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P. Ultchaswadi

O. Rodanant

S. Nirudthisard

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## Ropivacaine: an update in clinical use

Pornthip Ultchaswadi\*

Oraluxna Rodanant\* Supranee Nirudthisard\*

**Ultchaswadi P, Rodanant O, Nirudthisard S. Ropivacaine: an update in clinical use. Chula Med J 2001 Apr; 45(4): 347 - 64**

*Ropivacaine is a new aminoamide local anesthetic drug of the same group as bupivacaine and mepivacaine. It is the monohydrate of hydrochloride salt of 1-propyl-2',6' pipercoloxylidide. The pipercoloxylidides are called chiral drugs because of their asymmetric carbon atom. Unlike mepivacaine and bupivacaine, which are available for clinical use as a racemic mixture of left (sinister) and right (rectus) handed configuration, ropivacaine is prepared as a pure s-enantiomer (left handed configuration). Its clinical efficacy appears to be quite similar to that of bupivacaine but it posses a greater margin of safety.*

*Because of its better sensory-motor differential block and lesser cardiotoxicity than previous long acting amide local anesthetic drugs, ropivacaine may be a preferable local anesthetic drug particularly for extradural analgesia.*

**Key words:** *Ropivacaine, Clinical use.*

Reprint request : Ultchaswadi P, Department of Anesthesiology, Faculty of Medicine,  
Chulalongkorn University, Bangkok 10330, Thailand.

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### Objective

Our purpose was to review properties, pharmacology and current use of ropivacaine, a new local anesthetic agent.

\* Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University

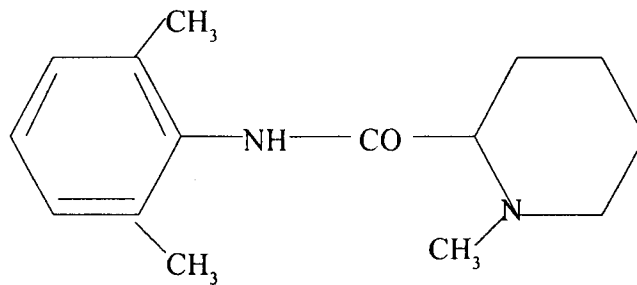
**พรทิพย์ อัชชสวัสดิ์, อรลักษณ์ รอดอนันต์, สุปราณี นิรุตติศาสน์. Ropivacaine: ที่ใช้ในทางคลินิกในปัจจุบัน. จุฬาลงกรณ์เวชสาร 2544 เม.ย; 45(4): 347 - 64**

*Ropivacaine* เป็นยาชาเฉพาะที่ชนิด *aminoamide* ตัวใหม่ ซึ่งเป็นยาในกลุ่มเดียวกับ *Bupivacaine* และ *Mepivacaine* *Ropivacaine* เป็น *Monohydrate* ของเกลือ *Hydrochloride* ของ *1-propyl-2',6'-pipecoloxylidide* *Pipecoloxylidides* เป็นยาชนิด *Chiral* เพราะว่ามีคาร์บอนอะตอมที่ไม่สมมาตรกัน *Ropivacaine* ต่างจาก *Mepivacaine* และ *Bupivacaine* ตรงที่ *Ropivacaine* เป็น *S-enantiomer* บริสุทธิ์ ประสิทธิภาพของยา *Ropivacaine* คล้ายกับ *Bupivacaine* แต่มีช่วงของความปลอดภัยมากกว่า (*greater margin of safety*) เนื่องจาก *Ropivacaine* มีข้อดีกว่ายาชาเฉพาะที่กลุ่ม *Amide* ตัวเดิมที่ออกฤทธิ์นาน ตรงที่มีความสามารถแยกระงับประสาทความรู้สึกละประสาทการเคลื่อนไหว และมีภาวะเป็นพิษต่อหัวใจน้อยกว่า *Ropivacaine* จึงเป็นยาชาเฉพาะที่ที่น่าใช้โดยเฉพาะอย่างยิ่งในการระงับความรู้สึกลแบบ *Extradural*

