NEW MODES OF OBSTETRIC ANALGESIA: DOES PIEB MODE BRING A REAL BENEFIT?

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SERVICE D’ANESTHÉSIE. HÔPITAL LOUIS MOURIER, COLOMBES.
LABOR PAIN


Chronic pain syndromes and labor pain

- Causalgia
- Nulliparas (no prepared childbirth training)
- Nulliparas (prepared childbirth training)
- Multiparas (trained and untrained)
- Chronic back pain
- Cancer pain (nonterminal)
- Phantom limb pain
- Postherpetic neuralgia
- Toothache
- Arthritis

McGill questionnaire pain scores (PRI)

- Pain after accidents
- Digit amputation
- Bruise
- Fracture
- Cut
- Laceration
- Sprain
LABOR STAGES

- **First Stage**
  - Latent phase
  - Active phase

- **Second Stage**

- **Post Partum**

Graph showing cervical dilatation (cm) with phases of labor.
LABOR PAIN

PARTICULARITIES

- Intense or intolerable
- Variable from one woman to another
- Increases during labor
- Is increased by oxytocin/prostaglandins
EPIDURAL ANALGESIA (EA)

« IDEAL » EA

- Effective throughout the work
- Flexible
- Little or no re-injection by caregivers
- No motor blockade
- No impact on labor and delivery
- No side effects: hypotension, pruritus, nausea-vomiting...
EPIDURAL ANALGESIA (EA)

« IDEAL » EA = MATERNAL SATISFACTION !!
HOW TO OBTAIN « IDEAL » EA ?
WHICH AGENTS / WHICH CONCENTRATIONS?

Wong CA. Int J Wom Health 2009

**AGENTS**
- A local anesthesia (LA)
- An opioid
- ± Clonidine

**CONCENTRATIONS**
- Ropivacaïne: 0.08 – 0.15 %
- LEvobupivacaïne: 0.0625 – 0.125 %
- Bupivacaïne: 0.0625 – 0.125 %
- Sufentanil: 0.25 – 0.50 µg/mL
- Clonidine: 1 - 2 µg/mL
WHICH MODES OF ADMINISTRATION?

Evolution of modes of administration

- Continuous epidural Infusion (CEI)
- PCEA
- PCEA + PIEB
- INTERACTIVE PCEA
PCEA vs CONTINUOUS EPIDURAL INFUSION (CEI)

Van der Vyver M, Halpern S. BJA 2002; 89: 459-65

Number of patients without supplemental intervention

<table>
<thead>
<tr>
<th>Study (first author)</th>
<th>PCEA (n/N)</th>
<th>Infusion (n/N)</th>
<th>Risk difference (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sia</td>
<td>17/20</td>
<td>16/20</td>
<td></td>
</tr>
<tr>
<td>Butros</td>
<td>42/48</td>
<td>34/50</td>
<td></td>
</tr>
<tr>
<td>Gambling</td>
<td>34/55</td>
<td>5/13</td>
<td></td>
</tr>
<tr>
<td>Purdie</td>
<td>38/75</td>
<td>16/84</td>
<td></td>
</tr>
<tr>
<td>Collis</td>
<td>27/44</td>
<td>12/46</td>
<td></td>
</tr>
<tr>
<td>Curry</td>
<td>29/30</td>
<td>17/30</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>187/272</td>
<td>100/243</td>
<td></td>
</tr>
</tbody>
</table>

Less intervention (top up) with PCEA
**PCEA vs CONTINUOUS EPIDURAL INFUSION (CEI)**

