EXPERIENCES WITH ROPIVACAINE

Brunello BRUNETTO
San Paolo Hospital
Savona Italy
...thanks for your sympathy!...
in LIGURIA 21 Hs  for 1.575.000 res.
## San Paolo & San Giuseppe Hospitals

### Department of Anesthesiology & ICU

**Head Dr. Brunello BRUNETTO**

<table>
<thead>
<tr>
<th><strong>Hospital San Paolo</strong></th>
<th><strong>Town of Savona 61.500 res.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>OR of great surgery</td>
<td>8</td>
</tr>
<tr>
<td>OR of day surgery</td>
<td>2</td>
</tr>
<tr>
<td>OR of ambulatory surgery</td>
<td>1</td>
</tr>
<tr>
<td>Beds of ICU</td>
<td>13</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Hospital San Giuseppe</strong></th>
<th><strong>Town of Cairo Montenotte 13.200 res.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>OR of day surgery</td>
<td>2</td>
</tr>
</tbody>
</table>
San Paolo & San Giuseppe Hospitals  
Department of Anesthesiology & ICU  
Head Dr. Brunello BRUNETTO

<table>
<thead>
<tr>
<th>People of the team</th>
<th>People of the team</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>1</td>
</tr>
<tr>
<td>Anesthesists</td>
<td>30</td>
</tr>
<tr>
<td>Head Nurses</td>
<td>4</td>
</tr>
<tr>
<td>Nurses</td>
<td>97</td>
</tr>
<tr>
<td>Social Health Operators</td>
<td>17</td>
</tr>
<tr>
<td>Technical Health Assistants</td>
<td>1</td>
</tr>
<tr>
<td>Auxiliaries</td>
<td>1</td>
</tr>
<tr>
<td><strong>People of the team</strong></td>
<td><strong>151</strong></td>
</tr>
</tbody>
</table>
Nowadays around 1:100,000 anesthesias

Safety improvement

Anesthesia-related mortality
(Beecher & Todd)

Around 1:2680 anesthesias

Nowadays around 1:100,000 anesthesias
• Preoperative optimization of the patient’s conditions
• Monitoring (capnography, pulse oximetry etc.)
• **Safer drugs**
• PACU
• Training and CME...
EVOLUTION OF ANAESTHETIST

2000 BC

ETHER

1846

1950

2000

2014

Copyright 66: www.facebook.com/laughingdoses

Dr GANESH CHOU DHARI
M.D.(ANAE), SOLAPUR
THE ITALIAN ANESTHESISTS-INTENSIVISTS ARE IN FRONT LINE TO PREVENT THE COMPLICATIONS.
Controlling postoperative pathophysiology

Information and teaching

Stress

Pain Relief

Exercise

Enteral Nutrition

Growth Factors

Reduced morbidity and
Accelerated convalescence

KEHLET Br J Anesthesia  78, 606: 1997
Albert Niemann (chemical) isolated COCAINE in 1858.
Koller, first, invented topical anesthesia through intraocular injection of cocaine and also used cocaine as local anesthetic for a tooth extraction.

Mattison JB
Cocaine poisoning

1884

1888

1905

Procaine

1943

Lidocaine

1957

Bupivacaine

1980s

Ropivacaine and Levobupivacaine
• a lipophilic pole
• an hydrophilic pole
• an intermediate chain, with an amide or ester link
LOCAL ANAESTHETICS
CHEMICAL STRUCTURE

**aminoesters**
- cocaine
- tetracaine
- procaine
- clorprocaine
- benzocaine

**aminoamides**
- lidocaine, mepivacaine
- bupivacaine, levobupivacaine
- ropivacaine
- prilocaine
IDEAL PECULIARITIES OF A LOCAL ANESTHETIC

1 excellent potency at low concentrations
2 good penetrability
3 short onset
4 long offset
5 low systemic toxicity
6 lack of neurotoxicity
7 absolute reversibility of action
8 ease of sterilizing
9 safety

D. Celleno et al. 2007
IDEAL PECULIARITIES OF A LOCAL ANESTHETIC

1 excellent potency at low concentrations
2 good penetrability
3 short onset
4 long offset
5 low systemic toxicity
6 lack of neurotoxicity
7 absolute reversibility of action
8 ease of sterilizing
9 safety

