium (BIS >80 vs 50)  NNT 4.7
- Reduced duration of delirium (0.5±1.5 days vs 1.4±4.0 days)

Neuroleptics
- Haloperidol prophylaxis reduced duration of delirium after hip surgery
- Risperidone 1 mg in cardiac surgery – 11% vs 32%; NNT 4.9
- Olanzapine 10 mg in joint arthroplasty – 14% vs 40%; NNT 4
- Gabapentin 900 mg pre and post spine surgery – 0/9 vs 5/12 p=0.045
  No differences in length of stay

$\alpha_2$ agonists
- Dexmedetomidine reduced duration of delirium and intubation
- 3% vs 50% delirium post cardiac valve replacement

Nerve block (Fascia Iliaca compartment) in hip surgery
- 10.8% vs 23.8% delirium
- Greatest effect for intermediate risk
- Reduced duration and severity of delirium
Cost Benefit Analyses

- Depends on settings, comparisons, drug costs, LOS, assumptions

- Unsedated colonoscopy less expensive than sedated
  - Propofol (+/- narcotic) recovery time 15 min vs 55 min (BZD + narcotic)

- Isoflurane ICU sedation €122 vs €171 (midazolam/sufentanil)

- ED propofol vs midazolam savings of CAD $17.33/patient

- Lower total costs post cardiac surgery with dexmedetomidine vs propofol midazolam (attributed to shorter ICU LOS)
Conclusions

- Procedural sedation frequently required in hospitalized perioperative and ICU patients
- Many drug options and administration techniques
- Theoretical and practical advantages
- No perfect single agent
- Procedural sedation can improve clinical course and outcome
Thanks for your attention!
Monitoring for Procedural Sedation

• Patient
  - Airway patency and protection
  - Oxygenation/ventilation
  - Hemodynamics

• Level of Sedation
  - Sedation scales (SAS, Ramsay, MAAS)
  - Processed EEG (BIS)
Optimizing sedation/analgesia is a difficult job
Optimizing sedation/analgesia is a difficult job
A Randomized, Controlled, Double-Blind Trial of Patient-Controlled Sedation with Propofol/Remifentanil Versus Midazolam/Fentanyl for Colonoscopy

50 colonoscopy patients randomized to midazolam/fentanyl (MF) or propofol/remifentanil (PR) Patient Controlled Sedation.

• Patient, nurse, and gastroenterologist perceptions equivalent between the groups.

• 2 patients in group PR required anesthesiologist intervention for arterial desaturation

Mandel JE Anesth Analg 2008;106:434–9