Standards of Care in Perioperative Patient Management: Anesthesiology Clinical Case Challenge

Mark D. Antoszyk, CRNA, BS
Director
Anesthesia Services
Department of Anesthesiology
Carolina’s Medical Center Northeast
Concord, North Carolina

Mark D. Antoszyk, CRNA, BS, is director of anesthesia services in the Department of Anesthesiology at Carolina’s Northeast Medical Center in Concord, North Carolina.

Mark received his Bachelor of Science degree from La Roche College in Pittsburgh, Pennsylvania. He has worked in a variety of settings utilizing general and regional anesthesia techniques for cardiovascular, ear, nose and throat, neurosurgical, obstetrics, gynecology, ophthalmology, pediatric, plastic, reconstructive, orthopedic, and general surgery.

Mark is a member of the American Association of Nurse Anesthetists and has served on the National Advisory Council for Novations. Mark is a certified instructor for cardiopulmonary resuscitation, pediatric advanced life support, advanced cardiac life support, and is also a licensed paramedic.
Standards of Care in Perioperative Patient Management: Anesthesiology Clinical Case Challenge

Slide Booklet
Learning Objectives

- Discuss opportunities to provide improved perioperative pain control in anesthesia practice
- Describe the advantages and disadvantages of short-acting opioids as part of a general anesthesia regimen
- Identify opportunities to improve hemodynamic control and postoperative recovery time with opioid-based anesthesia

Good Anesthesia = Titration to Effect

- Pharmacodynamic approach
  - Titrating drugs to effect
- Pharmaceutical approach
  - Choosing “forgiving drug”
- Pharmacokinetic approach
  - Knowledge of concentration-effect relationship

Preanesthesia Considerations Prior to Using a Short-acting Opioid
Preanesthesia Evaluation

- Notable history and physical
- Comorbidities
- Concomitant medications
- Type of surgery
- Previous history of anesthesia
- Allergies
- Venous access
- Airway

Rationale for & Comparison of Available Short-acting Opioids

Opioid Receptors and Response to Stimulation

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mu-1</td>
<td>Supraspinal analgesia</td>
</tr>
<tr>
<td>Mu-2</td>
<td>Depression of ventilation</td>
</tr>
<tr>
<td></td>
<td>Cardiovacular effects</td>
</tr>
<tr>
<td></td>
<td>Physical dependence</td>
</tr>
<tr>
<td></td>
<td>Euphoria</td>
</tr>
<tr>
<td>Delta</td>
<td>Modulate Mu receptors</td>
</tr>
<tr>
<td>Kappa</td>
<td>Spinal analgesia</td>
</tr>
<tr>
<td></td>
<td>Sedation</td>
</tr>
<tr>
<td></td>
<td>Miosis</td>
</tr>
<tr>
<td>Sigma</td>
<td>Dysphoria</td>
</tr>
<tr>
<td></td>
<td>Hypertonia</td>
</tr>
</tbody>
</table>
Opioid Benefits

- Analgesia
  - Blunt neuroendocrine activation
- Hemodynamic stability
  - No direct myocardiac depression
  - Blunt catecholamine response to noxious stimuli
- Decreased need for hypnotic anesthetics

Development of Newer Opioids

- Goals for opioids have been to:
  - Increase potency, safety, & therapeutic index
  - Improve PK/PD effects → titratability
  - Improve overall patient satisfaction
- Considerations?
  - Superior intraoperative control
  - Respiratory compromise (OSA)
  - Emergence & recovery
  - Decrease risk for preoperative adverse events

Structure of Synthetic μ-Opioids

- Alfentanil
- Fentanyl
- Remifentanil
- Sufentanil
- Remifentanil


OSA, obstructive sleep apnea

Desirable Characteristics of µ-Opioids

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Alfentanil</th>
<th>Fentanyl</th>
<th>Remifentanil</th>
<th>Sufentanil</th>
</tr>
</thead>
<tbody>
<tr>
<td>µ-Opioid receptor selectivity</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>No histamine release</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Rapid response to titration</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid, predictable offset of opioid effects (5-10 min)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elimination independent of renal or hepatic function</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Onset and Offset Rates of µ-Opioids