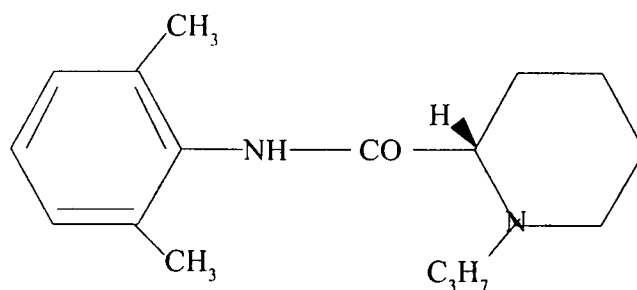
### History

Ropivacaine (1-propyl-2',6'-pipecoloxylidide) is a new amide local anesthetic drug. Ropivacaine is a member of the mepivacaine family (pipecolyl xylidides), well known members of which include mepivacaine and bupivacaine (Fig 1).<sup>(1,2)</sup> Far from being a me-too drug, ropivacaine is the only local

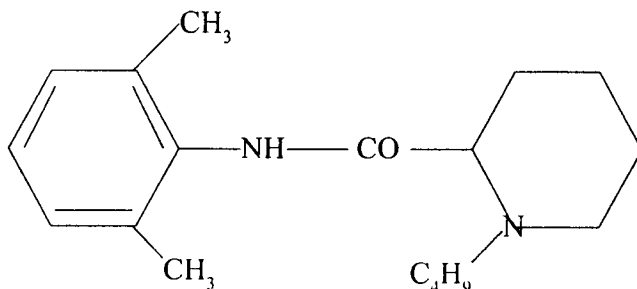
anesthetic drug prepared as a pure left-rotating S(-) enantiomer since thus, it is less arrhythmic and more potent.<sup>(1,3)</sup> It has an enantiomeric purity of 99.5 %.<sup>(2)</sup> Ropivacaine was first synthesized during the development of bupivacaine and its first clinical trials were in 1988.<sup>(4)</sup>



Mepivacaine



Ropivacaine



Bupivacaine

**Figure 1.** Chemical structure of local anesthetic drugs: the mepivacaine family (pipecolyl xylidides).<sup>(1,2)</sup>

### Physiochemical properties

Upon comparison of the physiochemical properties of ropivacaine, mepivacaine, bupivacaine and lidocaine (Table 1)<sup>(4,6)</sup>, the pKa of ropivacaine is equal to that of bupivacaine so that the onset of action is similar. The percentage of protein binding of ropivacaine is marginally lower than that of bupivacaine, so the duration of action is equal to or shorter than that of bupivacaine. The potency of ropivacaine is below that of bupivacaine, but above that of lidocaine, based on its partition coefficient.

### Pharmacodynamics

At low concentrations below 0.5% ropivacaine induces more profound and rapid blockade of pain fibers (A delta and C fibers) than bupivacaine. At higher concentrations, the blocking activity is not different from that of bupivacaine.<sup>(7,8)</sup>

Based on a biphasic vascular effect of local anesthetics ropivacaine also has this effect, causing vasoconstriction at low concentrations and vasodilatation at high concentrations.<sup>(9,10)</sup> This effect was found in both pigs and in human studies.<sup>(9-12)</sup>

Italic studies in pigs and dogs indicate that

ropivacaine has lower effects on cardiac rhythm than equianalgesic doses of bupivacaine but that it affects cardiac rhythm more than lidocaine.<sup>(13,14)</sup> When administering equipotent high doses of ropivacaine, bupivacaine and lidocaine (5.33, 4 and 16 mg, respectively) into the left anterior descending artery in anesthetized pigs, the hemodynamic changes (such as decreased left ventricular dP/dT, increased LVEDP, decreased MAP) were not different between groups. But only ropivacaine significantly increased the great cardiac venous blood flow. All of these three drugs had no significant effect on either heart rate or cardiac output.<sup>(13)</sup> Ropivacaine and bupivacaine did not significantly compromise the uteroplacental blood flow or deteriorate the fetal condition either intravenous infusion into pregnant ewes<sup>(15)</sup> or epidural administration for cesarean section in human.<sup>(16)</sup> Ropivacaine and bupivacaine cross the human placenta at a similar rate. The placental transfer of both drugs increases significantly as the fetal pH decreases and significantly decreases as the maternal plasma protein binding increases.<sup>(17)</sup> When ropivacaine, bupivacaine or levobupivacaine were infused intravenously into pregnant ewes, the placental transfer rate was not