IDEAL FOR ALL THE LOCAL ANESTHETICS?
IDEAL FOR ALL THE SURGERIES?
• **pKa**

(the pH at which the 50% of a LA is not-ionized and the other 50% is ionized)

Local Anesthetics with a **pKa** near the physiological pH have a **faster onset** because soluted in larger part not-ionized. Increasing pKa becomes soluted in larger part the ionized fraction, that gives a **slow onset**.
<table>
<thead>
<tr>
<th></th>
<th>pka</th>
<th>% not ionized form at pH 7.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIDOCAINE</td>
<td>7.9</td>
<td>24</td>
</tr>
<tr>
<td>MEPIVACAINE</td>
<td>7.8</td>
<td>39</td>
</tr>
<tr>
<td>BUPIVACAINE</td>
<td>8.1</td>
<td>17</td>
</tr>
<tr>
<td>LEVOBUPIVACAINE</td>
<td>8.1</td>
<td>17</td>
</tr>
<tr>
<td>ROPIVACAINE</td>
<td>8.1</td>
<td>17</td>
</tr>
</tbody>
</table>
HOW CHANGING THE ONSET

WARNING: changes pKa

ADDITION of NaHCO$_3$: prolongs the onset changing the pH of solution
CONSTANT OF DISSOCIATION

ONSET OF THE BLOCK
• **Liposolubility**

Anaesthetics with higher liposolubility are also the most potent; this is due to the ability to cross the fosfolipidic matrix of the cellular membranes, so a low liposolubility results in a low degree of motor blockade and in a high motor sensory differentiation.
<table>
<thead>
<tr>
<th></th>
<th>liposolubility</th>
<th>equivalent concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIDOCAINE</td>
<td>2.9</td>
<td>2%</td>
</tr>
<tr>
<td>BUPIVACAINE</td>
<td>28</td>
<td>0.5%</td>
</tr>
<tr>
<td>LEVOBUPIVACAINE</td>
<td>30</td>
<td>0.5%</td>
</tr>
<tr>
<td>ROPIVACAINE</td>
<td>3</td>
<td>0.75%</td>
</tr>
</tbody>
</table>
Ropi is less lipophilic than Bupi and that, together with its stereoselectives properties, contributes to Ropi having a significantly higher threshold for cardiotoxicity and CNS toxicity than bupivacaine in animals and healthy volunteers.

Knudsen K. et al
Central nervous and cardiovascular effects of i.v. infusions of ropivacaine, bupivacaine and placebo in volunteers.
• **Proteic bond**

(the most part of LA binds to acid alfa-glicoproteins, reduced in pregnancy)

Takes an important effect on the **length** of the blockade. An high percentage of LA bond to proteins means a great affinity of binding to the receptor proteins. **The most potent local anaesthetics have also the longer length of action.**
<table>
<thead>
<tr>
<th></th>
<th>proteic bond %</th>
<th>duration min</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIDOCAINE</td>
<td>64</td>
<td>100</td>
</tr>
<tr>
<td>MEPIVACAINE</td>
<td>75</td>
<td>100</td>
</tr>
<tr>
<td>BUPIVACAINE</td>
<td>95</td>
<td>175</td>
</tr>
<tr>
<td>LEVOBUPIVACAINE</td>
<td>97</td>
<td>190</td>
</tr>
<tr>
<td>ROPIVACAINE</td>
<td>94</td>
<td>150</td>
</tr>
</tbody>
</table>
PROTEIC BOND

LENGTH OF THE BLOCK

BG Covino Pharmacology of local anaesthetic agents Br J Anaesth 1986;58:701-16
Brachial plexus block with a new local anaesthetic: 0.5 per cent ropivacaine

