Labor Epidural: Local Anesthetics and Beyond
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The Changing Practice of Anesthesia
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Goals:
- Review Concept of MLAC
- Local anesthetic efficacy
- Local anesthetic sparing effects:
  - opiates
  - epinephrine
  - other adjuvants

Why not just Local Anesthetics
Local anesthetics (LA) alone associated with:
- Motor block

IJOA 1995;4:82-8

Why not just Local Anesthetics
Local anesthetics (LA) alone associated with:
- Motor block
- Increased instrumental delivery
- Decreased maternal satisfaction

IJOA 1995;4:82-8
Why not just Local Anesthetics

Local anesthetics (LA) alone associated with
Motor block
Motor Block associated with:
increased instrumental delivery
decreased maternal satisfaction
May contribute to maternal neurologic
injury from malpositioning

IJOA 1995;4:82-8

MLAC

Determination of the Minimum Local Analgesic Concentrations of Epidural Bupivacaine and Lidocaine in Labor

Malachy O. Columb, FRCA, and Gordon Lyons, FRCA

Minimum Local Anesthetic Concentration (MLAC)
Effective concentration in 50% of patients in 1st stage of labor (EC_{50})
Clinicial model to allow determination of relative potency of LAs
Allow measurement of LA sparing effects of other drugs

Anesth Analg 1995;81:833-7

MLAC

First Stage of Labor epidural request
Cervical dilation not exceeding 5cm
Lumbar epidural, LOR saline (2ml)
No test dose
20mL bolus of solution over 5 minutes
VAPS of 10 or below (0-100 range) within 60 min
Up-Down sequential allocation

Anesth Analg 1995;81:833-7

MLAC

After initial bolus:

Effective: Achieve VAPS of 10 or below (0-100 range)

Ineffective: Unable to achieve VAPS of 10 or below but responsive to predetermined rescue dose

Rejected: Unresponsive to initial or rescue dose (segmental pain, unilateral block etc...)

Curr Opin Anaesthesiol 2005;18:241-5
MLAC - Bupivacaine

- MLAC of bupivacaine was 0.065% (95% CI 0.045-0.085) (Dixon and Massey formula)

MLAC - Lidocaine

- MLAC of lidocaine was 0.37% (95% CI 0.32-0.42) (Dixon and Massey formula)

MLAC - Bupivacaine/Lidocaine

- Designed only to obtain ED50
- ED95 would be more clinically useful

Anesth Analg 1995;81:833-7
MLAC Limitations

Possible variations in dose-response curve

![Dose-response curve diagram](image)

Curr Opin Anaesthesiol 2005;18:241-5

MLAC Limitations

- Designed only to obtain ED50
- ED95 would be more clinically useful
- A snap-shot of labor pain at that particular cervical dilation

Values depend on patient population and the study center (parity, induction vs. spontaneous labor)

MLAC increases with labor progression

Early labor (2cm cervical dilation)
MLAC bupivacaine 0.048%

Late labor (5cm cervical dilation)
MLAC bupivacaine 0.140%

BJA 1998:80:11-13
MLAC Limitations

- Designed only to obtain ED50
  - ED95 would be more clinically useful
- A snap-shot of labor pain at that particular cervical dilation
- Values depend on patient population and the study center
- Only valid in labor epidural setting

Bupivacaine vs. Ropivacaine

- MLAC of bupivacaine 0.067% (95% CI 0.052 - 0.082)%
- MLAC of ropivacaine 0.111% (95% CI 0.100 - 0.122)%
- Ropivacaine is 60% as potent as Bupivacaine
- No difference in motor blockade, side effects

Anesthesiology 1999;90:944-50

Bupivacaine vs. Ropivacaine

- MLAC of Bupivacaine 0.093% (95% CI 0.076 - 0.110)%
- MLAC of Ropivacaine 0.156% (95% CI 0.136 - 0.176)%
- Ropivacaine is 60% as potent as Bupivacaine

BJA 1999;82:371-3
**(Summary)**

**Bupivacaine vs. Ropivacaine**

- **MLAC bupivacaine**
  - 0.048% (0.037-0.058%) - 0.104% (0.09-0.117%)

- **MLAC ropivacaine**
  - 0.089% (0.081-0.094%) - 0.156% (0.136-0.176%)

Absolute MLAC values depend on cervical dilation and study center.

