

Ropivacaine and levobupivacaine: A review of the adult and nonobstetrical literature "I remember"

MICHEL GIRARD, MD, MHPE, FRCPC

Every comprehensive article on the use of ropivacaine or levobupivacaine includes a sentence about their lesser toxicity in relation to bupivacaine. In general, this short sentence seems sufficient to justify, from the authors' point of view, their use for postoperative analgesia, as well as for different types of anesthesia blocks in the operating room (O.R.). While this advantage seems obvious in the O.R. when single injections are used to induce blocks, this is not necessarily the case for postoperative analgesia.

Ropivacaine (ropi) and bupivacaine (bupi), both derivatives of mepivacaine, were synthesized in 1957. At that time, it was decided to develop and market bupi. As a long-acting local anesthetic, this molecule reigned supreme until 1979 when Albright,¹ in a surprising editorial, established a relation between bupi and cases of toxicity that included a cardiac effect making resuscitation difficult. Other reports, including several cases in obstetrical anesthesia, confirmed Albright's warnings. Over the following years, the main consequence was withdrawal of FDA approval of bupi 0.75% for obstetrical anesthesia. In addition to this official measure, two other significant changes in clinical practice led to a decrease in bupi-associated complications. These were the use of the *test dose* and the divided, rather than bolus, dose of local anesthetic. Meanwhile, the industry was trying to develop less toxic local anesthetics. The first clinical articles describing ropi were published at the end of the 1980s and those describing levobupivacaine (L-bupi) in the early 1990s. However, the clinical measures taken to decrease the frequency of bupi-related complications were so successful that certain authors suggested that the additional cost of these new agents in the clinical setting was not justified. This opinion was not shared by everyone.³

GENERAL CONSIDERATIONS

Ropi and bupi are produced when the methyl group ($-\text{CH}_3$), situated on the nitrogen ion of mepivacaine, is replaced by a $-\text{C}_3\text{H}_7$ group in the case of ropi (propivacaine = ropivacaine) and by a butyl group ($-\text{C}_4\text{H}_9$) in the case of bupi. These 3 molecules have an asymmetrical carbon enabling them to exist in 2 distinct forms that are mirror images of each other without being superimposable. The first of the 2 principal nomenclatures of these asymmetrical molecules⁴ is based on the *Sequence Rule Notation*. In a 3-dimensional molecular model, the smallest of the 4 atoms bound to carbon is placed at the back. Of the 3 remaining atoms, the smallest and the largest are identified. In this situation, if the arrow connecting them goes in a clockwise direction, it is labeled the "R" enantiomer. If it goes counterclockwise, it is labeled the "S" form. The second label is based on the rotation of a plane of polarized light passing through a solution of

Committee for Continuing Medical Education
Department of Anesthesiology
University of Montreal

Pierre Drolet, MD
Chairman and Editor
Maisonneuve-Rosemont Hospital

Jean-François Hardy, MD
Chairman of the
Department of Anesthesiology,
University of Montreal

François Donati, MD
Maisonneuve-Rosemont Hospital

Edith Villeneuve, MD
Ste-Justine Hospital

Robert Blain, MD
Montreal Heart Institute

Normand Gravel, MD
CHUM

Robert Thivierge, MD
Vice-Dean
Continuing Education
University of Montreal

University of Montreal
Department of Anesthesiology
Faculty of Medicine
C.P. 6128, Succursale Centre-Ville
Montréal (Québec) H3C 3J7
Pavillon principal, bureau S-712
Tel: (514) 343-6466
Fax: (514) 343-6961
E-mail: anesth@medclin.
umontreal.ca

Université 
de Montréal
Faculty of Medicine
Department of Anesthesiology

The editorial content of *Anesthesiology Rounds* is determined solely by the Department of Anesthesiology of the University of Montreal Faculty of Medicine

Available on the Internet
www.anesthesiologyrounds.ca

the molecule. The “+” sign is used when the rotation is clockwise, and the “-” sign is used when it is counterclockwise. The first method is said to be absolute, whereas the second is relative. As the results are non-superimposable, both methods are used to identify the enantiomers.

The discovery that the “L” (L = S) form of these molecules was less toxic led to the development of solutions containing only the “L” enantiomer of the molecule. Commercial ropi and L-bupi are almost pure solutions of the “S” enantiomer, but bupi is a racemic mixture in that it contains equal quantities of the “R” and “S” enantiomers of the molecule.

ROPIVACAINE AND LEVOBUPIVACAINE

Toxicity and potency

In terms of the central nervous and cardiac systems, the “S” enantiomers of these two molecules are recognized as being less toxic than the bupi racemic form. This has been demonstrated *in vitro* in animals and in volunteer subjects. Anecdotal reports of accidental intravenous administration of these medications seems to confirm the experimental data. However, while toxicity may be less, it still exists. In pigs, a lethal dose by intracoronary injection is: ropi \approx L-bupi \approx 0.5 x bupi.⁵ There are several extensive reviews on the subject.⁶⁻⁸

For clinical purposes, it is acknowledged that L-bupi is equivalent to racemic bupivacaine, both in terms of its potency and duration of action.⁶ The situation is more complex for ropi. In general, it is considered to be less potent than bupi.⁶ However, certain clinical studies using equal doses of the two medications produced similar results, which points to equal potency.⁹⁻¹² However, these studies were generally done on plexus blocks, a more complex technique, with results that are more difficult to reproduce and interpret in the clinical setting than studies done on spinal anesthesia, the epidural, or the infiltration of surgical wounds. In experimental models, the potency of ropi is estimated to be 50% - 66% that of bupi.¹³⁻¹⁷ Another characteristic of ropi appears to be a better separation of sensory and motor blocks, particularly at low concentrations (eg, <0.2%). Certain authors have taken advantage of this characteristic, as noted below.