A new local anaesthetic, ropivacaine hydrochloride, was used in a concentration of 0.5 per cent in 32 patients receiving a subclavian perivascular block for upper extremity surgery. One group (n = 15) received 0.5 per cent ropivacaine without epinephrine and a second group (n = 17) received 0.5 per cent ropivacaine with epinephrine in a concentration of 1:200,000. Anaesthesia was achieved in 87 per cent of the patients in both groups in all of the C7 through T1 brachial plexus dermatomes. Motor block was profound with 100 per cent of patients in both groups developing paresis at both the shoulder and hand and 100 per cent developing paralysis at the shoulder. There was a rapid initial onset of sensory block (a mean of less than four minutes for analgesia) with a prolonged duration (a mean of greater than 13 hr of analgesia). The addition of epinephrine did not significantly affect the quality or onset of sensory or motor block. The duration of sensory block was reduced by epinephrine at T1 for analgesia and at C7, C8, and T1 for anaesthesia. The duration of sensory block in the remaining brachial plexus dermatomes as well as the duration of motor block was not affected by epinephrine. There was no evidence of cardiovascular or central nervous system toxicity in either group with a mean dose of 2.5–2.6 mg·kg⁻¹ ropivacaine.

Key words
ANAESTHETICS, LOCAL: ropivacaine;
ANAESTHETIC TECHNIQUES: regional, brachial plexus.

From the Department of Anesthesiology, *University of Texas, Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas 78284. and the Department of Anesthesiology, †University of Illinois, College of Medicine at Chicago, 3200 West 1740 Taylor Street, Chicago, Illinois 60612.

The study was supported by a grant from Astra Ab AB and was conducted at Audie L. Murphy Memorial Veteran’s Administration Hospital (San Antonio, Texas), Medical Center Hospital (San Antonio, Texas), West Side Veteran’s Administration Hospital (Chicago, Illinois), and University of Illinois Hospital (Chicago, Illinois).

Address correspondence to: Rosemary Hickey, The University of Texas, Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas 78284-7838.

Ropivacaine is a new local anaesthetic with a chemical formula similar to that of other amino amides in clinical use (Figure 1). The physical properties of ropivacaine are listed in Table 1. In vitro studies have demonstrated that ropivacaine is a potent blocker of Aδ and C fibres (pain fibres). Preliminary animal studies have also shown that ropivacaine is an effective local anaesthetic for infiltration, epidural, spinal, and brachial plexus anaesthesia. In a guinea pig model of brachial plexus block Akerman et al. demonstrated that ropivacaine was similar to bupivacaine in terms of onset and duration of sensory block and frequency of motor block. It has been reported to be less toxic than bupivacaine but more toxic than lidocaine. No previous studies have evaluated ropivacaine for brachial plexus anaesthesia in man. The purpose of this study was to determine the efficacy and safety of 0.5 per cent ropivacaine with and without epinephrine in patients receiving subclavian perivascular brachial plexus blocks. The rapidity of onset as well as duration of sensory and motor block were also determined.

Ropivacaine is a new local anesthetic...
ROPIVACAINE 0.2%

POSTOPERATIVE PAIN
Lumbar epidural (cont. Inf.) 6-10 ml/h
Thoracic epidural (cont. Inf.) 6-14 ml/h
Peripheral nerve block (cont. Inf.) 5-10 ml/h
Peripheral minor nerve block 1-100 ml

LABOUR PAIN (Lumbar epidural)
Bolus 10-20 ml
Intermittent top-up 10-15 ml
Continuous infusion 6-14 ml/h

IN CHILDREN
Caudal epidural block (below T12) 1 ml/Kg
ROPIVACAINE 0.5%

SURGICAL ANESTHESIA
Intrathecal administration 3-4 ml

IN CHILDREN
Peripheral nerve block (ilioinguinal block)
0.6 ml/kg
ROPIVACAINE 0.75%

SURGICAL ANESTHESIA
Lumbar epidural 15-20 ml
Thoracic epidural single block 5-15 ml
Peripheral major nerve block 10-40 ml
Peripheral minor nerve block or infiltr. 1-30 ml

POSTOPERATIVE PAIN
Intra-articular injection 20 ml
ROPIVACAINE 1%

SURGICAL ANESTHESIA
Lumbar epidural 15-20 ml
Motor sensory differentiation

It’s favourable for:

• **Labour analgesia**: is kept the walking, that encourages the progress of the labour, and the women can take part actively.

• **In the treatment of post operative pain**: the lack of pain in the course of physiotherapy’s practices it’s mandatory, to avoid the stop of them.