*Van der Vyver M, Halpern S. BJA 2002; 89: 459-65*

**Dose of LA (mg. h⁻¹)**

<table>
<thead>
<tr>
<th>Study (first author (yr))</th>
<th>PCEA (n)</th>
<th>Mean (sd)</th>
<th>Infusion (n)</th>
<th>Mean (sd)</th>
<th>Weighted mean difference (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrante (1991)</td>
<td>20</td>
<td>9(4)</td>
<td>20</td>
<td>16(4)</td>
<td></td>
</tr>
<tr>
<td>Ferrante (1994)</td>
<td>15</td>
<td>9(4)</td>
<td>15</td>
<td>17(4)</td>
<td></td>
</tr>
<tr>
<td>Curry</td>
<td>30</td>
<td>8(3)</td>
<td>30</td>
<td>14(4)</td>
<td></td>
</tr>
<tr>
<td>Gambling</td>
<td>55</td>
<td>5(2)</td>
<td>13</td>
<td>9(3)</td>
<td></td>
</tr>
<tr>
<td>Sia</td>
<td>20</td>
<td>18(3)</td>
<td>20</td>
<td>21(5)</td>
<td></td>
</tr>
<tr>
<td>Collis</td>
<td>44</td>
<td>9(2)</td>
<td>46</td>
<td>12(3)</td>
<td></td>
</tr>
<tr>
<td>Butros</td>
<td>48</td>
<td>13(4)</td>
<td>50</td>
<td>15(4)</td>
<td></td>
</tr>
<tr>
<td>Smedvig</td>
<td>25</td>
<td>8(5)</td>
<td>27</td>
<td>8(0.4)</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>257</td>
<td>221</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reduction of LA doses by 25% - 30% with PCEA
PCEA vs CONTINUOUS EPIDURAL INFUSION (CEI)

Van der Vyver M, Halpern S. BJA 2002; 89: 459-65

NO DIFFERENCE FOR:

✓ Duration of labor
✓ Instrumental deliveries
✓ Caesarean sections
✓ Neonatal outcomes
« IDEAL » PCEA ?
PCEA: BOLUS VOLUME?

Yokoyama M et al. Anesthesiology 2004; 100: 1504 - 10

10 ml vs 5 ml  ➔ Diffusion on more metamers
           ➔ More homogeneous distribution
Reduction in LA concentrations for larger boluses with less risk of toxicity

(Lyons GR et al. Anesth Analg 2007; 104: 412-5)

Bupivacaine 0.25% w/v

MLAV = 9.2 ml (95% CI 6.9-11.5)
MLAD = 23 mg (95% CI 17.2-28.9)

Bupivacaine 0.125% w/v

MLAV = 13.6 ml (95% CI 12.4–14.8) *
MLAD = 17 mg (95% CI 15.5-18.5)**

*P = 0.002  **P = 0.045
PCEA BOLUS VOLUME

- Larges volumes of diluted solution (8 -10 ml) with long lockout periods to improve:
  - Analgesia
  - Maternal satisfaction

- Maximal doses to prevent the risk if there is an unrecognized intrathecal KT
  - bupivacaïne ≤ 5-6 mg ropivacaïne ≤ 7-8 mg

RCP SFAR 2006 « Blocs périmédullaires chez l’adulte »
<table>
<thead>
<tr>
<th>References</th>
<th>N</th>
<th>Local anesthetic concentrations, bolus volume, and lockout interval</th>
<th>N/group; infusion rates</th>
<th>Comments</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paech (^{11})</td>
<td>50</td>
<td>B 0.125%, F 3 (\mu g/\text{mL}), bolus 4 mL, lockout 15 min</td>
<td>(N = 25); 0 mL/h</td>
<td>Parturients and caregivers blinded.</td>
<td>All outcomes reported. Higher proportion of total dose given by clinicians in the no-infusion group (17% vs 9%).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(N = 25); 4 mL/h</td>
<td></td>
<td>Maternal satisfaction was not reported. There were fewer clinician rescue bolus doses in the 6 mL/h group than the 0 or 3 mL/h group.</td>
</tr>
<tr>
<td>Ferrante et al.(^{8})</td>
<td>45</td>
<td>B 0.125%, F 2 (\mu g/\text{mL}), bolus 3 mL, lockout 10 min</td>
<td>(N = 15); 0 mL/h</td>
<td>Double blind; mixed parity.</td>
<td>All outcomes were reported. No difference between groups in any outcome.</td>
</tr>
<tr>
<td>Petry et al.(^{12})</td>
<td>74</td>
<td>B 0.125%, S 0.75 (\mu g/\text{mL}), E 1:800,000, bolus 3 mL, lockout 12 min</td>
<td>(N = 37); 0 mL/h</td>
<td>? blinding.</td>
<td>All outcomes were reported. No difference between groups in any outcome. No significant dose trend.</td>
</tr>
<tr>
<td>Boselli et al.(^{6})</td>
<td>133</td>
<td>R 0.1%, S 0.5 (\mu g/\text{mL}), bolus 5 mL, 5-min lockout, total 22 mL/h including infusion</td>
<td>(N = 34); 0 mL/h</td>
<td>Parturients and caregivers blinded.</td>
<td>Clinician workload not reported. Increased incidence of pain &gt;4/10 in the no-infusion group. No other differences between groups.</td>
</tr>
<tr>
<td>Bremerich et al.(^{7})</td>
<td>66</td>
<td>R 0.16%, S 0.5 (\mu g/\text{mL}), bolus 4 mL</td>
<td>(N = 33); 0 mL/h</td>
<td>Parturients blinded.</td>
<td>All outcomes reported. More clinician interventions in the no-infusion group.</td>
</tr>
<tr>
<td>Missant et al.(^{9})</td>
<td>78</td>
<td>R 0.15%, S 0.75 (\mu g/\text{mL}), bolus 4 mL, lockout 15 min</td>
<td>(N = 38); 0 mL/h</td>
<td>Parturients and caregivers blinded.</td>
<td>All outcomes were reported. No differences in any outcomes.</td>
</tr>
<tr>
<td>Vallejo et al.(^{10})</td>
<td>127</td>
<td>R 0.10%, F 2 (\mu g/\text{mL}), bolus 5 mL</td>
<td>(N = 63); 0 mL/h</td>
<td>Parturients and data collectors were blinded.</td>
<td></td>
</tr>
</tbody>
</table>