CLINICAL USE

Ophthalmology: Peribulbar block

In a study involving 2000 patients that compared 9 ml of ropi (0.75%) to a mixture of 4 ml of bupi (0.5%) and 4 ml of mepivacaine (2%), (each solution

containing 1 ml of hyaluronidase), Luchetti observed fewer arrhythmias and less pain on injection with ropi. Akinesia was of better quality with this group, thus allowing fewer re-injections.¹⁸

Deep cervical plexus blocks

In a comparison study between ropi (0.75% and 1.0%) and mepivacaine (2.0%), it was concluded that ropi 0.75% produced as good, if not better, results as ropi 1.0% and a longer-lasting block than mepivacaine.¹⁹ In a comparison study with ropi 0.75% and bupi 0.5%, all of the clinical characteristics of both solutions were comparable, with the exception that bupi induced longer postoperative analgesia.²⁰

Spinal anesthesia

In a comparison between L-bupi at doses of 4 mg, 8 mg and 12 mg and hyperbaric bupi, an analysis of several clinical indicators revealed completely superimposable results.²¹ In a comparison of 17.5 mg of an isobaric solution (0.5%) of these two medications for arthroplasty of the hip (THR), both groups of patients reacted in a comparable manner.²² Therefore, for spinal anesthesia, L-bupi and bupi may be considered to be interchangeable.

In a study with isobaric solutions, Gautier compared 8, 10, 12, and 14 mg doses of ropi with 8 mg of bupi. He demonstrated that the block with 12 mg of ropi is comparable to that with 8 mg of bupi. There was no difference between the blocks associated with the 12 mg and 14 mg doses of ropi, except that the delay in time before urination was 30 minutes longer in the 14 mg group. In a study on endourological surgery comparing 10 mg of isobaric bupi to 15 mg of isobaric ropi, Malinovsky noted a higher level (two dermatomes) with bupi and a greater need for intravenous morphine with ropi. The motor blocks and hemodynamic effects were comparable.²³ Thus, there does not appear to be any advantage in using ropi for spinal anesthesia.

Epidural

Surgical anesthesia

During lower abdominal surgery, a comparison between 20 ml (0.75%, 150 mg) of L-bupi and bupi revealed few differences in terms of intraoperative and postoperative results. Thus, the times required for the regression of two dermatomes and regression to T-10 were comparable; the time necessary for complete regression of the block was 45 minutes longer with L-bupi (550 min \pm 87 min vs 505 min \pm 71 min). Although the onset of the block was slower in the L-bupi group, the total duration was comparable.

The authors concluded that the effects of the two medications were “indistinguishable.”²⁴ The addition of adrenaline (1:200,000 or 1:400,000) to L-bupivacaine did not change the clinical results in comparison to a group not receiving adrenaline. The blood-serum levels of L-bupivacaine were not significantly decreased in the group receiving adrenaline as compared to the group not receiving adrenaline, with neither of the two adrenaline solutions being more efficacious.²⁵

Generally, before proceeding with an injection of local anesthetic, the administration of a *test dose* is recommended. In the case of an epidural, the intent is to verify the effects not only of the intravascular injection, but also of the intrathecal injection. Ngan Kee suggests that ropivacaine is not the ideal agent for a test dose since the onset of the spinal block is too long (8 min) and the mixture with adrenaline is not specific enough as an intravenous injection marker.²⁶ With either ropivacaine or bupivacaine, a concentration of at least 0.5% is necessary to produce adequate anesthesia via the epidural route. In general, a comparison of these 2 agents at this concentration or higher, does not reveal any important differences. Some reports indicate that the motor block with ropivacaine is a little less and that bupivacaine produces a longer-lasting block,^{27,28} however, others report no differences whatsoever.²⁹⁻³¹ Even in a study of forced expiratory volume (exhaled in 1 second) and vital capacity in patients suffering from severe chronic obstructive pulmonary disease, no differences were revealed between a thoracic epidural using ropivacaine 0.75% or bupivacaine 0.75%.³²

Postoperative analgesia

The literature on postoperative anesthesia via an epidural must be divided into two categories: local anesthetics used alone or local anesthetics combined with opioids. The fact is, the administration of a local anesthetic without opioids is associated with a failure rate that is too high, and an incidence of motor block and hypotension too significant, for clinicians to have adopted this method.³³ While there is a theoretical interest in comparing solutions without narcotics, we will limit this discussion to studies in which opioids are combined with low concentrations of local anesthetics.

After surgery for THR and total knee replacement (TKR), 3 solutions were compared:

- L-bupivacaine 0.125%
- fentanyl 4 µg/mL
- L-bupivacaine 0.125% + fentanyl 4 µg/mL

The infusion flow rate was 4 mL/hr and the patient could self-administer bolus doses of 2 mL/10 min. The combination of L-bupivacaine and fentanyl was

the most effective and the incidence of side effects was not higher in this group.³⁴

Crews et al also compared 3 solutions for analgesia following major abdominal surgical procedures:

- L-bupivacaine 0.25% + morphine 0.005%
- L-bupivacaine 0.25%
- morphine 0.005%.