<table>
<thead>
<tr>
<th>Pharmacokinetics</th>
<th>Alfentanil</th>
<th>Fentanyl</th>
<th>Remifentanil</th>
<th>Sufentanil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset: blood-effect site equilibration, mean</td>
<td>0.96 min</td>
<td>6.6 min</td>
<td>1.6 min</td>
<td>6.2 min</td>
</tr>
<tr>
<td>Organ-independent elimination</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Nonspecific esterase metabolism</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Offset: context-sensitive half-time, mean*</td>
<td>&gt;50 min</td>
<td>&gt;100 min</td>
<td>3-6 min</td>
<td>30 min</td>
</tr>
</tbody>
</table>

*The time required for drug concentrations in blood or at effect site to decrease by 50%. Based on a 3-hour infusion.
†Increases with increasing infusion duration due to accumulation.


Infusion Front-end Kinetics

Quick to steady-state…
Infusion Back-end Kinetics

Mean Concentration Over Time With Short-acting IV Opioids

Context-Sensitive Half-time
Ideal Characteristics of Short-term Opioids for Anesthesia

- To provide precise control you need:
  - Rapid onset of action
  - Predictable control of hemodynamic response (HR)
  - Rapid titration, providing rapid response to intraoperative stress
  - Control of sympathomimetic response
  - Predictable duration and offset of action

Opioid Pharmacodynamic Variability

![Graph showing probability of no response to surgical incision vs. plasma alfentanil concentration](image)

Probability of No Response to Surgical Incision (%) (n=37)

- Intubation
- Skin Incision
- Skin Closure

Blood and Effect Site Concentrations of Remifentanil After Titration


Metabolism of Remifentanil

Metabolism by Hydrolysis (Facilitated by Esterases)
What Are the Current Risks with Opioids?

**Opioid Risks**
- Respiratory depression
- Bradycardia
- Chest wall/laryngeal muscle rigidity
- Postoperative nausea and vomiting (PONV)
- Pruritus
- Delayed emergence
- Dependency

Where Do Short-acting Opioids Fit Best in Our Practice?
Why Choose a Short-lived Opioid Intraoperatively?

- Minimize effects of drug accumulation
- Predictable and rapid onset and offset
- Rapid patient response to titration (up or down)
  - Manage intraoperative hemodynamic changes from surgical manipulation or pain
- Generally unaffected by gender or renal/hepatic function or by age or weight
- Significant potential for reduced PONV

General Inhalational Anesthesia vs Total Intravenous Anesthesia (TIVA)

- How do we determine which technique is most appropriate for which patient?
- What are the primary considerations for each?

What Anesthesia Technique You Use Should Be Based on Your Goals

- "Balanced" anesthesia with opioid and volatile agent
  - Safe
  - Ubiquitous
  - Practiced for decades
- TIVA
  - Safe
  - Relative newcomer to the OR
    - Outpatient > inpatient
    - Need to consider patient satisfaction
Inhalation vs TIVA

- Major issues:
  - Decreased PONV with propofol TIVA
    - Significant for patient satisfaction
  - Greater patient satisfaction with IV induction
    - Less PONV with IV induction and inhalational maintenance than with inhalational induction and maintenance
  - Emergence and exiting facility for outpatients essentially identical


IV, intravenous.

Specific Case Considerations
& Personal Experience

Case Considerations Using TIVA: Head and Neck Dissection

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Induction</th>
<th>Maintenance</th>
<th>Emergence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and neck</td>
<td>Propofol and a short-acting opioid relevant for intubation only.</td>
<td>Continuous infusion with 100 µg/kg/min propofol plus a short-acting opioid initially. Then titrate to needed level.</td>
<td>Assuming no expectation of tracheal or laryngeal edema, remove the ET after return of spontaneous respiration and patient arousal</td>
</tr>
</tbody>
</table>

ET, endotracheal tube.
Surgery
Induction
Maintenance
Emergence

- **Tonsillectomy, female 7 years old**
- Inhalation of sevoflurane 8% inhaled and a nitrous oxide to oxygen mix
- Following IV placement, switch to an IV opioid-based maintenance regimen
- Remove ET as patient awakens after spontaneous respiration has been established