Faster offset

Foster RH. Drugs 2000; 59(3):551-79
Epidural analgesia in abdominal surgery: 0.2% ropivacaine with sufentanil

G. DE COSMO, P. PRIMIERI, E. ADDUCCI, M. FIORENTI, G. BECCIA

Department of Anesthesiology and Critical Care
Catholic University of Rome, Rome, Italy

Aim. Combining an opioid with peridural local analgesia is an excellent technique to control post-operative pain. Sufentanil is a widely used opioid agent, but its optimal dosage has not yet been defined. In this study we wanted to determine the best dose of epidural sufentanil in major surgery.

Methods. Before the operation, 45 major abdominal surgery patients received blended anesthesia through an epidural catheter. The patients were randomized into 3 groups of 15 subjects according to different sufentanil doses [0.2% ropivacaine combined with sufentanil at a dose of 0.5 µg/ml⁻¹, 0.75 µg/ml⁻¹, or 1 µg/ml⁻¹ (groups A, B and C, respectively)] administered through an epidural catheter connected to an elastometric pump (5 ml/h) for the first 36 post-operative hours. The level of postoperative analgesia in motion and at rest was measured using an analog visual scale (VAS-R, VAS-I).

Results. Analgesia was best in group A, and similar in groups B and C; 2 cases of paresthesia were noted in group C. The VAS-I scores were <3 across all 3 patient groups.

Conclusion. Epidural analgesia is an efficacious and reliable technique. The combination of 0.2% ropivacaine and 0.75 µg/ml⁻¹ sufentanil was found to be the optimum choice between analgesic efficacy and minor side effects, which correlated with the higher dose of sufentanil given to group C.

Key words: Analgesia, epidural - Sufentanil - Pain postoperative, prevention and control.

The co-administration of ropivacaine and sufentanil is an appropriate technique for postoperative analgesia. To avert the motor block that has been reported with high-volume continuous lumbar epidural infusion of 0.1% ropivacaine, the anesthetic can be given at higher doses (0.2%) and at reduced volumes at the level of the chest metamere.² Optimal analgesia with reduced infusion volumes can be obtained only by associating the local anesthetic with an opioid. One such agent is sufentanil, a drug ideally suited for metameric administration; however, its optimal concentration has not yet been fully determined.

The normally used dose of epidural sufentanil is 1 µg ml⁻¹. Several studies³ have shown that a dose of 0.75 µg/ml⁻¹ sufentanil and 0.125% bupivacaine provide a better analgesic effect than that with 0.5 µg/ml⁻¹ but one similar to that at 1 µg/ml⁻¹.³ The duration of epidural administration of an anesthetic depends on numerous factors, an important one being hospital or organization; subsequently, epidural analgesia can be limited to the first 36 postoperative hours, and then intravenous opi-
EPI added to 20 mL ROPI 0.5% and 0.2% on postop analgesia via a femoral catheter after total knee replacement under combined peripheral block/general anesthesia.

After surgery, patient-controlled analgesia (PCA) with Ropi 0.2% plus Epi 1:200.000 for Group ROPI-EPI and plain Rop 0.2% for Group ROPI was available via the femoral catheter (Ropi 0.2% bolus 20 mL, lockout 120 min). The patients were instructed to use PCA when the knee pain score was >3.

Epinephrine does not influence the duration of analgesia of the ropivacaine concentrations investigated.
0.75% and 0.5% Ropivacaine for Axillary Brachial Plexus Block: A Clinical Comparison With 0.5% Bupivacaine

Laura Bertini, M.D., Vincenzo Tagariello, M.D., Stefania Mancini, M.D., Alma Ciaschi, M.D., Carla Maria Posteraro, M.D., Pia Di Benedetto, M.D., and Ornella Martini, M.D.