The thoracic infusion flow rate was 4 mL/hr, and at the patient’s request, a bolus dose of 2 mL was administered and the flow rate was increased by 2 mL/hr. The combination of the 2 medications induced better analgesia, as is reflected in the results of pain evaluation at rest and with movement, as well as fewer requests for drug rescue (ketorolac).³⁵

In another study, the effect of clonidine on L-bupivacaine was studied after THR surgeries. Again 3 solutions were compared:

- L-bupivacaine 0.125%
- clonidine 8.3 µg/mL
- L-bupivacaine 0.125% + clonidine 8.3 µg/mL

An infusion of 6 mL/hr was used. Use of a rescue drug (morphine) was less in the L-bupivacaine + clonidine group and no significant side effects were noted with the use of clonidine, except for a slightly lower blood pressure (10 mm Hg) requiring no particular treatment.³⁶

Ropivacaine 0.2% is the concentration most frequently used for epidural postoperative analgesia. When combined with sufentanil 0.5 µg/mL during a 72-hour postoperative infusion, ropivacaine 0.2% induced less motor block than bupivacaine 0.25% when used alone or with sufentanil. The ropivacaine-sufentanil combination is more effective in decreasing pain than either of these two medications alone. The main side effects associated with epidural opioids were more frequent when sufentanil was used.³⁷ In a comparison of ropivacaine 0.2% and bupivacaine 0.125% after major abdominal surgery – both were combined with fentanyl 2 µg/mL – no difference in motor block was noted, which in fact was almost absent. However, patients in the bupivacaine group made more requests for this epidural solution.³⁸ Scott demonstrated that, in combination with ropivacaine 0.2%, the optimal concentration of fentanyl is 4 µg/mL.³⁹ Brodeur, however, recommends the addition of sufentanil at a concentration of 0.75 µg/mL.⁴⁰ These 2 studies involved patients who had undergone major abdominal surgery. When ropivacaine 1.0% is used after THR, Kampe suggests that combining it with sufentanil 1µg/mL is more effective than ropivacaine used alone. In each group, the motor block is described as “negligible”.⁴¹

After major abdominal surgery, Hodgson and Liu compared 4 solutions: bupivacaine 0.05%, bupivacaine 0.1%, ropivacaine

0.05%, and ropi 0.1%, all of which contained fentanyl 4 µg/mL. Administration was controlled by the patient. The authors concluded that the four were efficacious and equivalent, and while there were few motor blocks, they recommend solutions of 0.05% to limit them.⁴² However, adding opioids to ropi may not be without consequences. A study by Finucane demonstrated that following colon surgery, a solution containing fentanyl 2 µg/mL provided better analgesia, but was associated with late discharge from the hospital.⁴³ Adrenaline (2 µg/mL) may also be added to the combination of ropi 0.1% and fentanyl 2 µg/mL. Niemi demonstrated that analgesia was better, with no increase in side effects, when this combination was used at the thoracic level after major abdominal or thoracic surgery.⁴⁴

The accumulation of ropi during prolonged postoperative infusions may cause harmful effects for patients if the free plasma concentration responsible for the toxic effects is increased proportionally during the infusion. In a study on the infusion of ropi 0.2% over a period of 120 hours, Wiedemann demonstrated that the free plasma fraction after an initial increase, stabilized at the 70-hour point, and diminished slightly thereafter. This may be explained by the constant increase (except for a decrease during the first hours) of α 1-acid glycoprotein to which ropi binds with great affinity.⁴⁵

Plexus blocks

Upper limb

Axillary block

Few pharmacokinetic or clinical differences were noted in a comparison of equal doses of ropi 0.5% and bupi 0.5% in an axillary brachial plexus block.^{10, 46, 47} In a study comparing ropi 0.75% to bupi 0.5% (40 mL each), Raeder noted comparable onset and duration of action. However, subjective evaluation of the quality of the analgesia at the end of surgery and of the motor block by the anesthetist and surgeon was more positive with ropi, even if skin infiltrations were used for 7 patients in the ropi group, and only 4 in the bupi group. One patient in the ropi group convulsed following an accidental intravenous injection.⁴⁸

Interscalene block

In a comparison of ropi 0.5% and 0.75% with bupi 0.5% using the interscalenic approach, Klein did not demonstrate a difference in the onset or duration of action, regardless of the concentration of ropi.⁴⁹ In a study using the same medications at the same concentrations, Bertini concluded that ropi

performed better than bupi in terms of onset of action and quality of the sensory block, but found no advantage in using ropi 0.75% as opposed to 0.5%.⁵⁰ In a study with ropi 1.0%, a faster onset of action was demonstrated, but it did not prolong postoperative analgesia beyond what was obtained with concentrations of 0.5% or 0.75% of ropi or 0.5% of bupi.^{51,52} Urmeý demonstrated a 100% incidence of phrenic nerve block, lasting for 3 to 5 hours, following administration of 34 to 52 mL of mepivacaine 1.5% with adrenalin and bicarbonate.⁵³ Administration of ropi 0.5% and 0.75% induced paresis of the hemidiaphragm and a moderate decrease in the forced vital capacity of 40% \pm 17% (0.5%) and 41% \pm 22% (0.75%), respectively. The maximum forced expiratory volume/second also fell by 30% \pm 19% (0.5%) and 38% \pm 28% (0.75%), respectively.⁵⁴ The smaller decrease in values, in relation to Urmeý's findings, can be explained primarily by the methodological differences in measuring these values. It is in this context, among others, that the block differential attributed to ropi can be used to advantage. While ropi concentrations required for surgical purposes induce significant paresis of the hemidiaphragm, the situation is different when lower concentrations are used in postoperative analgesia. Therefore, the comparison of self-administered ropi 0.2% via interscalene catheter with intravenous morphine for postoperative analgesia is interesting. On the side of the surgery, the diaphragmatic excursion, in normal or forced respiration, is no different from control values at 24 and 48 hours after initiating the block. On the nonsurgical side, these values are diminished. Secondly, the incidence of nausea was 5.5% in the ropi group versus 60% in the morphine IV group.⁵⁵

The successful use of a continuous bilateral interscalene block for the purpose of postoperative analgesia was reported in a 61-year-old female patient suffering from systemic lupus erythematosus, without pulmonary involvement. Ropi 0.2% at 7 mL/hr on both sides was used. The spirometric data decreased by 60%, but the patient remained eupneic. The authors suggest limiting this technique to patients with normal pulmonary function.⁵⁶