**Case Considerations Using TIVA: Tonsillectomy**

**Maintenance Infusion Rates**

- **1.0 \( \mu \text{g/kg/min} \)**
  - Profound analgesia
- **0.5 \( \mu \text{g/kg/min} \)**
  - Paralysis required
- **0.25 \( \mu \text{g/kg/min} \)**
  - Ventilation required
  - > 50% MAC reduction
- **0.1 \( \mu \text{g/kg/min} \)**
  - Works well with nitrous
  - May be satisfactory for spontaneous ventilation

**ENT**

- Hemodynamic stability without vasodilators
- Decreased bleeding, improved operative conditions during nasal/sinus surgery
- Rapid awakening, rapid ability to protect airway, rapid recovery
Case Considerations Using TIVA: Open Inguinal Hernia Repair

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Induction</th>
<th>Maintenance</th>
<th>Emergence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open inguinal hernia repair, male 45 years old, BMI = 38</td>
<td>Infusion of propofol plus short-acting opioid</td>
<td>Following intubation, 300 µg/kg/min of propofol as the base along with a short-acting opioid</td>
<td>Turn off the infusion during skin closure for quick wake up at time of dressing being placed.</td>
</tr>
</tbody>
</table>

BMI, body mass index.

MAC

- Marked decrease in propofol use
  - Much more cooperative for blocks
  - Rapid recovery
- Decreased need for GA for inadequate local/block

Infusion Rates for MAC Sedation

- 0.2 µg/kg/min
  - Apnea likely
- 0.1 µg/kg/min
  - Respiratory depression
- 0.05 µg/kg/min
  - Little likelihood of respiratory depression
- 0.025 µg/kg/min
  - Few problems expected
Neuroanesthesia

- Hemodynamic stability without vasodilators
- Improved ability to rapidly change anesthetic depth
- Rapid recovery with early ability to assess neurologic function
- Improved SSEP monitoring with TIVA

SSEP: somatosensory evoked potential

Emergency Cases

- Rapid sequence induction
- Awake fiber-optic intubation
- Intensive care unit ET changes

Induction
- Midazolam, 2 mg
- Remifentanil, 0.1 µg/kg
- Propofol, bolus 2 mg

Maintenance
- Remifentanil, 0.1 µg/kg/min
- Propofol, 100 µg/kg/min
- At ~45 min, intraoperative spike in hemodynamic response from surgical stimulus, titrated remifentanil to 0.2 µg/kg/min and propofol to 140 µg/kg/min, then backed off
- Intraoperative medications
  - At ~30 min, ondansetron, 4 mg
  - At ~45 min, ketorolac, 30 mg

Emergence
- ~30 min prior to end of surgery, bolus morphine (2 mg)
- Infusion stopped
- Bolus morphine, 2 mg, repeated again at the end of the surgery

16-Year Old with Muscular Dystrophy: Cholecystectomy (1 hour, 50 min; BIS)

Induction
- Midazolam, 2 mg
- Remifentanil, 0.1 µg/kg
- Propofol, bolus 2 mg

Maintenance
- Remifentanil, 0.1 µg/kg/min
- Propofol, 100 µg/kg/min
- At ~45 min, intraoperative spike in hemodynamic response from surgical stimulus, titrated remifentanil to 0.2 µg/kg/min and propofol to 140 µg/kg/min, then backed off
- Intraoperative medications
  - At ~30 min, ondansetron, 4 mg
  - At ~30 min, ketorolac, 30 mg

Emergence
- ~30 min prior to end of surgery, bolus morphine (2 mg)
- Infusion stopped
- Bolus morphine, 2 mg, repeated again at the end of the surgery
14-Month Old: Sigmoid Colectomy with Central Line (2 hours, 40 min)

- **Induction**
  - Sevoflurane, 2.8%
  - Midazolam, 0.5 mg
  - Remifentanil, 0.1 µg/kg
  - Propofol, bolus 40 µg
- **Maintenance**
  - Sevoflurane, 1.25%-1.45%
  - Remifentanil, 0.15 µg/kg/min
- **Emergence**
  - ~1 hr to 30 minutes prior to the end of surgery
    - Morphine, 0.8 mg
    - Ondansetron, 1 mg
    - Ketorolac, 4 mg
  - Infusion stopped