Ropivacaine 60% as potent as bupivacaine.

*Curr Opin Anaesthesiol 2005;18:241-5*

**Motor Blockade**

- **MLAC bupivacaine**
  - 0.326% (0.285-0.367)

- **MLAC ropivacaine**
  - 0.497% (0.431-0.563)

P = 0.0008 Ropivacaine 66% as potent as bupivacaine in producing motor block.

*Anesth Analg 2002;95:204-8*

**MLAC Chloroprocaine and Fentanyl**

- 20mL bolus, VAS of 10 or less (0-100) in 30 min

- CPC: 0.43% (95 CI 0.29-0.56)

- CPC with 3mcg/ml fentanyl: 0.26% (95 CI 0.2-0.32)

- 3mcg/ml (60mcg) of fentanyl leading to 0.17% reduction in CPC MLAC.

1.65 times increase in relative potency

40% dose reduction

*Anesth Analg 1996;83:987-90*

**Bupivacaine and Fentanyl (IV vs. epidural)**

- 20mL of bupivacaine and 60mcg IV fentanyl vs 20mL bupivacaine and 3mcg/ml fentanyl (60mcg/20ml)

- Fentanyl dose constant in both IV and epidural groups

- MLAC bupivacaine and IV fentanyl 0.064% (95 CI 0.049 - 0.080)%

- MLAC of bupivacaine and epidural fentanyl 0.034% (95 CI 0.017 - 0.050)%

*Anesthesiology 2000;93:122-8*
Bupivacaine Fentanyl (IV vs. epidural)

- Epidural fentanyl increase analgesic potency of bupivacaine by 1.88 compared to IV dose
- Epidural fentanyl increased occurrence of pruritus
- Epidural fentanyl had higher cephalad spread of block

Epidural fentanyl increase analgesic potency of bupivacaine by 1.88 compared to IV dose

Epidural fentanyl increased occurrence of pruritus

Epidural fentanyl had higher cephalad spread of block

All suggesting primarily a spinal site of action
Fentanyl Site of Action

<table>
<thead>
<tr>
<th>Systemic site of action</th>
<th>Spinal site of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse Analgesia</td>
<td>Segmental Analgesia</td>
</tr>
<tr>
<td>Same efficacy (IV vs. Epidural)</td>
<td>Epidural route more efficacious</td>
</tr>
<tr>
<td>Plasma levels identical, analgesia depends on plasma levels</td>
<td>Analgesia independent of plasma levels</td>
</tr>
<tr>
<td>Same side-effect profile</td>
<td>Different side-effect profile</td>
</tr>
</tbody>
</table>

Epidural route more efficacious.
Plasma levels identical, analgesia depends on plasma levels.
Same side-effect profile.

Bupivacaine infusion
Epidural vs IV Fentanyl

Anesth Analg 2003;97:1439-45

Bupivacaine infusion with the addition of IV vs. Epidural infusion of fentanyl (30mcg/hr):

MLAC\text{infusion} with IV fentanyl infusion
0.063\% (0.058-0.067)

MLAC\text{infusion} with epidural fentanyl infusion
0.019\% (0.000-0.034)

Bupivacaine and Epidural Fentanyl

- MLAC bupivacaine plain
  0.069\%
- MLAC bupivacaine with 1mcg/ml fentanyl
  0.057\%
- MLAC bupivacaine with 2mcg/ml fentanyl
  0.048\%
- MLAC bupivacaine with 3mcg/ml fentanyl
  0.031\%
- MLAC bupivacaine with 4mcg/ml fentanyl
  0.015\%

Pruritus incidence 27.5\% with 4mcg/ml, 10\% with 3mcg/ml and 5\% with both 2mcg/ml and 1mcg/ml.