Lower limb

No difference in intraoperative and postoperative data was demonstrated in a comparison of L-bupi (20 ml, 0.5%) and ropi (20 ml, 0.5%) for sciatic nerve block.⁵⁷ The average length of time before the first request for narcotics following a THR was compared after ropi 0.75% or bupi 0.75% was administered for femoral and sciatic nerve blocks. The average dura-

tion with ropi was 781 min [267-1725] and with bupi was 912 min [235-1895] N.S.⁵⁸ In comparing bupi 0.5% to ropi 0.75% for a sciatic nerve block during surgery of the foot, the average duration before the first request for narcotics was comparable to within a few minutes. These results could be superimposed on those obtained in the previous study, although the concentration of bupi was 0.5% in the second study.⁵⁹ In another study, Ng examined the quality of analgesia for up to 48 hours after TKR. At rest and with movement, a “3 in 1” block achieved with 30 mL of ropi 0.25%, ropi 0.5%, or bupi 0.25%, decreased opioid use for up to 48 hours in comparison with the control group. No difference in analgesia was noted between the 3 experimental groups.⁶⁰ In a study using ropi 0.2% or 0.5% for “3 in 1” blocks, Weber did not demonstrate a lengthening of analgesic effect with the addition of adrenaline 1:200,000. The authors explained that the lack of effect, also noted for brachial plexus and epidural anesthesia, was due either to the long duration of action of ropi or by its intrinsic vasoconstricting effect.⁶¹ Finally, Casati demonstrated that clonidine (1 µg/kg) prolongs the duration of action of ropi 0.75% when used for femoral and sciatic nerve blocks.⁶² Therefore, it may be concluded that there is little advantage in using solutions at higher concentrations than ropi or bupi 0.5% for plexus blocks.

Intravenous blocks (Bier’s block)

Three studies⁶³⁻⁶⁵ compared ropi 0.2% to lidocaine 0.5% for intravenous regional anesthesia of the upper limb. The authors concluded that the incidence of neurological manifestations was higher with lidocaine; however, it should be noted that these were benign manifestations with blood serum levels of lidocaine at about 1.7 µg/mL. The duration of postoperative analgesia with ropi was only 30 minutes longer than with lidocaine in 1 of the 5 nerve regions studied; the disappearance of the sensory block was comparable 3 min after discontinuation of the tourniquet in the other 4 regions. A report estimating the ropi/lidocaine cardiac toxicity ratio at 6.7⁶⁶ in pigs anesthetized by intracoronary injection makes one question the appropriateness of using this technique, given the marginal advantages gained.

MISCELLANEOUS

Bay-Nielson compared bupi to L-bupi (0.25%) for cutaneous infiltration during inguinal hernia repairs under local anesthetic. No significant difference was noted between the two groups.⁶⁷

The use of ropi has been reported in various clinical contexts with mixed results. Among the most recent are: scalp blocks in neurosurgery,⁶⁸ intraperitoneal instillation after gynecological endosurgery,⁶⁹ intraperitoneal instillation and infiltration after endocholecystectomy,^{70,71} ilioinguinal block during surgery for inguinal hernia,^{72,73} self-administration into an inguinal surgical wound,⁷⁴ infiltration of a wound and irrigation via a surgical drain after shoulder surgery,⁷⁵ and intra-articular instillation after knee surgery.^{76,77} This list is not exhaustive and for more details, the reader should consult the publications cited.

COMPLICATIONS

Convulsions are the most frequently reported complication following absorption of too high a dose of ropi or its accidental intravascular injection, either partial or complete, during the induction of a block. These intravascular injections may occur even when particular care is taken, their occurrence during research projects attests to this.^{48,78} Convulsions and severe cardiac arrhythmias have occurred following the administration of 30 ml of ropi 0.75% for a sciatic nerve block in a 74-year-old male patient (90 kg). The entire dose was not intravenous since a partial block was achieved.⁷⁹ A frequent comment in describing these cases is that the reported event, while unfortunate, attests to the safety of ropi, since the patient only manifested convulsions. It should be remembered that these cases are usually reported in an anecdotal manner, that the doses administered are generally large, and that the likelihood of patients developing serious complications also depends on their medical condition.

The intrinsic vasoconstricting effect of ropi has the advantage of prolonging its effect.⁸⁰ It is probably better to avoid its administration in cases where the arterial circulation is terminal, as in the case of circumcision.⁸¹ A case of transitory radicular irritation was reported following the intrathecal administration of ropi.⁸² There were serious reservations about this diagnosis⁸³ and it is probably better to wait before adding ropi to the list of local anesthetics responsible for this phenomenon.

GENERAL RECOMMENDATIONS

The bupi/ropi ratio for cardiac toxicity after intracoronary injection in pigs is 2.⁵ While the role of the central nervous system in bupi intoxication is likely significant,⁶ the situation is not as clearly defined for ropi. In order to take advantage of its lesser toxicity, ropi should be given in doses that are similar to

TABLE 1: Patients described by Albright¹

Patient	Technique	Local Anesth.	Volume administered
Man/ 68 kg*	Caudal	Etidocaine 1%	Test dose 5 ml Followed by 20 ml
	Interscalene	Bupivacaine 0.5%	40 ml
Woman (Caeserean)	Epidural	Bupivacaine 0.75%	2 ml then 10 ml after 5 minutes
	Axillary	Bupivacaine 0.5%	40 ml
	Interscalene	Bupivacaine 0.5%	40 ml
	Bier's block		Bupivacaine 0.5%
		2-chloroprocaine 2%	25 ml

* The author mentions that aspiration through the Crawford needle before, during and after injection of the therapeutic dose was negative.

those described for bupi, without looking for the marginal advantages associated with higher doses and concentrations. As for L-bupi, the situation is more simple; it should be administered in the same doses and concentrations as bupi since it is equally potent and less toxic. Therefore, the following reasoning should be avoided: "Ropivacaine is less cardiotoxic than bupivacaine and may be used in higher doses in order to increase the quality of a block."⁴⁸

There are studies with experimental protocols in the literature where the doses of ropi are 1.5 to 2 times that of bupi (0.5%), as reported by Albright (Table 1). Solutions of ropi with concentrations ranging from 0.75% to 1% were used in these experiments. Thus, in equal doses, the use of increasing concentrations of local anesthetic solutions causes rapid increases in the blood serum level of the local anesthetic and the slope of the increase plays a significant role in the severity of toxic manifestations. Furthermore, the percentage that is protein-bound decreases as the blood serum level of local anesthetic increases,⁸⁴ and this can increase the risks during an accidental injection of these higher concentrations of ropi. A long-acting local anesthetic is not always necessary. The prudent clinician is completely justified in using a less toxic local anesthetic such as lidocaine, or even 2-chloroprocaine if the clinical situation allows. Table 2 gives suggestions for limiting the risks of toxic effects from long-acting local anesthetics.