---

**Postoperative Analgesia**

- Opioids prior to emergence (not comprehensive list)
  - Morphine 0.1 to 0.2 mg/kg IV ~ 20 to 30 min
  - Fentanyl 1 to 1.5 µ/kg IV ~ 5 min
- Activate epidural
- Infiltrate with long-acting local anesthetic
- Major Nerve Block (often done before procedure)
- Continue remifentanil 0.05 to 0.1 µg/kg/min
- IV Acetaminophen 1000 mg (or 15 mg/kg)
  - Ketorolac 30 mg IV ~ 30 min

---

**A Debate on Techniques and Monitoring: Current Thoughts**
**Manual Controlled Infusion vs Target Controlled Infusion (TCI)**

- A contemporary debate
  - Fifty ASA grade I or II patients, aged 18 to 65 years, scheduled for elective orthopedic or body surface surgery lasting >30 min
  - TCI: Commonly higher propofol doses administered within first 30 min of anesthesia (may delay recovery)
  - TCI: Lower Bispectral Index Score (BIS) in first 15 min
- Reflect on European vs small US experience
  - TCI: Lower dosing; better on elderly; surgery specific

---

**Monitoring Strategies for Anesthesia Depth: Pros and Cons**

- Attempts to quantify patient awareness with depth of anesthesia (to ensure zero recall)
  - Glasgow Coma Scale (GCS) test (not used in anesthesia routinely)
  - Electroencephalogram (EEG) monitoring/computed analytics
    - BIS
    - Spectral Edge Frequency (SEF)
    - State Entropy (SE) Index
    - Patient State Analyzer – 4-channel EEG (PSA 4000)
  - Auditory evoked potential (AEP) monitor
- Anesthesiologists agree that none are the "gold standard" or are sufficiently sensitive to guarantee that patients will not awaken during surgery

---

**Considerations for Emergence & Recovery**
Emergence and Recovery:
Considerations

- Goal is to prepare for and have smooth transition to postoperative analgesia
- Early planning important because some agents have rapid offset of action (within 5-10 minutes)
  - Benefit of lack of cumulative effects, but may be disadvantage in postoperative setting when considering pain control
  - Need to be prepared
- Identify risk for pulmonary aspiration of gastric contents

Propofol Emergence Data

![Plasma Propofol Concentration over Time](image)

Target plasma concentration
Recovery after:
- 10-day infusion
- 1-hour infusion
Awakening

Minutes After End of Infusion

Short-acting Opioid Improves Time to Orientation Compared With N₂O

![Proportion of Oriented vs Time](image)

- Remifentanil
- Nitrous oxide

During ambulatory orthopedic surgery with a desflurane-fentanyl general anesthetic

Infusion of remifentanil 0.085 µg/kg/min compared with 66% N₂O
Postoperative Management

Postoperative Analgesia Management Options

- Choice of analgesia should depend upon patient and type of surgery:
  - Nonsteroidal agent administered IV or IM
  - IV acetaminophen
  - Major nerve block
  - Local anesthetic wound infiltration
  - Long-acting opioids administered 20 to 30 minutes before discontinuation of certain short-acting opioids
  - Epidural administration of an opioid and/or local anesthetic

Considerations for Special Populations
Considerations for Special Populations

- Age
- Comorbidities
- Body mass effects

Practical Considerations

Rapid Onset

ADVANTAGES
- Rapid response to titration and bolus
- Control of anesthetic depth
- Hemodynamic stability
- Predictable plasma & receptor level

DISADVANTAGES
- Increased risk for:
  - Bradycardia
  - Hypotension
  - Chest wall rigidity
  - Apnea
**Practical Considerations: Rapid Offset**

<table>
<thead>
<tr>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Rapid response to titration</td>
<td>• No residual analgesia</td>
</tr>
<tr>
<td>• Predictable emergence</td>
<td></td>
</tr>
<tr>
<td>• High-dose opioid technique without need for post-op ventilation</td>
<td>• Hemodynamic instability</td>
</tr>
<tr>
<td>• Ideal for TIVA</td>
<td></td>
</tr>
</tbody>
</table>

**Summary**

- Newer opioids have the potential to improve therapeutic index, titratability, recovery, and overall patient experience & satisfaction
- Short-acting opioids:
  - Decrease drug accumulation
  - Provide rapid onset, offset, and response to titration
  - Unaffected by patient gender, age, or weight
- Early planning is essential to ensure a smooth emergence & recovery, and proper postoperative analgesia
- Understanding and anticipating the potential side effects of short-acting opioids allows the practitioner to potentially eliminate them from practice