Hyperbaric prilocaine
Expanding the indications in neuroaxial anesthesia

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The rationale

• New local anesthetics with new combination of features
• Benefit and safety considerations
• General trends in healthcare
  • Structure of patients’ collective
  • Shift towards ambulatory surgery
  • Economical limitations
History of local anesthetics

- 3000 B.C. Coca plant (*erythroxylum coca*) leaves used by amerindians
- 1750 Coca leaves arrive in Europe
- 1859 Isolation of cocaine alkaloid
- 1884 First clinical use of cocaine in ophthalmology by Sigmund Freud
- 1905 Procaine
- 1932 Tetracaine
- 1943 Lidocaine
- 1952 2-Chlorprocain
- 1957 Mepivacaine
- 1960 Prilocaine
- 1963 Bupivacaine
- 1970 Articain
- 1972 Etidocaine
- 1996 Ropivacaine
- 1999 Levobupivacaine
Nomenclature & Chemistry

**Amínoamídes (2 x i)**

![Chemical structure of aminoamides](diagram)

- 1943 Lidocaine
- 1957 Mepivacaine
- 1960 Prilocaine
- 1963 Bupivacaine
- 1970 Articain
- 1972 Etidocaine
- 1996 Ropivacaine
- 1999 Levobupivacaine

**Amínoesters (1 x i)**

![Chemical structure of aminoesters](diagram)

- 1905 Procaine
- 1932 Tetracaine
- 1952 2-Chlorprocain
Onset of action

Fast

• Lidocaine
• 2-Chlorprocain
• Mepivacaine
• **Prilocaine**
• Articain
• Etidocaine

Slow

• Procaine
• Tetracaine
• Bupivacaine
• Ropivacaine
• Levobupivacaine
Duration of action

**Long**
- Mepivacaine 1.5-3 h
- Tetracaine 1-3 h
- Bupivacaine 4-5 h
- Etidocaine 4-6 h
- Ropivacaine 4-6 h

**Variable**
- Articaine 0.5-5 h

**Short**
- 2-Chlorprocain 30-40 min
- Procaine 40-60 min
- Prilocaine 1-1.5 h
- Lidocaine 1-2.5 h
Combined onset and duration

**Fast & Short**
- Procaine
- Tetracaine
- Bupivacaine
- Ropivacaine
- Levobupivacaine

**Slow & Long**
- Procaine
- Tetracaine
- Bupivacaine
- Ropivacaine
- Levobupivacaine

**Fast & Long**
- Mepivacaine
- Articain
- Etidocaine
Combined onset and duration

**Fast & Short**
- 2-Chlorprocain
- Prilocaine
- Lidocaine

**Slow & Long**
- Procaine
- Tetracaine
- Bupivacaine
- Ropivacaine
- Levobupivacaine

**Slow & Short**
- Procaine
- Tetracaine

**Fast & Long**
- Mepivacaine
- Articain
- Etidocaine
Toxicity and side effects

**Aminoesters**: metabolite paraaminoibenzoic acid is responsible for allergic reactions. Therapy by antiallergic medication and measures.

**All local anesthetics**: systemic effects such as peri-oral numbness, dysgeusia, preconvulsive neurological effects (tremor, tinnitus, nystagmus, somnolence), convulsive neurological effects (cloni), coma, apnea, arrhythmias, cardiac arrest. Prevention by dosage limit, therapy by anticonvulsants and symptomatic measures.
**Toxicity and side effects**

**Prilocaine:** if given in large dose (> 10 mg/kg) produces o-toluidine which converts Hb to metHb (tissue hypoxemia). Prevention by dosage limit, therapy by i.v. methylene blue or ascorbic acid.

For a 60 kg adult the limit is at 600 mg

For spinal anesthesia one needs 2-3 ml of 2% solution = 40 - 60 mg
Day case surgery (DCS)

- Ambulatory surgery
- Same-day surgery
- Come and go surgery
- Outpatient surgery

The patient returns home on the day of surgery, thus keeping the in-hospital postoperative stay very short (and spending most of the postoperative recovery at home).

