Sedation For Cardiac Procedures – A Review of Sedative Agents

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Aims of Sedation

- Provide patient comfort
  - Anxiolysis
  - Analgesia
- Amnesia
- Immobilization to facilitate procedure
- Suppress sympathetic response
Stages of Sedation

Minimal sedation (Anixolysis)  Moderate Sedation (Conscious Sedation)

General Anaesthesia  Deep Sedation
## Level of sedation

<table>
<thead>
<tr>
<th></th>
<th>Minimal sedation</th>
<th>Moderate sedation</th>
<th>Deep sedation</th>
<th>General anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Responsive to verbal</strong></td>
<td><strong>Normal</strong></td>
<td><strong>Purposeful response</strong></td>
<td><strong>Only on repeated or pain stimulus</strong></td>
<td><strong>No response even with pain stimulus</strong></td>
</tr>
<tr>
<td>stimulus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Airway</strong></td>
<td><strong>Unaffected</strong></td>
<td><strong>No intervention required</strong></td>
<td><strong>Intervention may reqd</strong></td>
<td><strong>Intervention often reqd</strong></td>
</tr>
<tr>
<td><strong>Spontaneous ventilation</strong></td>
<td><strong>Unaffected</strong></td>
<td><strong>Adequate</strong></td>
<td><strong>May be inadequate</strong></td>
<td><strong>Frequently inadequate</strong></td>
</tr>
<tr>
<td><strong>CVS function</strong></td>
<td><strong>Unaffected</strong></td>
<td><strong>Usually maintained</strong></td>
<td><strong>Usually maintained</strong></td>
<td><strong>May be impaired</strong></td>
</tr>
</tbody>
</table>
Optimal level of sedation

- Depends on procedure type
- Moderate Sedation (Conscious sedation) in most situation
- Controlled state of depressed consciousness which allows
  - the patient the ability to independently and continuously
    maintain an airway and
  - respond appropriately to physical stimulation and verbal command
- Deep sedation may be needed transiently for short but painful procedure, such as AICD
Cardiovascular Effect Sedatives

- Direct effect on myocardium and vasculature
- Direct effect on conduction system of the heart
- Indirect effect on autonomic nervous system
- Indirect effect on respiration with resultant hypercarpia and/or hypoxia
Ideal Sedative Agent for Cardiac Procedures

- Provides hypnotic, analgesia, anxiolysis and amnesia
- Favourable pharmacokinetic properties
  - Rapid onset and offset
  - Absence of cumulative effect
  - Easy titration
- Absence of direct/indirect cardiovascular and electrophysiological effect
- Stable IV preparation with long shelf life
- No pain on injection
- Easy administration – bolus vs infusion
- Cost
Drugs commonly used for sedation

• Benzodiazepine
• Opioids
• Intravenous anaesthetics
  – Propofol, etomidate, ketamine
• Other sedatives
  – Dexmedetomidine, anti-histamine, droperidol
Benzodiazepine - Midazolam

*provide*

- Sedation
- Anxiolysis
- Anterograde amnesia
- No analgesia
Midazolam

- Short duration (half life 100 min) and onset 2-5 min
- Less pain on injection when compared with diazepam
- Cardiovascular stable in clinical dose if used alone and no direct electrophysiological effect
- May have marked resp depression with opioid
- Dosage
  - titration against level of sedation with 1 mg iv bolus (adult) at 2 min intervals total 0.1mg/kg
- Antagonist
  - flumazenil
Opioids

• Analgesia & sedation
• Side effects
  – Respiratory depression
  – Nausea / vomiting
  – Lightheadedness
  – Dysphoria / Euphoria
• Choice
  – Morphine / pethidine / fentanyl
  – Alfentanil, remifentanil
• Antagonist
  – naloxone
Morphine

- Onset after IV bolus 10-15 min with half-life 3-4 hours
- May develop hypotension after bolus injection due to histamine release and/or suppression of sympathetic tone
- No direct electrophysiology effect
- Dosage – titration with 1 mg bolus up to 0.15mg/kg
Fentanyl