BJA 1997;78:493-7

Bupivacaine and Epidural Fentanyl

Anesth Analg 2003;97:1439-45
**Bupivacaine and Epidural Sufentanil**

- MLAC bupivacaine plain 0.104%
- MLAC bupivacaine with 0.5mcg/ml sufentanil 0.048%
- MLAC bupivacaine with 1.0mcg/ml sufentanil 0.021%
- MLAC bupivacaine with 1.5mcg/ml sufentanil 0.009%

*Anesthesiology 1998;89:626-32*

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**Bupivacaine and Epidural Epinephrine**

- MLAC bupivacaine plain 0.091%
- MLAC of bupivacaine with epi 1/300K 0.065%
- 29% reduction of MLAC

*Anesthesiology 2002;96:1123-8*

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**Epinephrine Effect**

- Vasoconstriction not a major role
- Bupivacaine decreases spinal and dural blood flow
- Addition of epi does not further decrease blood flow
- Epinephrine alone has analgesic properties
- Strong evidence for $\alpha_2$ mechanism

*Anesthesiology 2002;96:1123-8*
Bupivacaine and Epidural Epinephrine

- 29% reduction in MLAC of bupivacaine
- No difference in motor block
- No difference in time to onset/cephalad spread
- Prolonged analgesia 69 min (epi group) vs. 62 mins
  (not statistically significant)

Anesthesiology 2002;96:1123-8

Bupivacaine and Epidural Epinephrine

- Stat. significant reduction in FHR and maternal BP
- Lowest Maternal MAP 79mmHg (epi group) vs. 84
- Likely a peripheral β effect
- FHR 134 bpm (epi group) vs. 140
- At higher concentrations, epinephrine may have a tocolytic effect (β adrenergic effect)

Anesthesiology 2002;96:1123-8

Epidural Clonidine

“I recommend an epidural, at least until they’re off to school.”

“Because it’s the best way to manage labor pain.”
Epidural Clonidine

Indications and Usage

“Duraclon is indicated in combination with opioids for the treatment of severe pain in cancer patients that is not adequately relieved by opioid analgesics alone. Epidural clonidine is more likely to be effective in patients with neuropathic pain than somatic or visceral pain........ In a rare patient, the potential benefits may outweigh the known risks (see WARNINGS).”

Clonidine package insert, Revised August 2010
Bioniche Pharma USA LLC. Lake Forest, IL

Addition of clonidine (100mcg vs 150mcg) to 0.0625% Bupivacaine containing 1/200K epinephrine and 10mcg of sufentanil

- Significant decrease in maternal MAP with both doses
- Clonidine 150mcg was associated with more frequent variable and late FHR decelerations
- Clonidine 100mcg was associated with more frequent early FHR decelerations

BJA 1996;77:458-62
Epidural Clonidine

- Shown to have spinal site of action for analgesia
- Efficacy with opioid-resistant pain
- Efficacy with neuropathic/sympathetically mediated pain
- Less respiratory depression than opiates at equivalent analgesic doses

*Anesthesiology 1993;78:277-87*

Ropivacaine and Epidural Clonidine

- MLAC ropivacaine plain 0.097%
- MLAC ropivacaine with 30mcg clonidine 0.081%
- MLAC ropivacaine with 60mcg clonidine 0.035%

- 16% decrease in MLAC with 1.5mcg/ml (30mcg)
- 64% decrease in MLAC with 3mcg/ml (60mcg)

*A&A 2002;95:735-40*

Ropivacaine and Epidural Clonidine

- No difference in SBP between control and 30mcg
- Lowest SBP in 60mcg group

<table>
<thead>
<tr>
<th></th>
<th>Ropivacaine</th>
<th>Ropiv + 30mcg Clonidine</th>
<th>Ropiv + 60mcg Clonidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest SBP (mm Hg)</td>
<td>112</td>
<td>114</td>
<td>104</td>
</tr>
<tr>
<td>Hypotension Incidence</td>
<td>13%</td>
<td>11%</td>
<td>26%</td>
</tr>
<tr>
<td>Sedation Score</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

No difference in motor blockade, APGAR scores, operative/instrumental deliveries

*A&A 2002;95:735-40*

Ropivacaine and Epidural Clonidine

- MLAC Ropivacaine 0.099%
- MLAC Ropivacaine + Sufentanil 5mcg 0.036%
- MLAC Ropivacaine + Clonidine 75mcg 0.036%

- Significant local anesthetic sparing effect with low dose sufentanil and clonidine

*IJOA 2009;17:315-21*
**Future Directions**

- Intrathecal neostigmine studied in 1940's
- Spinal site of action for acetylcholine
- Analgesia for experimental, labor, post-op, chronic pain
- High incidence of severe nausea/vomiting (10mcg dose)
- Epidural neostigmine has less GI side effects