Not to be confounded with Day Care Surgery = return home from surgery within 24 h (usually on the next day)

The surge of day case surgery

1990

10%

2015

65%
Some good reasons

Surgery & anesthesia duration prolongs the stay in the hospital. Duration of staying in the hospital correlates with postoperative complications...

- Pain
- PONV
- Thromboembolic events
- Delayed discharge
- Unanticipated readmissions
- Infections

*Fast ambulation is associated with faster and better recovery.*
Even more good reasons

...better surgical techniques
...better anesthetics and more sophisticated techniques

Conditions

- Patient is considered fit for discharge according to local standardized protocol
- No signs of hemorrhage, surgical wound looks normal
- Transport is available (patient doesn’t drive)
- Postoperative medication is assured (compliance)
- Patient is accompanied by an adult person who is able to take care, and is present for 24 h
- Patient refrains from driving, operating machines, signing contracts and drinking alcohol for 24 h
- Ability of contacting the surgeon & anesthetist (or emergency) for 24 h
- Ability of return to hospital if necessary in due time (distance and means of transportation)
Advantages of DCS

- Reduction in medical costs and need for healthcare resources
- Increased availability of indoor beds and capacity
- Better comfort (at home finer than in the hospital)
- Less hospital acquired infections
- Less vein thrombosis
- Less social disruption for the patient
- Less separation-induced anxiety and stress (esp. in children)
- Faster recovery

Disadvantages of DCS

- The restriction of DCS to experienced senior staff (little opportunity for junior staff to practice)
- Necessity of more expensive drugs and equipment
- The need for a responsible person to oversee the day care patient at home for the first 24-48 hours
- Maintenance of close communication from home to clinic
- Extra work for the general practitioner in the postoperative period; patients often ring them for advice or treatment
- Risk of delayed recognition of complications and delayed treatment
- Risk of unexpected readmission

The complication rates in day surgery, resulting in unexpected readmissions are equally divided between problems with the surgery and anaesthesia:

- Haemorrhage, pain in 50%
- Nausea and vomiting, dizziness in 50%

Anesthesia in DCS

In hospital surgery

Day case surgery

Size, duration & invasiveness of surgery

60%
Anesthesia in DCS

Size, duration & invasiveness of surgery

In hospital surgery

Day case surgery

General anesthesia

Regional anesthesia

Regional anesthesia

General anesthesia

Regional anesthesia
Regional anesthesia in DCS

**Institution**
- Less intensity of care (economical), higher turnover
- Less duration of care (economical), lower facility costs

**Surgeon**
- Accurate assessment of operation result and function
- Easy communication about findings and treatment options

**Patient**
- Easy communication about findings and treatment options
- Less suffering by pain and PONV
- Better comfort at home than in the hospital
- Less complications (hospital acquired infections, vein thrombosis)
- Less social disruption for the patient
- Less separation-induced anxiety and stress (esp. in children)
- Earlier mobilization, faster recovery
Complications

The complication rates in day surgery, resulting in unexpected re-admissions are equally divided between problems with the surgery and anaesthesia:

- Haemorrhage, pain in 50%
- Nausea and vomiting, dizziness in 50%

Typical for GA

- Postspinal headache
- Urinary retention

Typical for RA

An inherent dilemma
of spinal anesthesia for short procedures:

A short surgery requires a short anesthesia (just a bit longer than the operation). This results in...

- early return of motor function thus enabling early discharge
- also early return of sensibility & postoperative pain
**Discharge criteria (GA)**

Post anaesthetic discharge scoring system (PADSS) by Chung

1. **Vital signs**
   - 2 = Within 20% of preoperative value
   - 1 = 20–40% of preoperative value
   - 0 = >40% of preoperative value

2. **Activity and mental status**
   - 2 = Oriented x3 AND has a steady gait
   - 1 = Oriented x3 OR has a steady gait
   - 0 = Neither

3. **Pain, nausea and/or vomiting**
   - 2 = Minimal
   - 1 = Moderate, having required treatment
   - 0 = Severe, requiring treatment

4. **Surgical bleeding**
   - 2 = Minimal
   - 1 = Moderate
   - 0 = Severe

5. **Intake and output**
   - 2 = Has had PO fluids AND voided
   - 1 = Has had PO fluids OR voided
   - 0 = Neither