Table 1. Physiochemical properties of local anesthetic drugs.<sup>(4,5)</sup>

	Ropivacaine	Bupivacaine	Mepivacaine	Lidocaine
M.W.	274	288	246	234
pKa	8.07	8.1	7.6	7.7
Partition coefficient (N heptane/buffer)	2.9	10	-	1.0
Protein binding (%)	94	96	78	65

M.W. : Molecular weight

different between groups. There were no important hemodynamic changes in the pregnant ewes and fetuses.<sup>(18)</sup>

**Pharmacokinetics**

When 20, 40, 80 mg of ropivacaine were infused intravenously for 30 minutes lead to 94 % plasma protein binding, almost all protein binding is  $\alpha_1$ -acid glycoprotein. The volume of distribution at steady state (Vdss) was 42 litres. The elimination half life was 1.7 hours and mean plasma clearance was 400 ml/min.<sup>(19)</sup>

In patients undergoing hysterectomy, upon epidural administration of ropivacaine 125, 187.5, 250 mg or bupivacaine 125 mg, the C<sub>max</sub> is 0.69, 1.11, 1.77, 0.60 mg/L, respectively. The half life (T1/2) is 4.8, 5.8, 3.6 and 7.88 hours, respectively. The greater C<sub>max</sub> of ropivacaine than bupivacaine is most likely explained by the greater V<sub>d</sub> of bupivacaine. The shorter T1/2 of ropivacaine could be explained by the higher lipophilicity of bupivacaine.<sup>(20)</sup>

Ropivacaine is extensively metabolized by microsomal cytochrome P450 in the liver.<sup>(21,22)</sup> There are various metabolites, 2',6'-pipecoloxylidide (PPX), 3' hydroxyropivacaine (3'-OH Ropivacaine) and 4-hydroxyropivacaine (4'-OH Ropivacaine). PPX is a major

metabolite<sup>(21,23)</sup> with a cardiotoxicity 1/8 that of ropivacaine.<sup>(1)</sup> Ropivacaine and its metabolites are excreted in the urine (86 ± 3 %) and in the feces (9 ± 1 %). The major metabolite identified in the urine is conjugated 3-OH-ropivacaine (37±3 %). Only 1±0.6 % is excreted in the urine with its chemical composition unaltered.<sup>(21)</sup>

Systemic toxicity of intravenous ropivacaine was studied in various species of animals. Non-pregnant and pregnant ewes received an intravenous infusion of ropivacaine or bupivacaine at a rate of 0.5 mg/kg/min until circulatory collapse. Compared to bupivacaine, a greater dose of ropivacaine was needed to produce significant toxic manifestations in pregnant ewes, but no clinical significance was observed in nonpregnant ewes. The margin of safety defined as the CC/CNS ratio (dose causing circulatory collapse versus the dose causing convulsive activity) was similar in both drugs (Table 2).<sup>(24)</sup> Hence, we can conclude that the systemic toxicity of ropivacaine or bupivacaine is not enhanced by gestation in sheep. This is in contrast to an earlier study in which cardiotoxicity of bupivacaine was enhanced by pregnancy in sheep<sup>(25)</sup> and in vitro study in rabbits' myocardium.<sup>(26)</sup>

**Table 2.** CC/CNS ratio.<sup>(23)</sup>

	Dose ratio	Concentration ratio
Nonpregnant		
Ropivacaine	2.13 ± 0.26	1.77 ± 0.15
Bupivacaine	2.03 ± 0.16	1.39 ± 0.09
Pregnant		
Ropivacaine	1.78 ± 0.17	1.61 ± 0.11
Bupivacaine	1.74 ± 0.17	1.37 ± 0.18

There is only one study in humans regarding systemic toxicity by IV infusion of ropivacaine, bupivacaine and placebo. The average maximum tolerated dose with respect to central nervous system symptoms was higher with ropivacaine (115mg) than with bupivacaine (103mg), but this was not clinically significant. The maximum tolerated unbound plasma concentration after ropivacaine infusion was significantly higher than that after bupivacaine ( $p < 0.001$ ). The time required for all symptoms to disappear was shorter after ropivacaine infusion.<sup>(27)</sup>