*A&A 2009;109:293-95*

**Epidural Neostigmine**

- VAS score starting at 51-65 (0-100)
- Reduction in VAS 20min

<table>
<thead>
<tr>
<th>Ropiv 20mg</th>
<th>VAS Score 20min</th>
<th>Reduction in VAS 20min</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td></td>
<td>62%</td>
</tr>
<tr>
<td>Ropiv 10mg, Suf 5mcg</td>
<td>6.5</td>
<td>89%</td>
</tr>
<tr>
<td>Ropiv 10, Suf 5, Neost 2mcg/kg</td>
<td>6.0</td>
<td>90%</td>
</tr>
<tr>
<td>Ropiv 10, Suf 5, Neost 4mcg/kg</td>
<td>1.6</td>
<td>98%</td>
</tr>
<tr>
<td>Ropiv 10mg, Neost 4mcg/kg</td>
<td>21</td>
<td>59%</td>
</tr>
</tbody>
</table>

*Highest motor blockade with Ropivacaine 20mg*

*A&A 2003;96:1161-66*

**Epidural Neostigmine**

- Combined sufentanil/neostigmine

- Sufentanil 10mcg
- Sufentanil 20mcg
- Sufentanil 10mcg + neostigmine 250mcg
- Sufentanil 10mcg + neostigmine 500mcg
- Sufentanil 10mcg + neostigmine 750mcg

*Anesthesiology 2004;101:439-44*
**Epidural Neostigmine**

- Doses below 250mcg (2-4mcg/kg) shown minimally effective
- 500mcg dose shown effective
- 750mcg no additional benefit

Anesthesiology 2004;101:439-44

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**Dexmedetomidine**

- Case Reports:
  - ICU sedation of parturient with respiratory failure requiring non-invasive ventilation (Respir Care 2012 in press)
  - Awake fiberoptic intubation of parturient with spinal muscular dystrophy for cesarean section (IJOA 2009;18:403-7)
  - Adjunct for labor analgesia and cesarean delivery in a parturient with a tethered spinal cord (IJOA 2009;18:258-61)

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**Epidural Dexmedetomidine**

- Intra-Op/Post-Op analgesia
  - RCT
  - Vaginal hysterectomies Intra-op/post-op analgesia
  - Ropivacaine + (dexmedetomidine vs. clonidine)
    - 1.5mcg/kg
    - 2mcg/kg
  
  More sedation, faster onset sensory and motor block

Indian J Anaesth 2011;55:116-21
Epidural Dexmedetomidine
Intra-Op/Post-Op analgesia

<table>
<thead>
<tr>
<th></th>
<th>RD</th>
<th>RC</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to T10 level</td>
<td>8.52 ± 2.36</td>
<td>9.72 ± 3.44</td>
<td>0.032</td>
</tr>
<tr>
<td>onset (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max sensory level</td>
<td>T5-6</td>
<td>T6-7</td>
<td>-</td>
</tr>
<tr>
<td>Time to max sensory</td>
<td>13.14 ± 3.96</td>
<td>15.80 ± 4.86</td>
<td>0.018</td>
</tr>
<tr>
<td>level (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to complete</td>
<td>17.24 ± 5.16</td>
<td>19.52 ± 4.06</td>
<td>0.041</td>
</tr>
<tr>
<td>motor block</td>
<td></td>
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<td></td>
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Indian J Anaesth 2011;55:116-21

Epidural Dexmedetomidine
Intra-Op/Post-Op analgesia

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<th>RD</th>
<th>RC</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to T10 level</td>
<td>7.12 ± 2.44</td>
<td>9.14 ± 2.94</td>
<td>0.016</td>
</tr>
<tr>
<td>onset (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max sensory level</td>
<td>T4-6</td>
<td>T5-7</td>
<td>-</td>
</tr>
<tr>
<td>Time to max sensory</td>
<td>13.38 ± 4.48</td>
<td>16.61 ± 4.36</td>
<td>0.021</td>
</tr>
<tr>
<td>level (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to complete</td>
<td>18.16 ± 4.52</td>
<td>22.98 ± 4.78</td>
<td>0.033</td>
</tr>
<tr>
<td>motor block</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Saudi J Anaesth 2011;5:365-70

Summary

- Local anesthetics bupivacaine/ropivacaine
- Opiates fentanyl/sufentanil
- Epinephrine
- Clonidine
- Neostigmine ???
- Dexmedetomidine ???