One may attempt to justify the use of long-acting local anesthetics for short surgical procedures because postoperative analgesia is also obtained. However, this usually lasts only a few hours and, while the patient may be satisfied on leaving the hospital, it will be a another story late in the evening or during the night when he has to adjust his oral medication to get pain relief. The use of a continuous block, with the help of an intermediate-acting local anesthetic, may be a judicious choice when it

TABLE 2: Suggestions to limit toxicity of local anesthetics

1. Select the local anesthetic according to the duration of the procedure; an intermediate-acting local anesthetic may be used for many procedures.
2. When contemplating the use of a long-acting local anesthetic, think of using a continuous block with an intermediate-acting local anesthetic to initiate the block.
3. When executing a single-injection block of a long-acting local anesthetic, replace bupi with ropi or L-bupi.
4. Use lower concentrations of long-acting local anesthetics that have been demonstrated to be effective, without looking for marginal advantages associated with higher concentrations.
5. Unless it is contraindicated, always combine opioids with local anesthetic infusions for postoperative analgesia by epidural.
6. Unless it is contraindicated, always use a test dose and divide the dose injected.

replaces a single, more toxic injection of local anesthetic. When a long-acting local anesthetic is used to induce a block by single injection, it is generally more advantageous to replace bupi with L-bupi or ropi.

CONCLUSION

The new local anesthetics have much to offer our patients. However, when using them, one should remember the cases of serious toxicity described since 1979 and not forget that there are less toxic local anesthetics that are often appropriate for our clinical needs. Nicolas M. Greene wrote in 1976, "If he (the complete anesthetist) cares for 750 patients a year, he orchestrates and selects anesthetic drugs to assure that each of his 750 patients receives the best that anesthesia has to offer... he gives 750 anesthetics a year, not one anesthetic 750 times,"⁸⁵ *I remember.*

References

1. Albright GA. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. *Anesthesiology* 1979;51:285-7.
2. D'Angelo R. Are the new local anesthetics worth their cost? *Acta Anaesthesiol Scand* 2000;44:639-41.
3. Wildsmith JA. New local anaesthetics – how much is improved safety worth? *Acta Anaesthesiol Scand* 2001;45:652-3.
4. Whiteside JB, Wildsmith JA. Developments in local anaesthetic drugs. *Br J Anaesth* 2001;87:27-35.
5. Morrison SG, Dominguez JJ, Frascarolo P, Reiz S. A comparison of the electrocardiographic cardiotoxic effects of racemic bupivacaine, levobupivacaine, and ropivacaine in anesthetized swine. *Anesth Analg* 2000; 90:1308-14.
6. Mather LE, Chang DH. Cardiotoxicity with modern local anaesthetics: is there a safer choice? *Drugs* 2001;61:333-42.
7. McClellan KJ, Faulds D. Ropivacaine: an update of its use in regional anaesthesia. *Drugs* 2000;60:1065-93.
8. Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. *Drugs* 2000;59:551-79.
9. Marhofer P, Glaser C, Koinig H, Mayer N, Kapral S. The use of ropivacaine in brachial plexus anaesthesia. *Anaesthesia* 1998;53:14-5.
10. McGlade DP, Kalpokas MV, Mooney PH, Chamley D, Mark AH, Torda TA. A comparison of 0.5% ropivacaine and 0.5% bupivacaine for axillary brachial plexus anaesthesia. *Anaesth Intensive Care* 1998;26: 515-20.