When equipotent doses of ropivacaine, bupivacaine and lidocaine were injected into the left anterior descending coronary artery of anesthetized pigs, the cardiodepressant ratio of bupivacaine (B): ropivacaine (R): lidocaine (L) was 4 : 3 : 1 on a mg basis. The electrophysiological toxicity ratio of B:R:L, defined as the amount of local anesthetic agent required to equally prolong the QRS interval was 15:6.7:1 on a milligram basis. The electrophysiological toxicity ratio of B:R in equipotent doses was 1.7:1. Hence, ropivacaine should be expected to have an approximately 70 % greater margin of safety than bupivacaine.<sup>(13)</sup>

### Clinical Use

There are many clinical uses of ropivacaine as following

1. Epidural anesthesia : painless labor, cesarean section, postoperative continuous epidural infusion, abdominal surgery and lower extremities surgery
2. Intrathecal anesthesia
3. Caudal anesthesia
4. Peripheral nerve block : Brachial plexus block, etc.

5. Intravenous regional anesthesia (Bier's block)

6. Infiltrative anesthesia

**1. Epidural anesthesia :** As for epidural anesthesia, there are many clinical uses such as

1.1 Epidural analgesia in labor or painless labor

In 2 studies, the analgesic potency of ropivacaine was 0.60 relative to bupivacaine.<sup>(28-29)</sup> The minimal recommended concentration was 0.2 %.<sup>(30)</sup> At this concentration, the optimal infusion rate was 6-8 ml/h.<sup>(31)</sup> Most studies<sup>(22,32-37)</sup> reported the onset of ropivacaine was not different from the onset of bupivacaine, but McCrae, et al<sup>(38)</sup> compared 0.5 % ropivacaine (10 ml) with 0.5 % bupivacaine (10 ml). The onset of 0.5 % ropivacaine showed a 50 % delay when measured against that of 0.5 % bupivacaine. In sensory block, all studies revealed similar duration and qualities upon comparison with bupivacaine.<sup>(22,32-39)</sup>

In a prospective meta-analysis of patients receiving epidural analgesia with 0.25 % ropivacaine or 0.25 % bupivacaine, the drugs were administered as intermittent boluses in four studies and by continuous infusion in two studies. The intensity of motor block was lower in the ropivacaine group. Spontaneous vaginal deliveries occurred more frequently with ropivacaine than bupivacaine (58 % vs 49 %) and instrumental deliveries (forceps and vacuum extraction) less frequently (27 % vs 40 %) (Table 3).<sup>(39)</sup> This may be due to the less profound motor blockade in the ropivacaine group allowing normal labor. With neonatal outcome, the NACS (Neurological and adaptive capacity scores) at 24 hours in the ropivacaine group were better than in the bupivacaine group. But the NACS at 2 hours were not significantly different. These may be explained by the lower lipid solubility and shorter half life of ropivacaine resulting in more rapid

**Table 3.** Effects of epidural ropivacaine and bupivacaine on motor block and mode of delivery.<sup>(34)</sup>

	0.25 % Ropivacaine	0.25 % Bupivacaine	P-value
No motor block	51 %	42 %	P < 0.05
Spontaneous delivery	58.3 %	48.9 %	P < 0.05
• Primigravida	45 %	39 %	
• Multiparae	80 %	64 %	P < 0.05
Instrument delivery (Forceps or vacuum extraction)	27.1 %	40 %	P < 0.01
• Primigravida	36 %	47 %	
• Multiparae	12 %	28 %	P < 0.05
Cesarean section rate	14.6 %	11.2 %	NS

excretion. Hence, ropivacaine seems to be safer for application in obstetrics.<sup>(39)</sup>

Current study in ambulatory labor epidural analgesia compared the efficacy of 20 ml of either 0.08 % bupivacaine plus 2 µg/ml fentanyl with 0.08 % ropivacaine plus 2 µg/ml fentanyl. No significant difference between group in onset and quality of analgesia was revealed. Spontaneous micturition was observed in 65 % of bupivacaine group compared with 100 % of ropivacaine group. Ambulation was observed in 75 % of bupivacaine group and 100 % of ropivacaine group. The incidence of forceps delivery was 35 % in bupivacaine group and 10 % in ropivacaine group. Ropivacaine as compared with bupivacaine in same concentration in painless labor provided better ability to ambulate and micturate. Thus, ropivacaine seems to be a good drug for ambulatory epidural analgesia for women in labor.<sup>(40)</sup>