\(B = \) Bupivacaine; \(F = \) Fentanyl; \(S = \) Sufentanil; \(E = \) Epinephrine; \(R = \) Ropivacaine
PCEA: INTEREST IN CEI?


YES

- Reduction of care provider rescue bolus
- Improve maternal satisfaction
- Especially if low bolus volumes (≤ 5ml)
MODE PIEB
« Programmed Intermittent Epidural Bolus »
MODE PIEB

- Administration at regular intervals of a programmed bolus ± associated with PCEA mode
- Currently possible with some pumps (CADD®-Solis v3.0 Smiths medical)

- PIEB: bolus volume, lockout interval, infusion rate (250 – 500 mL/h)
- No CEI!
PIEB: Why this concept?

Kaynar AM et al. Anesth Analg 1999; 89: 531 - 8

- Multiorifice epidural KT
- Continuous (10.5 ml/h) vs bolus (3-5 ml sur 1 min / 20 min)
- KT placed onto a piece of white semiabsorbent paper over 1h

Area of diffusion $\rightarrow$ bolus (1.2 in$^2$) $>$ continuous infusion (0.3 in$^2$)
Perfusion continue
Accumulation dans le nerf
avec le temps car persistance
d’A locaux à l’extérieur
du fait débit du continu

Bolus
Répartition harmonieuse
Pénétration et équilibration,
Chute régulière de la
concentration des A locaux
du fait des bolus:
Pas de surdosage

PIEB: Why this concept?
PIEB + PCEA vs PCEA + CEI

Capogna G et al. Anesth Analg 2011; 113: 826 - 31

PCEA
- Bupi 0.125%
- 5 ml / 10 min
- 15 ml max / h

+ PIEB
- Levobupi 0.0625% + suf 0.5 μg/ml
- 10 ml bolus every h
- N = 75 nulliparous

+ CEI
- Levobupi 0.0625% + suf 0.5 μg/ml
- 10 ml / h
- N = 70 nulliparous

✓ Primary outcome: incidence of motor block throughout labor
✓ Secondary outcome: incidence instrumental deliveries
1. Complete block (unable to move feet or knees)
2. Almost complete block (able to move feet only)
3. Partial block (just able to move knees)
4. Detectable weakness of hip flexion while supine (between scores 3 and 5)
5. No detectable weakness of hip flexion while supine (full flexion of knees)
6. Able to stand and to perform partial knee bend

Motor block if score < 6 !!
Motor block more frequent throughout labor in CEI group

Figure 2. Percentage of patients from programmed intermittent epidural bolus (PIEB) or continuous epidural infusion (CEI) groups who had any motor block versus time after induction of labor analgesia. Data were censored for delivery. The groups were significantly different, $P < 0.001$. 