Background and Objectives. Although ropivacaine has been extensively studied for epidural anesthesia, very few reports exist on brachial plexus block. We therefore decided to investigate the clinical features of axillary brachial plexus anesthesia with two different concentrations of ropivacaine (0.5% and 0.75%) and to compare the results with those obtained with 0.5% bupivacaine. Methods. Three groups of patients were randomized and prospectively studied. They received, in a double-blind fashion, 12 mL of the local anesthetic solution into the midaxilla, by a nerve-stimulator technique. Onset time in each of the stimulated nerves was recorded both for the sensory and motor block. Peak time (ready to surgery), rate of supplemental blocks, need for intraoperative opioids, duration of sensory and motor block, postoperative analgesic requirements, and patient satisfaction were also recorded. Results. The rate of complete sensory and motor block observed with both ropivacaine groups was higher at 10, 15, and 20 minutes postinjection (P < .001). The mean peak time was shorter with ropivacaine than with bupivacaine (R50 = 16.37 minutes, R75 = 14.7 minutes, B = 22.3 minutes, P < .05). The quality of the anesthesia was higher with ropivacaine, as measured by the intraoperative needs for opioids and the overall patient's satisfaction (P < .05). No significant differences were noted with all the other studied parameters. Conclusions. Ropivacaine showed advantages over bupivacaine for axillary brachial plexus block. Because no statistical differences were found between the two ropivacaine groups, we therefore conclude that 0.75% does not add benefit and that 0.5% ropivacaine should be used to perform axillary brachial plexus blocks. Reg Anesth Pain Med 1999; 24:514-518.

Key words: ropivacaine, bupivacaine, brachial plexus block.

Ropivacaine is an amide-type local anesthetic manufactured as the hydrochloride monohydrate of the (S)-enantiomer (1). Although ropivacaine has been tested extensively in epidural anesthesia in animals and humans, few studies have been done with peripheral nerve blocks. Previous studies demonstrated that no significant difference existed in clinical use between ropivacaine and bupivacaine when equal concentrations were used in sciatic or axillary plexus block (2-4). Comparison of the physicochemical properties of ropivacaine and bupivacaine suggest that ropivacaine will have a similar onset and duration time, but that it might be slightly less potent in action (5). The goal of this study is to compare ropivacaine in two different concentrations (0.5% and 5 mg/mL), to bupivacaine 5 mg/mL in

Randomized, prospective and double-blind

Bupi 0.5% (B)
Ropi 0.5% (R50)
Ropi 0.75% (R75)

peak time:
R75 = 14 min
R50 = 16 min
B = 22 min

evaluating:

intraoperative needs for opioids
overall patients satisfaction

ROPI better than BUPI
0.5% Ropivacaine 15 mg can be used successfully for lower limb surgeries where early motor recovery is required and well appreciated by the patients too.
Gautier P.

Comparison of the effects of intrathecal ropivacaine, levobupivacaine and bupivacaine for Caesarean section.

Br J. Anaesth 2003;91:684-89

Levo 0,5% 8mg  
vs Bupi 0,5% 8mg  
vs Ropi 0,5% 12mg

Longer duration of motor block with Bupi
Spinal anaesthesia: comparison of plain ropivacaine 5 mg ml±1 with bupivacaine 5 mg ml±1 for major orthopaedic surgery

D. A. McNamee1*, A. M. McClelland1, S. Scott1, K. R. Milligan2, L. Westman3 and U. Gustafsson3
1Department of Anaesthetics and Intensive Care Medicine, The Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL, UK. 2Department of Anaesthetics, Musgrave Park Hospital, Stockmans Lane, Belfast, UK. 3AstraZeneca R&D, Sodertalje, Sweden

A more rapid postoperative recovery of sensory and motor function was seen in Group R compared with Group B.
Ropivacaine provides faster onset of sensory and motor block with **less duration of motor block**, higher safety profile and **equal postoperative analgesia** as compared to bupivacaine when used in brachial plexus block.

Less duration of motor block with ropivacaine is a desirable property as it enhances patients self-caring and comfort.
Ropivacaine less pronounced inhibits sympathetic activity than bupivacaine

Svitlyk, Y.; Harbar, M.; Svitlyk, H.; Pidhirnyy, Y.

Ropivacaine characterized by less pronounced inhibition of sympathetic activity. In our opinion due to this is less pronounced disorders of baroreflexive regulation of the heart under the influence of ropivacaine and, thereafter, less pronounced clinical manifestations of sympathectomy (decreasing of blood pressure and bradycardia).
ROPIVACAINE VS BUPIVACAINE

< cardiotoxicity
< neurotoxicity
> vasoconstriction

BUPI

High toxicity with low therapeutic index (margin between effective dose and toxic dose) and strict margin between the toxic convulsivant dose and the lethal cardiac dose

High number of deaths due to accidental venous injection of bupivacaine
**Table 1. Maximum doses of local anaesthetics in adults.**