#### 1.2 Epidural anesthesia in cesarean section

Upon comparison with bupivacaine, most studies<sup>(16,41-43)</sup> found no significant difference in the sensory blocking profile (onset, duration and maximum

height of sensory block) and observed that ropivacaine led to a slower onset and more rapid recovery of the motor block than bupivacaine. These results may demonstrate the advantage of ropivacaine over bupivacaine. Based on most studies<sup>(42-45)</sup>, the recommended concentration is 0.5 % - 0.75 %. According to two studies<sup>(44,45)</sup>, when increasing the concentration to 0.75 %, ropivacaine produced equally effective anesthesia for cesarean section as 0.5 % bupivacaine. Ropivacaine will potentially replace bupivacaine due to its lower cardiotoxicity<sup>(13)</sup>, which does not appear to be enhanced by pregnancy.<sup>(24,26,46,47)</sup>

#### 1.3 Postoperative continuous epidural infusion

Because of higher incidence of ineffective analgesia with 0.1 % concentrations of ropivacaine, studies in healthy volunteers and postoperative patients have established 0.2 % ropivacaine as the best balanced concentration for infusion.<sup>(48-52)</sup> Even with 0.3 % concentrations, most studies found an increase in motor block and side effects i.e. hypotension, bradycardia and urinary retention compared with lower concentrations.<sup>(50-53)</sup> At 0.2 %



concentrations of ropivacaine, the optimal infusion rate was 8 -10 ml/hr. Urinary retention and increased motor block were observed more frequently with infusion rates of 12 and 14 ml/hr, whereas the 6 ml/hr group failed to block all lumbar segments.<sup>(54)</sup> When 0.2 % ropivacaine was compared with 0.2 % bupivacaine at the same infusion rate, the bupivacaine group produced significantly more frequent and intense motor blocks. Whereas it showed no difference from the ropivacaine group with respect to analgesia.<sup>(55)</sup> Even when 0.3 % ropivacaine was administered, the recovery of postural control was faster than that of 0.25 % bupivacaine.<sup>(56)</sup>

Epidural infusion with ropivacaine had many benefits over PCA morphine in terms of more effective analgesia, less nausea/vomiting and earlier discharge from PACU, but more side effects of the local anesthetic agent such as hypotension and bradycardia were found.<sup>(54,57)</sup>

#### 1.4 Lower extremities surgery<sup>(58-59)</sup>

In lower extremities surgery, there are multiple studies evaluated epidural anesthesia with ropivacaine versus bupivacaine. Two double-blind randomized studies compared the effects of ropivacaine in various concentration with 0.5 % bupivacaine. The volume of injected solution was 20 ml. No difference between two drugs group was found in onset of analgesia, except in one study, a longer duration and intensity of motor block was found in 1 % ropivacaine group comparing with 0.5 % bupivacaine. More patient received higher concentration of ropivacaine required treatment for hypotension and bradycardia. Although high concentration of ropivacaine provide more satisfactory motor block but it developed more side effects, which can be treated without complication.

#### 1.5 Abdominal surgery

As for lower abdominal surgery, there are three studies evaluated effects of epidural anesthesia with various concentration of ropivacaine versus bupivacaine. Wood and Rubin<sup>(60)</sup> compared 1 % ropivacaine with 0.75 % bupivacaine in fix volume, 20 ml injected epidurally in patient undergoing gynecologic surgery. No significant difference was found in any results (onset, extent and duration of motor or sensory block). Tuttle, et al<sup>(61)</sup> compared ropivacaine with bupivacaine in same concentration (0.75 %) and volume (20ml) in patient undergoing gynecologic surgery. Ropivacaine had a slower onset and shorter duration of motor block than bupivacaine, but no significant difference in satisfaction of surgeon. Ropivacaine also had shorter duration of sensory block than bupivacaine.