Capogna G et al. Anesth Analg 2011; 113: 826 - 31
Motor block at full cervical dilatation (p < 0.001)
- CEI = 25 / 55 (33%)
- PIEB = 5 / 61 (8%)

Incidence of instrumental delivery (p = 0.03 et RR = 2.9)
- CEI = 20%
- PIEB = 7%

Strong association between motor block at full cervical dilatation and instrumental delivery!
PIEB: bolus volume and lockout period?

Wong CA et al. Anesth Analg 2011; 112: 904-11

Programmed interval bolus + PCEA

<table>
<thead>
<tr>
<th>Group</th>
<th>Programmed interval (min)</th>
<th>Bolus volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5/15</td>
<td>15</td>
<td>2.5</td>
</tr>
<tr>
<td>5/30</td>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td>10/60</td>
<td>60</td>
<td>10</td>
</tr>
</tbody>
</table>

Solution = bupivacaine 0.625 ml/ml + fentanyl 11.95 µg/ml
Débit continu = 10 ml/h

Primary outcome = total dose of LA use
PIEB = bolus volume and lockout period?

**Wong CA et al. Anesth Analg 2011; 112: 904-11**

**PIEB at 10ml / h ➔ Réduction of total dose of LA ≈ 2mg/h Clinically significant??**

### Table 4. Analgesic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group 2.5/15 (n = 66)</th>
<th>Group 5/30 (n = 60)</th>
<th>Group 10/60 (n = 54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bupivacaine dose (mg/h)†</td>
<td>11.3 (9.5–13.6)</td>
<td>11.1 (9.2–13.3)</td>
<td>10.3 (8.9–11.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Adjusted bupivacaine dose per hour of labor (mg/h)†</td>
<td>10.4 (9.6–11.2)</td>
<td>10.0 (9.3–10.8)</td>
<td>8.8 (8.0–9.7)</td>
<td>0.005</td>
</tr>
<tr>
<td>PIB bupivacaine dose (mg/h)</td>
<td>6.6 (6.1–7.3)</td>
<td>6.8 (6.1–7.3)</td>
<td>6.5 (6.2–6.9)</td>
<td>0.31</td>
</tr>
<tr>
<td>Time to first PCEA request (min)</td>
<td>106 (59–193)</td>
<td>123 (65–180)</td>
<td>107 (76–211)</td>
<td>0.68</td>
</tr>
<tr>
<td>PCEA requests (n)</td>
<td>10 (3–17)</td>
<td>10 (3–17)</td>
<td>8 (4–11)</td>
<td>0.32</td>
</tr>
<tr>
<td>PCEA deliveries (n)</td>
<td>7 (3–11)</td>
<td>6 (4–10)</td>
<td>6 (4–8)</td>
<td>0.69</td>
</tr>
<tr>
<td>PCEA bupivacaine dose (mg/h)</td>
<td>2.9 (1.6–4.3)</td>
<td>2.9 (2.1–4.1)</td>
<td>2.4 (1.6–3.3)</td>
<td>0.32</td>
</tr>
<tr>
<td>Time to first manual bolus (min)</td>
<td>304 (189–429)</td>
<td>313 (178–479)</td>
<td>349 (253–493)</td>
<td>0.31</td>
</tr>
<tr>
<td>No. of manual bolus doses per subject (n)</td>
<td>24</td>
<td>30</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>17</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>11</td>
<td>7</td>
<td>0.72</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Manual bupivacaine dose, all subjects (mg)</td>
<td>12.5 (0–19.0)</td>
<td>0 (0–16.0)</td>
<td>0 (0–17.0)</td>
<td>0.13</td>
</tr>
<tr>
<td>Manual bupivacaine dose, subjects receiving a manual bolus (mg)</td>
<td>18.8 (12.5–28.8)</td>
<td>18.8 (12.5–25.0)</td>
<td>18.8 (12.5–28.8)</td>
<td>0.73</td>
</tr>
<tr>
<td>Satisfaction with analgesia (mm)</td>
<td>90 (78–99)</td>
<td>94 (80–100)</td>
<td>93 (92–98)</td>
<td>0.85</td>
</tr>
</tbody>
</table>
**No difference for analgesic efficacy, motor block, mode of delivery**