<table>
<thead>
<tr>
<th></th>
<th>Plain</th>
<th>+ Adrenalin</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Cloroprocaine</td>
<td>800 mg (11 mg/kg)</td>
<td>1000 mg (14 mg/kg)</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>300 mg (4–5 mg/kg)</td>
<td>500 mg (7 mg/kg)</td>
</tr>
<tr>
<td>Prilocaine</td>
<td>500 mg (7 mg/kg)</td>
<td>600 mg (8.5 mg/kg)</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>300 mg (4–5 mg/kg)</td>
<td>500 mg (7 mg/kg)</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>175 mg (2.5 mg/kg)</td>
<td>225 mg (3 mg/kg)</td>
</tr>
</tbody>
</table>


**Table 2. Maximum dose of bupivacaine, levobupivacaine and ropivacaine in adults.**

<table>
<thead>
<tr>
<th></th>
<th>Single dose(^a)</th>
<th>Total dose in 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupivacaine</td>
<td>150 mg (2 mg/kg)</td>
<td>400 mg (5.5 mg/kg)</td>
</tr>
<tr>
<td>Levobupivacaine</td>
<td>150 mg (2 mg/kg)</td>
<td>400 mg (5.5 mg/kg)</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>225 mg (3 mg/kg)</td>
<td>800 mg (11 mg/kg)</td>
</tr>
</tbody>
</table>

Data from Pharmacia Fennica 2002, Finland.
\(^a\)With or without adrenalin (epinephrine).
Pharmacokinetics of 450 mg ropivacaine with and without epinephrine for combined femoral and sciatic nerve block in lower extremity surgery. A pilot study†

Karin P. W. Schoenmakers,¹ Tom B. Vree,¹ Nigel T. M. Jack,¹ Bart van den Bertr, Jacques van Limbeek¹ & Rudolf Sünstra¹

¹Department of Anaesthesiology, Sint Maarten'skliniek, Hengstelweg 3, 6574 NA, Nijmegen; ²Department of Pharmacy, Sint Maarten'skliniek, Hengstelweg 3, 6574 NA, Nijmegen and ³Department Research Development and Education, Sint Maarten'skliniek, Hengstelweg 3, 6574 NA, Nijmegen, the Netherlands

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

• For peripheral nerve blocks, larger doses of local anaesthetic than recommended are frequently used, in the absence of pharmacokinetic data, using higher than recommended doses may pose a medico-legal problem in cases of local anaesthetic systemic toxicity.

WHAT THIS STUDY ADDS

• This is the only study describing the pharmacokinetic profile in serum of 450 mg ropivacaine with and without epinephrine for combined sciatic/femoral nerve block. Free serum concentrations of ropivacaine in both groups remained well below the assumed threshold of 0.56 μg ml⁻¹ for systemic toxicity.

AIMS

No pharmacokinetic data exist on doses of ropivacaine larger than 300 mg for peripheral nerve block in man, although in clinical practice higher doses are frequently used. The purpose of the present study was to determine the pharmacokinetic profile in serum of 450 mg ropivacaine with and without epinephrine in patients undergoing anterior cruciate ligament reconstruction.

METHODS

Twelve patients were randomly allocated to receive a single shot combined sciatic/femoral nerve block with 60 ml of either ropivacaine 0.75% alone (group R, n = 6) or ropivacaine 0.75% plus epinephrine 5 μg ml⁻¹ (group RE, n = 6).Venous blood samples for total and free ropivacaine serum concentrations were obtained during 48 h following block placement. Pharmacokinetic parameters were calculated using a non-compartmental approach.

RESULTS

Results are given as mean (SD) for group R vs. group RE (95% CI of the difference). Total ropivacaine, was 2.81 (0.94) μg ml⁻¹ vs. 2.76 (0.82) μg ml⁻¹; (95% CI -0.23, 1.53); tₚₕ was 1.17 (0.39) h vs. 1.67 (0.94) h (95% CI -1.40, 0.40). The highest free ropivacaine concentration per patient was 0.18 (0.08) μg ml⁻¹ vs. 0.12 (0.04) μg ml⁻¹ (95% CI -0.04, 0.12). tₚₕ was 0.82 (2.26) h vs. 5.48 (1.69) h (95% CI -1.23, 3.91). AUC was 28.35 (5.92) μg ml⁻¹ h vs. 29.12 (7.34) μg ml⁻¹ h (95% CI -9.35, 7.81).