11. Marhofer P, Oismuller C, Faryniak B, Sitzwohl C, Mayer N, Kapral S. Three-in-one blocks with ropivacaine: evaluation of sensory onset time and quality of sensory block. *Anesth Analg* 2000;90:125-8.
12. Casati A, Fanelli G, Magistris L, Beccaria P, Berti M, Torri G. Minimum local anesthetic volume blocking the femoral nerve in 50% of cases: a double-blinded comparison between 0.5% ropivacaine and 0.5% bupivacaine. *Anesth Analg* 2001;92:205-8.
13. Pettersson N, Berggren P, Larsson M, Westman B, Hahn RG. Pain relief by wound infiltration with bupivacaine or high-dose ropivacaine after inguinal hernia repair. *Reg Anesth Pain Med* 1999;24:569-75.
14. Gautier PE, De Kock M, Van Steenberge A, et al. Intrathecal ropivacaine for ambulatory surgery. *Anesthesiology* 1999;91:1239-45.
15. McDonald SB, Liu SS, Kopacz DJ, Stephenson CA. Hyperbaric spinal ropivacaine: a comparison to bupivacaine in volunteers. *Anesthesiology* 1999;90:971-7.
16. Capogna G, Celleno D, Fusco P, Lyons G, Columb M. Relative potencies of bupivacaine and ropivacaine for analgesia in labour. *Br J Anaesth* 1999;82:371-3.
17. Polley LS, Columb MO, Naughton NN, Wagner DS, van de Ven CJ. Relative analgesic potencies of ropivacaine and bupivacaine for epidural analgesia in labor: implications for therapeutic indexes. *Anesthesiology* 1999;90:944-50.
18. Luchetti M, Magni G, Marraro G. A prospective randomized double-blinded controlled study of ropivacaine 0.75% versus bupivacaine 0.5%-mepivacaine 2% for peribulbar anesthesia. *Reg Anesth Pain Med* 2000;25:195-200.
19. Leoni A, Magrin S, Mascotto G, et al. Cervical plexus anesthesia for carotid endarterectomy: comparison of ropivacaine and mepivacaine. *Can J Anaesth* 2000;47:185-7.
20. Junca A, Marret E, Goursot G, Mazoit X, Bonnet F. A comparison of ropivacaine and bupivacaine for cervical plexus block. *Anesth Analg* 2001;92:720-4.
21. Alley EA, Kopacz DJ, McDonald SB, Liu SS. Hyperbaric spinal levobupivacaine: a comparison to racemic bupivacaine in volunteers. *Anesth Analg* 2002;94:188-93.
22. Glaser C, Marhofer P, Zimpfer G, et al. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. *Anesth Analg* 2002;94:194-8.
23. Malinovsky JM, Charles F, Kick O, et al. Intrathecal anesthesia: ropivacaine versus bupivacaine. *Anesth Analg* 2000;91:1457-60.
24. Kopacz DJ, Allen HW, Thompson GE. A comparison of epidural levobupivacaine 0.75% with racemic bupivacaine for lower abdominal surgery. *Anesth Analg* 2000;90:642-8.
25. Kopacz DJ, Helman JD, Nussbaum CE, Hsiang JN, Nora PC, Allen HW. A comparison of epidural levobupivacaine 0.5% with or without epinephrine for lumbar spine surgery. *Anesth Analg* 2001;93:755-60.
26. Ngan Kee WD, Khaw KS, Lee BB, Wong EL, Liu JY. The limitations of ropivacaine with epinephrine as an epidural test dose in parturients. *Anesth Analg* 2001;92:1529-31.
27. Kerkkamp HE, Gielen MJ, Edstrom HH. Comparison of 0.75% ropivacaine with epinephrine and 0.75% bupivacaine with epinephrine in lumbar epidural anesthesia. *Reg Anesth* 1990;15:204-7.
28. Tuttle AA, Katz JA, Bridenbaugh PO, Quinlan R, Knarr D. A double-blind comparison of the abdominal wall relaxation produced by epidural 0.75% ropivacaine and 0.75% bupivacaine in gynecologic surgery. *Reg Anesth* 1995;20:515-20.
29. McGlade DP, Kalpokas MV, Mooney PH, et al. Comparison of 0.5% ropivacaine and 0.5% bupivacaine in lumbar epidural anaesthesia for lower limb orthopaedic surgery. *Anaesth Intensive Care* 1997;25:262-6.
30. Brown DL, Carpenter RL, Thompson GE. Comparison of 0.5% ropivacaine and 0.5% bupivacaine for epidural anesthesia in patients undergoing lower-extremity surgery. *Anesthesiology* 1990;72:633-6.
31. Wood MB, Rubin AP. A comparison of epidural 1% ropivacaine and 0.75% bupivacaine for lower abdominal gynecologic surgery. *Anesth Analg* 1993;76:1274-8.
32. Groeben H, Schafer B, Pavlakovic G, Silvanus MT, Peters J. Lung function under high thoracic segmental epidural anesthesia with ropivacaine or bupivacaine in patients with severe obstructive pulmonary disease undergoing breast surgery. *Anesthesiology* 2002;96: 536-41.
33. Wheatley RG, Schug SA, Watson D. Safety and efficacy of postoperative epidural analgesia. *Br J Anaesth* 2001;87:47-61.
34. Kopacz DJ, Sharrock NE, Allen HW. A comparison of levobupivacaine 0.125%, fentanyl 4 microg/mL, or their combination for patient-controlled epidural analgesia after major orthopedic surgery. *Anesth Analg* 1999;89:1497-503.
35. Crews JC, Hord AH, Denson DD, Schatzman C. A comparison of the analgesic efficacy of 0.25% levobupivacaine combined with 0.005% morphine, 0.25% levobupivacaine alone, or 0.005% morphine alone for the management of postoperative pain in patients undergoing major abdominal surgery. *Anesth Analg* 1999;89:1504-9.
