Remifentanil: An Ultra Short Acting Opioid: “ESSENTIAL for Every Anesthesia Toolbox”

Mark J. Haffey MSN, CRNA, APN
OANA Spring Meeting
April 1, 2017
What's the strongest over-the-counter pain killer you got?
Objectives

- Describe the history of narcotics and the need for an ultra-short acting opioid.
- Discuss the pharmacokinetics and pharmacodynamics of Ultiva: an ultra short acting opioid.
- Identify select patients and procedures that remifentanil is the ideal opioid for.
- Discuss the role of remifentanil as a part of TIVA anesthetic
- Remi-Fentanil and Healthcare Reform
Progression of Fentanyl Analogs

- **Fentanyl**
  - 1960
  - (100x more potent than morphine)

- **Sufentanil**
  - 1974
  - (5-10x more potent than fentanyl)

- **Alfentanil**
  - 1976
  - (¼ as potent as fentanyl, 1/3 the duration of action)

- **Remi-Fentanil**
  - 1990
  - (2-3x as potent as fentanyl)
Pharmacodynamics and Pharmacokinetics

<table>
<thead>
<tr>
<th>Metabolized (Non-Specific)</th>
<th>Metabolyte</th>
<th>Volume of Distribution</th>
<th>Binding</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Plasma Esterase • Tissue Esterase</td>
<td>• Carboxylic Acid • RemiFentanil Acid</td>
<td>• Very Small</td>
<td>• μ2 receptor sites</td>
</tr>
</tbody>
</table>
Pharmacology of Remifentanil

- The ester tail makes the molecule susceptible to hydrolysis by plasma and tissue esterases.

- Remifentanil is metabolized to a carboxylic acid that has the potency of 1/1000 of the parent compound.

- Not a substrate for plasma cholinesterase, thus patients with atypical plasma cholinesterase have normal duration of action.
Pharmacokinetics of Remifentanil
Remifentanil: Contraindications

- Do not use Ultiva for Epidural, Intrathecal, or Regional Anesthesia due to glycine in the formulation
- Do not use in patients who have known hypersensitivity to fentanyl analogs
Why should Remifentanil be in my anesthesia toolbox?

- Rapid Onset
- High Potency
  - 3x more potent than Fentanyl
- Rapid Offset
  - 6-10min secondary to break down by non specific plasma and tissue esterases
- Total Dose has no effect rate of metabolism of Ultiva
- Metabolism not effected by hepatic and renal impairment
Remifentanil: A unique profile

- Nitrous oxide
- Desflurane
- Sevoflurane
- Isoflurane
- Halothane

Opioid analgesics

Proportion of Steady State Cm, %

Infusion begins at time zero

Infusion Duration, min

- Remifentanil
- Alfentanil
- Sufentanil
- Morphine
- Fentanyl
Remifentanil: Indications for Usage

- Induction of Anesthesia: 0.5-1.0 mcg/kg IV
- Maintenance of Anesthesia: 0.025-0.3 mcg/kg/min
- GETA with Inhalation Agents
- TIVA
- MAC
- Emergence of Anesthesia: 0.025-0.1 mcg/kg for immediate post-op pain control especially in the ICU setting.
Case Type: What, Why?

- **Neuro Cases**
  - Cases requiring intra-op or post-op neuro checks in the OR
    - Want timely wake-up and reliable neuro check
  - SSEP’s and MEP’s cases
    - No muscle relaxant
    - <.5 MAC of inhalation agent

- **Vascular Cases**
  - Carotid Endarterectomy
    - Post-op Neuro Check to verify no incidence of CVA
  - AV Fistula Creation
    - Renal Failure can lead to prolonged wake-up
Cases cont.

- ENT
  - Tracheal Stenosis
  - Vocal Cord Lesions
  - Radical Neck Tumor removal
  - Thyroidectomy
- Extremely Stimulating ENT cases where paralysis is contraindicated.
- Cases that are extremely stimulating or have significant intraoperative pain but have minimal post-op pain
- Cases where the patient has minimal residual effects from narcotic secondary to respiratory concerns.
Patient Focused

- Elderly
  - Decreased incidence of cognitive dysfunction*
  - Concerns with extubation criteria being met.
  - Decreased PACU Time

- Obesity
  - Blood Fat and Blood Muscle concentration of agent is decreased.
  - Decreased incidence of post-op respiratory complications

- Hepatic and Renal Failure patients
Patients (cont.)