CONCLUSIONS

Free serum concentrations of ropivacaine with and without epinephrine remained well below the assumed threshold of 0.56 μg ml⁻¹ for systemic toxicity. Changes in pharmacokinetics with epinephrine co-administration did not reach statistical significance.
Anesthesiology 2001

<table>
<thead>
<tr>
<th></th>
<th>Bupivacaine</th>
<th>Levobupivacaine</th>
<th>Ropivacaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiotoxic concentration</td>
<td>8.1 mmol/kg</td>
<td>9.9 mmol/kg</td>
<td>11.9 mmol/kg</td>
</tr>
</tbody>
</table>

1) distribution volume:  Bupi 73 L > Levo 67 L > Ropi 47 L

2) Bupi has high intrinsic toxicity: fast in, slow out

Best Practice & Research Clinical Anaesthesiology Vol. 17, No. 1, pp. 111±136, 2003 B. Cox MD Department of Anesthesiology, University Hospital Maastricht, PO Box 5800, 6202 AZ Maastricht, The Netherlands
LAST (Local Anesthetic Systemic Toxicity)

When the plasmatic levels of LA make toxicity, the effects reveal theirself on C.N.S. and on HEART because these are the only two organs in which the functioning is essentially due to cellular depolarization and ripolarization.
Local anesthetic systemic toxicity: update on mechanisms and treatment
John W. Wolfe  Current Opinion in Anesthesiology 2011, 24:561 – 566
First BRAIN and then HEART

• Neurotoxic plasmatic concentration is **lower** then the cardiotoxic concentration  
  (Affinity)

• The speed with which the concentration of LA increases in the central nervous system is **higher** respect the myocardium  
  (Perfusion)
Local Anesthetics

- Lightheadedness
- Confusion
- Tinnitus
- Unconsciousness
- Seizure
- Coma
- Peri-oral numbness

Toxicity Factors
1. Agent
2. Dose
3. Administration Rate
4. Injection Site
5. +/- Vasoconstrictor
6. Acidity (pH)

I'm the most toxic!
Only I can save you!
Lipidic rescue

**IMMEDIATELY**

Give an initial intravenous bolus injection of 20% lipid emulsion 1.5 ml.kg⁻¹ over 1 min

AND

Start an intravenous infusion of 20% lipid emulsion at 15 ml.kg⁻¹.h⁻¹

**AFTER 5 MIN**

Give a maximum of two repeat boluses (same dose) if:
- cardiovascular stability has not been restored or
- an adequate circulation deteriorates

Leave 5 min between boluses
A maximum of three boluses can be given (including the initial bolus)

AND

Continue infusion at same rate, but:
**Double** the rate to 30 ml.kg⁻¹.h⁻¹ at any time after 5 min, if:
- cardiovascular stability has not been restored or
- an adequate circulation deteriorates

Continue infusion until stable and adequate circulation restored or maximum dose of lipid emulsion given

*Do not exceed a maximum cumulative dose of 12 ml.kg⁻¹*

AAGBI Safety Guidelines http://www.aagbi.org
http://www.lipidrescue.org
TOTAL HIP REPLACEMENT

Intrathecal anesthesia L3-L4 with Ropivacaine 0.5% at standard doses
Or
Lumbar plexus anesthesia with Ropivacaine 0.75%

Post-op analgesia:
- Epidural through elastomeric pump (250 ml, 5-7 ml/h) with Ropivacaine 0.15% + morphine 8 mg or sufentanil 0.5-0.75 mcg/ml

- Perineural lumbar plexus block through elastomeric pump (250 ml, 5-7 ml/h) with Ropivacaine 0.4%. Repeating bolus with ropivacaine 0.75% 5-10 ml + NaCl 0.9% 3-4 ml max every 6 h.

Rescue dose (NRS>4) ketoprofen 100 mg ev repeating 3 times in 24 h.
TOTAL KNEE REPLACEMENT

Intrathecal anesthesia L3-L4 with Ropivacaine 0.5% at standard doses

Post-op analgesia:
- Epidural through elastomeric pump (250 ml, 5-7 ml/h) with Ropivacaine 0.15% + morphine 8 mg or sufentanil 0.5-0.75 mcg/ml
  or
- Perineural femoral nerve block through elastomeric pump (250 ml, 5-7 ml/h) with Ropivacaine 0.4%. Repeating bolus with ropivacaine 0.75% 5-10 ml + NaCl 0.9% 3-4 ml max every 6 h.