**Table 3. Labor Outcomes**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group 2.5/15 (n = 66)</th>
<th>Group 5/30 (n = 60)</th>
<th>Group 10/60 (n = 54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labor analgesia initiation to delivery interval (min)</td>
<td>487 (307–696)</td>
<td>412 (319–570)</td>
<td>519 (370–645)</td>
<td>0.22</td>
</tr>
<tr>
<td>Bromage scale score &gt;0, n (%)</td>
<td>9 (14)</td>
<td>6 (10)</td>
<td>4 (7)</td>
<td>0.54</td>
</tr>
<tr>
<td>VAS · time AUC (mm · h)</td>
<td>15 (6–29)</td>
<td>13 (5–26)</td>
<td>14 (8–25)</td>
<td>0.65</td>
</tr>
<tr>
<td>VAS score at vaginal delivery (mm)</td>
<td>26 (6–57)</td>
<td>29 (9–50)</td>
<td>18 (3–44)</td>
<td>0.31</td>
</tr>
<tr>
<td>Maximum oxytocin infusion during labor (mU/min)</td>
<td>8 (6–13)</td>
<td>8 (6–14)</td>
<td>12 (6–16)</td>
<td>0.70</td>
</tr>
<tr>
<td>Mode of delivery, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.39</td>
</tr>
<tr>
<td>NSVD</td>
<td>37 (56)</td>
<td>43 (72)</td>
<td>37 (68)</td>
<td></td>
</tr>
<tr>
<td>Forceps</td>
<td>11 (17)</td>
<td>8 (13)</td>
<td>7 (13)</td>
<td></td>
</tr>
<tr>
<td>Caesarean</td>
<td>18 (27)</td>
<td>9 (15)</td>
<td>10 (19)</td>
<td></td>
</tr>
</tbody>
</table>

Values are median (interquartile range) or n (percent).

VAS = visual analogue scale; AUC = area under the curve; NSVD = normal spontaneous vaginal delivery.
**PIEB: optimal programmation?**

Various PIEB programmations proposed

<table>
<thead>
<tr>
<th>Auteurs</th>
<th>mL</th>
<th>intervalles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wong</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>Capogna</td>
<td>10</td>
<td>60</td>
</tr>
<tr>
<td>Wong</td>
<td>2.5</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>60</td>
</tr>
<tr>
<td>Morau</td>
<td>8</td>
<td>60</td>
</tr>
<tr>
<td>Mavridou</td>
<td>8</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>60</td>
</tr>
</tbody>
</table>

Current trend = 8 – 10 mL / 60 min
Meta-analyse PIEB vs EA (CEI or PCEA)

- Randomized controlled studies, 2004 – 2011
- 9 studies:
  - PIEB, n = 350
  - Nulli et multiparous
### Principaux résultats

Principaux résultats

<table>
<thead>
<tr>
<th>Tableau 2. Summary of Randomized Controlled Trials Meta-analysis Findings Comparing PIEB and CEI or PCEA With a Background Infusion for Labor Analgesia^11</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIEB Versus CEI</strong></td>
</tr>
<tr>
<td>Local anesthetic consumption (MD)</td>
</tr>
<tr>
<td>Maternal satisfaction scores (MD)</td>
</tr>
<tr>
<td>Duration of second stage of labor (MD)</td>
</tr>
<tr>
<td>Mode of delivery</td>
</tr>
<tr>
<td>Instrumented delivery (OR)</td>
</tr>
<tr>
<td>Total duration of labor (MD)</td>
</tr>
<tr>
<td>Anesthesia interventions (OR)</td>
</tr>
</tbody>
</table>

Local anesthetic consumption presented as milligram of bupivacaine equivalents per hour; Satisfaction measured using 0–100 mm scale. Abbreviations: CEI, continuous epidural infusion; CI, confidence interval; MD, mean difference; OR, odds ratio; PCEA, patient-controlled epidural analgesia; PIEB, programmed intermittent epidural bolus.

^Favors PIEB over CEI.
EA is the most effective method for labor analgesia

PCEA = reference technique actually

PIEB = greater spread of LA solution in the epidural space ➞ better sensory blockade compared with CEI

PIEB = LA sparing effect ➞ fewer instrumental vaginal deliveries, less motor blockade, shorter duration of labor

PIEB = improvement in maternal satisfaction

PIEB = optimal regimen and pump settings remain unknown
Thank you for your attention