36. Milligan KR, Convery PN, Weir P, Quinn P, Connolly D. The efficacy and safety of epidural infusions of levobupivacaine with and without clonidine for postoperative pain relief in patients undergoing total hip replacement. *Anesth Analg* 2000;91:393-7.
37. Hubler M, Litz RJ, Sengebusch KH, et al. A comparison of five solutions of local anaesthetics and/or sufentanil for continuous, post-operative epidural analgesia after major urological surgery. *Eur J Anaesthesiol* 2001;18:450-7.
38. Berti M, Fanelli G, Casati A, et al. Patient supplemented epidural analgesia after major abdominal surgery with bupivacaine/fentanyl or ropivacaine/fentanyl. *Can J Anaesth* 2000;47:27-32.
39. Scott DA, Blake D, Buckland M, et al. A comparison of epidural ropivacaine infusion alone and in combination with 1, 2, and 4 microg/mL fentanyl for seventy-two hours of postoperative analgesia after major abdominal surgery. *Anesth Analg* 1999;88:857-64.
40. Brodner G, Mertes N, Van Aken H, et al. What concentration of sufentanil should be combined with ropivacaine 0.2% wt/vol for postoperative patient-controlled epidural analgesia? *Anesth Analg* 2000;90:649-57.
41. Kampe S, Weigand C, Kaufmann J, Klimek M, Konig DP, Lynch J. Postoperative analgesia with no motor block by continuous epidural infusion of ropivacaine 0.1% and sufentanil after total hip replacement. *Anesth Analg* 1999;89:395-8.
42. Hodgson PS, Liu SS. A comparison of ropivacaine with fentanyl to bupivacaine with fentanyl for postoperative patient-controlled epidural analgesia. *Anesth Analg* 2001;92:1024-8.
43. Finucane BT, Ganapathy S, Carli F, et al. Prolonged epidural infusions of ropivacaine (2 mg/mL) after colonic surgery: the impact of adding fentanyl. *Anesth Analg* 2001;92:1276-85.
44. Niemi G, Breivik H. Epinephrine markedly improves thoracic epidural analgesia produced by a small-dose infusion of ropivacaine, fentanyl, and epinephrine after major thoracic or abdominal surgery: a randomized, double-blinded crossover study with and without epinephrine. *Anesth Analg* 2002;94:1598-605.
45. Wiedemann D, MuhlNickel B, Staroske E, Neumann W, Rose W. Ropivacaine plasma concentrations during 120-hour epidural infusion. *Br J Anaesth* 2000;85:830-5.
46. Hickey R, Hoffman J, Ramamurthy S. A comparison of ropivacaine 0.5% and bupivacaine 0.5% for brachial plexus block. *Anesthesiology* 1991;74:639-42.
47. Vainionpaa VA, Haavisto ET, Huha TM, et al. A clinical and pharmacokinetic comparison of ropivacaine and bupivacaine in axillary plexus block. *Anesth Analg* 1995;81:534-8.
48. Raeder JC, Drosdahl S, Klaastad O, et al. Axillary brachial plexus block with ropivacaine 7.5 mg/ml. A comparative study with bupivacaine 5 mg/ml. *Acta Anaesthesiol Scand* 1999;43:794-8.
49. Klein SM, Greengrass RA, Steele SM, et al. A comparison of 0.5% bupivacaine, 0.5% ropivacaine, and 0.75% ropivacaine for interscalene brachial plexus block. *Anesth Analg* 1998;87:1316-9.
50. Bertini L, Tagariello V, Mancini S, et al. 0.75% and 0.5% ropivacaine for axillary brachial plexus block: a clinical comparison with 0.5% bupivacaine. *Reg Anesth Pain Med* 1999;24:514-8.
51. Casati A, Fanelli G, Cappelleri G, et al. A clinical comparison of ropivacaine 0.75%, ropivacaine 1% or bupivacaine 0.5% for interscalene brachial plexus anaesthesia. *Eur J Anaesthesiol* 1999;16:784-9.
52. Casati A, Fanelli G, Aldegheri G, et al. Interscalene brachial plexus anaesthesia with 0.5%, 0.75% or 1% ropivacaine: a double-blind comparison with 2% mepivacaine. *Br J Anaesth* 1999;83:872-5.
53. Urmey WF, Talts KH, Sharrock NE. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. *Anesth Analg* 1991;72:498-503.
54. Casati A, Fanelli G, Cedrati V, Berti M, Aldegheri G, Torri G. Pulmonary function changes after interscalene brachial plexus anesthesia with 0.5% and 0.75% ropivacaine: a double-blinded comparison with 2% mepivacaine. *Anesth Analg* 1999;88:587-92.
55. Borgeat A, Perschak H, Bird P, Hodler J, Gerber C. Patient-controlled interscalene analgesia with ropivacaine 0.2% versus patient-controlled intravenous analgesia after major shoulder surgery: effects on diaphragmatic and respiratory function. *Anesthesiology* 2000;92:102-8.
56. Maurer K, Ekatodramis G, Hodler J, Rentsch K, Perschak H, Borgeat A. Bilateral continuous interscalene block of brachial plexus for analgesia after bilateral shoulder arthroplasty. *Anesthesiology* 2002;96:762-4.
57. Casati A, Borghi B, Fanelli G, et al. A double-blinded, randomized comparison of either 0.5% levobupivacaine or 0.5% ropivacaine for sciatic nerve block. *Anesth Analg* 2002;94:987-90.
58. McNamee DA, Convery PN, Milligan KR. Total knee replacement: a comparison of ropivacaine and bupivacaine in combined femoral and sciatic block. *Acta Anaesthesiol Scand* 2001;45:477-81.
59. Connolly C, Coventry DM, Wildsmith JA. Double-blind comparison of ropivacaine 7.5 mg ml⁻¹ with bupivacaine 5 mg ml⁻¹ for sciatic nerve block. *Br J Anaesth* 2001;86:674-7.