Rescue dose (NRS>4) ketoprofen 100 mg ev repeating 3 times in24 h.
TOTAL KNEE REPLACEMENT

Intrathecal anesthesia L3-L4 with Ropivacaine 0.5% at standard doses

Post-op analgesia:
- Epidural through elastomeric pump (250 ml, 5-7 ml/h) with Ropivacaine 0.15% + morphine 8 mg or sufentanil 0.5-0.75 mcg/ml
  or
- Perineural femoral nerve block through elastomeric pump (250 ml, 5-7 ml/h) with Ropivacaine 0.375%. Repeating bolus with ropivacaine 0.75% 5-10 ml + NaCl 0.9% 5 ml max every 6 h.

Rescue dose (NRS>4) ketoprofen 100 mg ev repeating 3 times in24 h.
USUAL RULE TO DOSE THE LOCAL ANESTHETIC BY ULTRASOUND GUIDE

• TO IDENTIFY THE BLOCKING NERVES USING THE US GUIDE IN DYNAMIC WAY
• TO PUT THE NEEDLE’S TIP NEAR THE NERVOUS FIBRES AVOIDING TO PENETRATE INTO THE NERVE’S FASCICULES
• TO SURROUND THE NERVE WITH A FILM OF LOCAL ANESTHETIC. A RING OF LOCAL ANESTHETIC IS PREDICTIVE OF THE GOOD SUCCESS OF THAT NERVE’S BLOCK.
• FOR EVERY BLOCKING NERVE COULD BE ENOUGH 3-5 ML. OF LOCAL ANESTHETIC.
THE AXILLARY BRACHIAL PLEXUS BLOCK

• SURGERY ON SOFT TISSUES: mepivacaine 2% 20-30 ml

• SURGERY ON BONES: ropivacaine 0.2% 10-20 ml + ropivacaine 0.75% 10 ml
THE INTERSCALENIC BRACHIAL PLEXUS BLOCK

• SURGERY ON SOFT TISSUES OR NEEDS OF FAST REVERSAL: mepivacaine 2% 20 ml

• SURGERY ON BONES: ropivacaine 0.2% 10 ml + ropivacaine 0.75% 10 ml
ABDOMINAL SURGERY

INTRAFASCIAL CATHETER:

Ropivacaine 0.2% in elastomeric pump 5 ml/h for 48 hours
I'll decide if I want an epidural, when I want an epidural, and how many epidurals I want!

The secret life of termites
SAN PAOLO HOSPITAL (IN SAVONA) PROTOCOLS

ANALGESIA IN LABOUR

COMBINED SPINAL – EPIDURAL

- SPINAL: Sufentanil 2.5 – 3 mcg + NaCl 0.9 to 3 ml
- EPIDURAL CATHETER IN DILATATION PHASE: Ropivacaine 0.1% in top up (1 bolus every hour) until to 8-15 ml (max 20ml)
- EPIDURAL CATHETER IN EXPULSIVE PHASE: Ropivacaine 0.15 – 0.2% in top up until to 7-8 ml
Duration and Efficacy of Different Local Anesthetics on the Palmar Digital Nerve Block in Horses

Gabriele Biavaschi Silva et al.
Journal of Equine Veterinary Science.

Lido 2%
Bupi 0.5%
Ropi 0.75%

on experimental limping

ANESTHETIC EFFICACY: Ropi and Bupi > Lido

ANALGESIC EFFICACY: Ropi > Bupi and Lido
Ropi is less lipophilic than Bupi, and is less likely to penetrate large myelinated motor fibres, resulting in a relatively reduced motor blockade.

Thus, Ropi has a greater degree of motor sensory differentiation, which could be useful when motor blockade is undesirable.

The reduced lipophilicity is also associated with decreased potential for central nervous system toxicity and cardiotoxicity.

At low concentration ROPI, in comparison to the BUPI, shows good analgesia without involving the motility.

Clinical advantages of Ropivacaine must be considered in the cost effectiveness process.
...and thank you very much for your kind attention...