Upon an ascending dose study<sup>(62)</sup>, 0.5, 0.75, 1 % of ropivacaine and 0.5 % of bupivacaine 25 ml was injected epidurally in women undergoing abdominal hysterectomy. A dose-response relationship was observed with increasing dose of ropivacaine for all variables tested except analgesia and muscle relaxation. No difference was observed in distribution and onset of sensory block. The longer duration of sensory block in 1 % ropivacaine group was found. As for motor block, 1 % ropivacaine had longer duration than 0.75 % and 0.5 % ropivacaine respectively. Onset of motor block in 1 % ropivacaine group was faster than 0.5 % ropivacaine group.

## 2. Intrathecal anesthesia

Based on its lower cardiotoxicity on a milligram basis and shorter recovery time, ropivacaine may be a suitable substitute for bupivacaine. But most studies found ropivacaine only half as potent as bupivacaine

and in equipotent doses, ropivacaine offers no significant advantage over bupivacaine.<sup>(63-66)</sup>

### 3. Caudal anesthesia in pediatrics

The properties of ropivacaine, particularly its lower toxicity to the cardiovascular and central nervous systems, suggest advantages over bupivacaine regarding regional anesthesia especially caudal anesthesia in children. There are many studies comparing various concentrations with bupivacaine. Upon administration of 0.2 - 0.25 % concentrations of ropivacaine (0.7-1 ml/kg), neither motor block nor side effect was found, and likewise no difference in the quality of the sensory block when compared with 0.25 % bupivacaine. However, ropivacaine may have a benefit over bupivacaine due to its higher margin of safety.<sup>(67-69)</sup> Comparing 0.375 % (1 ml/kg) ropivacaine with bupivacaine at the same concentration and dose, the ropivacaine group showed a shorter duration of the motor block than the bupivacaine group.<sup>(70)</sup> Upon comparison of 0.25, and 0.5 % ropivacaine with 0.25 % bupivacaine a longer duration of analgesia was observed with 0.5 % concentration in the ropivacaine group. But 0.5 % ropivacaine was also found to delay voiding and standing.<sup>(71)</sup>

However in this study, neither concentration of ropivacaine showed any serious complication or significant difference in side effects upon comparison of an identical concentration of ropivacaine and bupivacaine.

### 4. Peripheral nerve block

#### 4.1 Brachial plexus block

Ropivacaine may potentially provide better success rates with brachial plexus block than bupivacaine, because its lower cardiotoxicity allows for larger doses to be used. Hence, 0.75 % ropivacaine

was compared with 0.5 % bupivacaine at the same volume of drugs for brachial plexus block. The concentration of 0.75 % ropivacaine showed a significantly higher quality of analgesia and motor block in two studies<sup>(72,73)</sup> but Vaghadia *italic* reported no statistical significance between groups.<sup>(74)</sup> The onset of analgesia with 0.75 % ropivacaine was faster than with 0.5% ropivacaine and was similar to that with 2 % mepivacaine when used for interscalene brachial plexus block.<sup>(75)</sup> When 0.5 % ropivacaine was compared with bupivacaine at the same concentration, no significant difference in terms of onset time, quality of blockade and duration of anesthesia were observed.<sup>(74,76)</sup> The concentration of 0.25 % ropivacaine is not suggested for brachial plexus block, because at this concentration a large number of supplemental peripheral nerve blocks is required.<sup>(77)</sup> One study has evaluated the effect of epinephrine on ropivacaine, the duration of the sensory block in the brachial plexus dermatomes as well as the duration of the motor block was not affected by epinephrine. However, adrenaline may be useful to provide a cardiovascular marker for intravascular injection when a test dose is administered.<sup>(78)</sup> As above studies have revealed that ropivacaine potentially provides a more effective analgesia and greater safety than bupivacaine, the drug often used in brachial plexus anesthesia nowadays.