*Total PADSS score is 10, ≥9 considered fit for discharge*

### Aldrete score

<table>
<thead>
<tr>
<th>Time</th>
<th>Before</th>
<th>After</th>
<th>Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moves 4 extremities voluntarily or on command</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Moves 2 extremities voluntarily or on command</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Moves 0 extremities voluntarily or on command</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Spontaneous, unlaboured respiration</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Apnea</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>BP ± 20% of preanaesthetic level</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>BP ± 20%–50% of preanaesthetic level</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>BP ± 50% of preanaesthetic level</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Awake and oriented x 3</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Arousable to verbal stimuli</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Not responsive</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Maintaining O₂ saturations &gt;90% on room air</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Needs O₂ inhalation to maintain O₂ saturations &gt;90%</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>O₂ saturation &gt;90% even with O₂ supplementation</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Total**

*Note:* A score of 10 was required for discharge from the endoscopy/recovery room.

*Chung et al. J Clin Anesth 1995; 7: 500-6*
Discharge criteria (RA)

- Return of anal tone
- Passage of urine
- Power of limbs (plantar flexion normal)
- Recovery of proprioception, ambulation without dizziness
- Upper level of temperature sensitivity loss < Th10
- Return of sympathetic tone

Prilocaine

- Fast onset of action
- Short duration of action, (but not too short)
- Very low TNS* rate
- metHb-toxicity only by doses far above routine use

*Transitory neurological symptoms
Hyperbaric Prilocaine

<table>
<thead>
<tr>
<th></th>
<th>Prilocaine hyperbar</th>
<th>40 mg</th>
<th>60 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast Onset of action</td>
<td>✔️</td>
<td>8 min</td>
<td>8 min</td>
</tr>
<tr>
<td>Fast Offset of Sensory Block</td>
<td>✔️</td>
<td>105 min</td>
<td>132 min</td>
</tr>
<tr>
<td>Fast Offset of Motor Block</td>
<td>✔️</td>
<td>92 min</td>
<td>118 min</td>
</tr>
<tr>
<td>Low Incidence of Side effects</td>
<td>✔️</td>
<td>0 TNS</td>
<td>0 TNS</td>
</tr>
<tr>
<td>Fast Discharge</td>
<td>✔️</td>
<td>208 min</td>
<td>256 min</td>
</tr>
</tbody>
</table>

- Fast onset of action
- Calculable duration
- Shorter motor blockade
- Very low TNS rate
Hyperbaric Prilocaine

- Available as 2% hyperbaric agent (20 mg / ml) for spinal (intrathekal) anesthesia
- Ideal for short surgical procedures, as they occur in day-case surgery
The main difference 1

Case 1
Case 2
Case 3
Case 4

Spinal puncture
Operability
Recovery

Spinal puncture
Operability
Recovery

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 hours
The main difference 2

Time to safe discharge

Spinal puncture
Operability
Recovery
Muscular weakness

Time to safe discharge

Spinal puncture
Operability
Recovery
Muscular weakness

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 hours
Variating the effect

- Influencing the spread by tilting the table
- Influencing the duration of action by
  - amount of drug (15-20-40-60 mg)
  - admixing fentanyl and/or clonidine
Variating the effect

- Limiting the spread to saddle block by sitting 10 min after puncture
- Ideal for perineal, anal and external genital interventions
- Very short stay in recovery room if power of legs preserved

When we put these items together...
When we put these items together...

- More frequent regional anesthesia
- More frequent day case surgery
- More frequent...
When we put these items together...

- More spinal anesthesia
- More frequent regional anesthesia
- More frequent day case surgery
When we put these items together...

- More frequent day case surgery
- More frequent regional anesthesia
- More spinal anesthesia
- Need for fast onset local anesthetic
When we put these items together...

- Need for fast onset local anesthetic
- More spinal anesthesia
- More frequent regional anesthesia
- More frequent day case surgery
- TNS with less
Hyperbaric Prilocaine

- Need for fast onset local anesthetic
- More spinal anesthesia
- More frequent regional anesthesia
- More frequent day case surgery
- Firm control & less short action