- Patients that are at risk for airway compromise in the PACU.
- Patients with history of prolonged sedation following general anesthesia.
RemiFentanyl: Rapid Onset and Offset
Offset: NO Effects Regarding TIME

- Regardless of the length of Infusion Time, Remifentanil is still Metabolized in 6-10 minutes.
- Remifentanil has no issues regarding potency of metabolites as byproduct remifentanil acid has 1/1000 potency.
Case Study:

- 18 y/o female with Scoliosis for T10-L3 spinal fusion. with intraoperative monitoring (SSEPs, MEPs)

- Hx of asthma and obesity (BMI 36). No previous anesthesia hx.

- No Muscle Relaxation requested and no more than .5 MAC inhalation agent (SSEPs and MEPs)

- Prone Position

- What is the Ideal Anesthetic?
The Extra Benefits

- Awake Fiberoptic Intubation - blunts tracheal stimulation.
- EBUS (Endobronchial ultra-sound)
  - 10mcg/ml concentration
- RSI in patients in which succinylcholine is contraindicated. (1.0 mcg/kg/min)
  - MH
  - Myasthenia Gravis
  - Muscular Dystrophy
  - Pseudocholinesterase Deficiency
- OB for patients unable to have epidural.
  - .05mcg/kg/min gtt
TIVA

- Remifentanil provides a potent analgesic.
- Dose or Rate does not affect emergence.
- Can be used for both General Anesthesia and MAC Anesthesia
  - MAC: .025-.1mcg/kg/min
  - GA: .05-.3mcg/kg/min
- Potentiated effect when used with Propofol or Precedex.
Ultiva and PONV

- Decreased incidence of PONV with Remi vs. other narcotics
- High dose Remi does not correlate to increased PONV
- Even though action is at μ-2 receptors, extremely fast metabolism = decreased side effects
Case Study

- 67 y/o F scheduled for vocal cord biopsy
- PMH: COPD (75 pack-year history), Stage 3 CKD, NIDDM, Obesity, and OSA
- PSH: Bilateral Knee Replacement, Appendectomy, Cholecystectomy
- Other Info: Pt was noted to have a history of slow wake-ups with GA and Hx of PONV.

WHAT NOW?
Why Ultiva?

- Extremely stimulating procedure
- Patient has Stage 3 CKD leading to decreased excretion of drugs
- Extremely concerned with patient respiratory status post-op secondary to procedure and OSA
- Pt is obese
  - increased retention of inhalation agents and drugs.
- Patient history of prolonged sedation
Concerns

- Hyperalgesia
- Acute Opioid Tolerance
- Opioid Induced Hyperalgesia
- Important to not overdose the patient as this leads to increased incidence of AOT/OIH
- Literature notes doses > .4mcg/kg/min
  - *MgSO4 has been shown to reduce RIH

- Bradycardia and hypotension

- Respiratory Depression
  - Apnea
Healthcare Reform, HCAHPS, and Remi-Fentanil

• Importance of Quality Care Initiatives

• ACA (2010)
  • ACO’s that meet performance standards will receive additional Medicare Payments.
  • Hospitals providing the best quality care for the best cost.
  • Increase access of Healthcare insurance to the uninsured.

• Quality Payment Program (QPP)
  • Payment on quality vs. quantity
  • HCAHPS
PEARLS OF WISDOM

- Use Ultiva for induction
  - Extremely effective in blunting response to laryngoscopy
  - Infusion vs Bolus

- Titrate maintenance dose to patient

- Potentiates other anesthetics

- Must administer long acting narcotic before stopping infusion if there is potential for post-op pain.

- Approved for Pediatrics
Summary

- Rapid onset
- Potent narcotic
- Extremely consistent rapid offset regardless of patient co-morbidities.
- Extremely non-potent metabolite meaning no narcotic induced depression post-op.
- Decreased PONV and more efficient patient throughput.
Questions and Answers