Remifentanil PCA in Labor

Jennifer Lucero, MD
Clinical Instructor
UCSF Department of Anesthesia

· Discuss the Pharmokinetics of Remifentanil
· Review literature on the use of Remifentanil in Labor
· Discuss Remifentanil PCA implementation
· Discuss Remifentanil as an alternative to epidural labor analgesia

Remifentanil Pharmacokinetics:

- Ultra short-acting mu-1 opioid receptor agonist
- Metabolized into inactive metabolite by non-specific esterases in plasma
- Rapid onset of analgesia = 30-60 sec; Peak at 2.5 min
- Context-sensitive half-life = 3.5 min
- "Respiratory depression" half-life = 2.5 min

Remifentanil and Pregnancy

- The placenta contains nonspecific esterases
- Fetal esterases nearly fully developed at birth
- Within 5-10 minutes of turning off an infusion there is virtually no residual remifentanil drug effect.
- Remifentanil can be turned off minutes before delivery without respiratory effect in the fetus

Remifentanil and Pregnancy:

- Plasma concentrations in pregnancy are ½ of non-pregnancy due to a larger volume of distribution and higher clearance
- Crosses the placenta rapidly but is rapidly metabolized and redistributed in fetus


Remifentanil Transfer

Kan, R. et al. Intravenous Remifentanil: Placental transfer, maternal and neonatal effects. Anesthesiology. 1998; 88: 1467-74
Remifentanil Transfer

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal</td>
<td>7.27</td>
<td>7.27</td>
<td>6.50 - 7.90</td>
</tr>
<tr>
<td>Maternal</td>
<td>7.92</td>
<td>7.92</td>
<td>7.00 - 8.80</td>
</tr>
</tbody>
</table>


Remifentanil vs. other opioids

- RCT: Remifentanil vs. meperidine vs. fentanyl PCA
- N = 159, 40 mcg bolus, 2 minute lockout for remifentanil
- Greatest decrease in pain scores with remifentanil but only significant at one hour
- Higher satisfaction, but more sedation and desaturation in remifentanil group

No difference in neonatal outcomes, n/v, Cesarean delivery


Remifentanil and Labor:

<table>
<thead>
<tr>
<th>Table 1. Summary of Remifentanil Studies for Labor Analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remifentanil PCA</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Hinova et al.</td>
</tr>
<tr>
<td>Nef et al.</td>
</tr>
<tr>
<td>Douma et al.</td>
</tr>
<tr>
<td>Velloso et al.</td>
</tr>
<tr>
<td>Hinova et al.</td>
</tr>
<tr>
<td>Nef et al.</td>
</tr>
<tr>
<td>Douma et al.</td>
</tr>
<tr>
<td>Velloso et al.</td>
</tr>
</tbody>
</table>

Side Effects of Remifentanil:

Remifentanil vs. Epidural

RCT: remifentanil PCA vs. epidural with levobupivacaine 0.625 mg/cc + fentanyl 2 mcg/cc

N=45

Lower pain scores in epidural group, but similar overall pain relief scores
More sedation and lower SpO2 in remifentanil group
Remifentanil vs. Epidural

### Table 1: Neonatal outcomes

<table>
<thead>
<tr>
<th></th>
<th>Remifentanil (n = 7)</th>
<th>Epidural (n = 8)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apgar score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 min</td>
<td>8.3 (1.3)</td>
<td>7.5 (1.3)</td>
<td>NS</td>
</tr>
<tr>
<td>5 min</td>
<td>9.0 (1.0)</td>
<td>8.0 (1.7)</td>
<td></td>
</tr>
<tr>
<td>&lt;7 at 1 min</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>umbilical artery</td>
<td>7.4 (0.1)</td>
<td>7.4 (0.1)</td>
<td>NS</td>
</tr>
<tr>
<td>pH umbilical artery base cord</td>
<td>-11.1 (6.6)</td>
<td>-8.8 (2.8)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are mean (SD) or n. NS: Not significant.


### VAS Scores: Remifentanil vs. Epidural

![VAS Scores Graph]

Fig 1: Visual Analogue Scale (VAS) used to evaluate pain levels and other variables. Higher scores indicate less pain. The VAS score for epidural analgesia was used to determine if the VAS score for epidural analgesia was used.


### Implementation

- Have pharmacy make the remifentanil in a standard concentration.
- Have a pre-printed Standardized form.
- Initial patient controlled dose should start at either 2.0 mcg/injection or weight based dosing of 0.2 mcg/kg (ideal body weight) and increase by 1.0-2.0 mcg until reach desired effect.
- Lockout of PCA q2 minutes, no basal rate, no PRN dose.
- All patients need supplemental O2 (at minimum 2L nasal cannula)
- Pediatricians should be present at delivery.
Routinely Available Remifentanil?

- Retrospective study in Ireland performed in 2007
- In 2005 remifentanil PCA for labor analgesia was routinely available
- During the two year period:
  - 28% opted for remifentanil
  - 22% opted for epidural
- Conversion from remifentanil to epidural was 10%

Neonatal Resuscitation

Table 3: Neonatal resuscitation effectiveness

<table>
<thead>
<tr>
<th>Method</th>
<th>Success</th>
<th>% Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual</td>
<td>99%</td>
<td>97%</td>
</tr>
<tr>
<td>Nasal</td>
<td>99%</td>
<td>97%</td>
</tr>
<tr>
<td>Oral</td>
<td>99%</td>
<td>97%</td>
</tr>
</tbody>
</table>

Note: Data from Boardwell et al. (2018) in International Journal of Obstetric Anesthesia.
Controversy still exists as to whether a routine use of remifentanil PCA should be used in labor. Literature supports neonatal outcomes similar with epidural and remifentanil. Literature supports the use of remifentanil in situations where a neuraxial block is contraindicated.

Current State:
Remifentanil PCA in Labor

- Remifentanil produces pain relief during the first stage of labor better than other opioids.
- Second stage of labor not as reliable.
- Prior to implementation at hospital, all health care providers should undergo and inservice on remifentanil and a protocol developed.

The Future of Remifentanil PCA in labor

- There exists a potential for the use of routine remifentanil PCA in labor in subgroups of laboring women.
  - Women who have fear of neuraxial block, but desire pain relief.
  - Multiparous women who need pain relief during first stage of labor.
- Research in the use in these subgroups of women would be beneficial to further delineate the use of remifentanil in labor.