- 100 times more potent than morphine
- Rapid onset (3-5 min) and short duration (15-30 min) due to redistribution
- Dosage – 0.1µg/kg up to 1.5 µg/kg
- Long biological half-life (7 hours) and will accumulate for repeated large dose (10 µg/kg) or infusion
- Cardiovascular stable and no direct effect
Remifentanil

- Ultra-short acting synthetic opioid, must be given by infusion (0.05-0.5 µg/kg/min)
- Potent analgesia and virtually will not accumulate – ideal for painful procedure
- Transient increase of parasympathetic tone – cardiovascular hypokinetiic with depression of SA node automaticity and even sinus arrest
- Pre-emptive vagolysis is recommended
  » Minerva Anesthesio 2003;69:673-9
Propofol

- Rapid onset (1-2 min) and short duration with half life (30-60 min)
- Dosage – 0.5-1mg/kg bolus and infusion 2-4mg/kg/hr
- Side effect
  - Pain on injection
  - Respiratory depression requiring ventilatory support
  - Hypotension due to vasodilatation with mild compensatory tachycardia
- No electrophysiological effect on AV node – suitable for ablation procedure
- Widely used due to its favourable pharmacokinetic, rapid awakening, easy titration and no nausea
Etomidate

- Rapid onset and half-life 75 min
- Minimal respiratory side effects and cardiovascular stable, no electrophysiology effect
- Ideal for procedure required short GA
- Dosage – 0.2-0.3mg/kg
- Side effect
  - Pain on injection
  - Myoclonus (reduce with low dose midazolam)
Ketamine

- Rapid onset (2-3 min) and half-life 2.5 hr
- Cardiovascular stability (activation of sympathetic) and maintenance of respiration/airway
- Dosage – 1-2mg/kg
- Side effect – arrhythmogenic, myocardial ischaemia, airway secretion, dissociation phenomena
Dexmedetomidine

• Central α2 agonist with resultant reduction in sympathetic outflow
• Sedative and analgesic properties
• Dosage – loading 1µg/kg/hr over 10-20min, then infusion 0.1-0.7 µg/kg/hr
• Onset 5-10 min, duration 3.5hr
• Initial hypertension followed by hypotension and bradycardia
• Found to depress SA and AV node function – not suitable for electrophysiology study in child
  » Anaesth Analg 2008;1(106):79-83
Combination of Sedatives

- Multi-modal sedation
- Lower dose of individual sedatives with fewer side effect
- Synergistic action
- BZ + opioid, BZ + IV anaesthetic
<table>
<thead>
<tr>
<th></th>
<th>Midazolam</th>
<th>Fentanyl</th>
<th>Morphine</th>
<th>Remifentanil</th>
<th>Propofol</th>
<th>Etomidate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset (min)</strong></td>
<td>2-5</td>
<td>3-5</td>
<td>10-15</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>2 hr</td>
<td>15-30 min</td>
<td>3-4 hr</td>
<td>Short</td>
<td>Short</td>
<td>short</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
<td>1mg</td>
<td>0.1µg/kg</td>
<td>1mg</td>
<td>No</td>
<td>0.5mg/kg</td>
<td>0.2mg/kg</td>
</tr>
<tr>
<td><strong>Infusion</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.05µg/kg/min</td>
<td>2mg/kg/h</td>
<td>-</td>
</tr>
<tr>
<td><strong>CVS S/E</strong></td>
<td>Stable</td>
<td>Stable</td>
<td>↓ BP</td>
<td>Brady ↓ BP</td>
<td>↓ BP</td>
<td>Stable</td>
</tr>
<tr>
<td><strong>Resp S/E</strong></td>
<td>Stable</td>
<td>Depress</td>
<td>Depress</td>
<td>Depress</td>
<td>Depress</td>
<td>Stable</td>
</tr>
</tbody>
</table>
Non Pharmacological

• Adequate local anaesthetic for painful procedure
  – New LA less cardiotoxic – levobupivacaine or ropivacaine compared with Marcaine
• Thorough explanation and reassurance with doctor-patient rapport
Summary

• Decide on the level of sedation in accordance to nature of procedure
• Choice of sedatives depends on experience, pharmacokinetic profile, equipment, CVS and respiratory side effect
• Always titrate with level of sedation
• Consider combination of sedative for synergic effect