60. Ng HP, Cheong KF, Lim A, Lim J, Puhaindran ME. Intraoperative single-shot "3-in-1" femoral nerve block with ropivacaine 0.25%, ropivacaine 0.5% or bupivacaine 0.25% provides comparable 48-hr analgesia after unilateral total knee replacement. *Can J Anaesth* 2001;48: 1102-8.
61. Weber A, Fournier R, Van Gessel E, Riand N, Gamulin Z. Epinephrine does not prolong the analgesia of 20 mL ropivacaine 0.5% or 0.2% in a femoral three-in-one block. *Anesth Analg* 2001;93:1327-31.
62. Casati A, Magistris L, Fanelli G, et al. Small-dose clonidine prolongs post-operative analgesia after sciatic-femoral nerve block with 0.75% ropivacaine for foot surgery. *Anesth Analg* 2000;91:388-92.
63. Atanassoff PG, Ocampo CA, Bande MC, Hartmannsgruber MW, Halaszynski TM. Ropivacaine 0.2% and lidocaine 0.5% for intravenous regional anesthesia in outpatient surgery. *Anesthesiology* 2001; 95:627-31.
64. Atanassoff PG, Hartmannsgruber MW. Central nervous system side effects are less important after iv regional anesthesia with ropivacaine 0.2% compared to lidocaine 0.5% in volunteers. *Can J Anaesth* 2002; 49:169-72.
65. Hartmannsgruber MW, Silverman DG, Halaszynski TM, et al. Comparison of ropivacaine 0.2% and lidocaine 0.5% for intravenous regional anesthesia in volunteers. *Anesth Analg* 1999;89:727-31.
66. Reiz S, Haggmark S, Johansson G, Nath S. Cardiotoxicity of ropivacaine – a new amide local anaesthetic agent. *Acta Anaesthesiol Scand* 1989;33:93-8.
67. Bay-Nielsen M, Klarskov B, Bech K, Andersen J, Kehlet H. Levobupivacaine vs bupivacaine as infiltration anaesthesia in inguinal herniorrhaphy. *Br J Anaesth* 1999;82:280-2.
68. Nguyen A, Girard F, Boudreault D, et al. Scalp nerve blocks decrease the severity of pain after craniotomy. *Anesth Analg* 2001;93:1272-6.
69. Goldstein A, Grimault P, Henique A, Keller M, Fortin A, Darai E. Preventing postoperative pain by local anesthetic instillation after laparoscopic gynecologic surgery: a placebo-controlled comparison of bupivacaine and ropivacaine. *Anesth Analg* 2000;91:403-7.
70. Labaille T, Mazoit JX, Paqueron X, Franco D, Benhamou D. The clinical efficacy and pharmacokinetics of intraperitoneal ropivacaine for laparoscopic cholecystectomy. *Anesth Analg* 2002;94:100-5.
71. Bisgaard T, Klarskov B, Kristiansen VB, et al. Multi-regional local anesthetic infiltration during laparoscopic cholecystectomy in patients receiving prophylactic multi-modal analgesia: a randomized, double-blinded, placebo-controlled study. *Anesth Analg* 1999;89: 1017-24.
72. Mulroy MF, Burgess FW, Emanuelsson BM. Ropivacaine 0.25% and 0.5%, but not 0.125%, provide effective wound infiltration analgesia after outpatient hernia repair, but with sustained plasma drug levels. *Reg Anesth Pain Med* 1999;24:136-41.
73. Wulf H, Behnke H, Vogel I, Schroder J. Clinical usefulness, safety, and plasma concentration of ropivacaine 0.5% for inguinal hernia repair in regional anesthesia. *Reg Anesth Pain Med* 2001;26:348-51.
74. Vintar N, Pozlep G, Rawal N, Godec M, Rakovec S. Incisional self-administration of bupivacaine or ropivacaine provides effective analgesia after inguinal hernia repair. *Can J Anaesth* 2002;49:481-6.
75. Horn EP, Schroeder F, Wilhelm S, et al. Wound infiltration and drain lavage with ropivacaine after major shoulder surgery. *Anesth Analg* 1999;89:1461-6.
76. Rautoma P, Santanen U, Avela R, Luurila H, Perhoniemi V, Erkola O. Diclofenac premedication but not intra-articular ropivacaine alleviates pain following day-case knee arthroscopy. *Can J Anaesth* 2000;47:220-4.
77. Convery PN, Milligan KR, Quinn P, Sjoval J, Gustafsson U. Efficacy and uptake of ropivacaine and bupivacaine after single intra-articular injection in the knee joint. *Br J Anaesth* 2001;87:570-6.
78. Vaghadia H, Chan V, Ganapathy S, Lui A, McKenna J, Zimmer K. A multi-centre trial of ropivacaine 7.5 mg x ml(-1) vs bupivacaine 5 mg x ml(-1) for supra clavicular brachial plexus anesthesia. *Can J Anaesth* 1999;46:946-51.
79. Ruetsch YA, Fattinger KE, Borgeat A. Ropivacaine-induced convulsions and severe cardiac dysrhythmia after sciatic block. *Anesthesiology* 1999;90:1784-6.
80. Cederholm I, Akerman B, Evers H. Local analgesic and vascular effects of intradermal ropivacaine and bupivacaine in various concentrations with and without addition of adrenaline in man. *Acta Anaesthesiol Scand* 1994;38:322-7.
81. Burke D, Joypaul V, Thomson MF. Circumcision supplemented by dorsal penile nerve block with 0.75% ropivacaine: a complication. *Reg Anesth Pain Med* 2000;25:424-7.
82. Ganapathy S, Sandhu HB, Stockall CA, Hurley D. Transient neurologic symptom (TNS) following intrathecal ropivacaine. *Anesthesiology* 2000; 93:1537-9.
83. de Jong RH. Ropivacaine neurotoxicity: a stab in the back? *Anesthesiology* 2001;95:1531.
84. de Jong R. Local anesthetics. St Louis: Mosby, 1994.
85. Greene NM. Editorial views: Familiarity as a basis for the practice of anesthesiology. *Anesthesiology* 1976;44:101-3.

Upcoming Scientific Meetings

31 January – 02 February 2003

41st Clinical Conference in Pediatric Anesthesiology
Anaheim, California

CONTACT: Herbert Zarco, Conference coordinator

Tel: 323 669-2262

Fax: 323 660-8983

Email: hzarco@chla.usc.edu

18-23 February 2003

American Academy of Pain Medicine
Annual Meeting

New Orleans, LA

CONTACT: American Academy of Pain Medicine

Tel: 847 375-4731

Fax: 877 734-8750

Email: aspm@amctec.com

20-24 June 2003

Canadian Anesthesiologists' Society 59th Annual
Meeting

Ottawa, ON

CONTACT: Susan Wilson, Coordinator

Tel: 416 480-0602

Fax: 416 480-0320

Email: meetings@cas.ca

Change of address notices and requests for subscriptions to *Anesthesiology Rounds* are to be sent by mail to P.O. Box 310, Station H, Montreal, Quebec H3G 2K8 or by fax to (514) 932-5114 or by e-mail to info@snellmedical.com. Please reference *Anesthesiology Rounds* in your correspondence. Undeliverable copies are to be sent to the address above.

This is an English translation of the original French article.

This publication is made possible by an educational grant from

Organon Canada Limited