#### 4.2 Intercostal nerve block

Kopacz et al compared 0.25 % ropivacaine with bupivacaine for bilateral intercostal blockade of T5 –T11 with 140 mg of either drug administered to volunteers. There was no significant difference in maximum plasma concentration. No toxic signs were observed. The motor block was less profound and of shorter duration with ropivacaine. The duration of the

sensory block was shorter when compared with bupivacaine.<sup>(79)</sup>

#### 4.3 Other peripheral nerve blocks

The recommended concentration of 0.5 - 0.75 % ropivacaine had a shorter duration of analgesia than bupivacaine, but a longer one than lidocaine. A 0.75 % ropivacaine concentration provided an onset time similar to 2 % mepivacaine and shorter than 0.5 % bupivacaine, and it also prolonged postoperative analgesia.<sup>(80-82)</sup>

#### 5. Intravenous regional anesthesia (IVRA), (Bier's block)

The local anesthetic most often used for IVRA is 0.5 % lidocaine, but analgesia is often rather brief. Compared with bupivacaine, ropivacaine causes less cardiovascular and central nervous system toxic effects suggesting that ropivacaine may be more useful for IVRA. There are two trials compared ropivacaine with lidocaine applied for IVRA, prolonged sensory block was observed with ropivacaine.<sup>(84-85)</sup> Hartmannsgruber et al compared 0.2 % ropivacaine (40 ml) with 0.5 % lidocaine (40 ml). They also found less CNS side effects (lightheadedness, tinnitus and drowsiness).<sup>(84)</sup> Ropivacaine causes prolonged analgesia with less CNS side effects. Hence, it seems

reasonable to consider ropivacaine a potential alternative for IVRA.

#### 6. Infiltrative anesthesia

Based on its vasoconstrictive properties, ropivacaine may be useful for infiltration. Cederholm, et al<sup>(9)</sup> compared intradermal administration of 0.25 %, 0.5 %, 0.75 % and 1 % ropivacaine with 0.25 %, 0.5 %, 0.75 % bupivacaine with or without addition of epinephrine (5 mg/ml) (Table 4).<sup>(9)</sup> The analgesic duration obtained with plain ropivacaine was longer than with plain bupivacaine at the same concentration due to the vasoconstrictive effect produced by 0.25-0.75 % ropivacaine. No increase in duration was observed with 1 % ropivacaine plain solution upon comparison with 0.75 % ropivacaine. This may be explained by a vasodilatory effect of the high concentration, 1 % ropivacaine.

Local anesthetic solutions with epinephrine shorten the onset time, increase the intensity and prolong the duration of the block. This is explained by epinephrine reducing the absorption and decreasing the peak blood concentration of the agent (Table 4).<sup>(9)</sup> In clinical use, ropivacaine produced no difference in postoperative analgesia or blood loss when compared with bupivacaine.<sup>(86-87)</sup>

**Table 4.** Duration of dermal analgesia after intradermal injection.<sup>(9)</sup>

	PLAIN SOLUTION (MIN)	WITH EPINEPHRINE (MIN)
0.25 % Ropivacaine	30	180
Bupivacaine	10	210
0.5 % Ropivacaine	60	210
Bupivacaine	10	180
0.75 % Ropivacaine	120	180
Bupivacaine	10	180
1 % Ropivacaine	60	240

### Complications and side effects

None of the serious adverse events was considered drug related. There was no significant difference between ropivacaine and bupivacaine by in terms of adverse events, e.g., hypotension, bradycardia, nausea.

In 1996, McClure has reported five cases of inadvertent intravenous injection (75 - 200 mg). One patient who had received 200 mg intravascularly developed convulsions, which resolved within 2 minutes with prompt treatment. None of the five patients developed cardiotoxicity.<sup>(2)</sup>

Since 1997, an additional 3 cases of inadvertent intravascular injection have been reported.<sup>(68-90)</sup> All of these had convulsions after receiving 120 - 225 mg intravenously. One patient who had received 225 mg intravascularly developed sinus bradycardia, supraventricular tachycardia (SVT), and transient atrial fibrillation. After about 20 minutes the patient was able to talk and subsequently fully recovered.

In conclusion, fractionating the total dose of local anesthetics or using a marker (i.e., epinephrine, lidocaine) is suggested.<sup>(90)</sup>

### Conclusions

Ropivacaine is a new, effective, long-acting amide local anesthetic agent and the firstly to be produced as a pure S-enantiomer. It is considered safer than bupivacaine, the currently used drug. Ropivacaine induces less motor block than bupivacaine at the same concentration. Current studies on ropivacaine suggest ropivacaine to offer a distinct advantage over bupivacaine in some clinical use as above from its greater sensory-motor differential block and lower toxic properties. On the other hand, bupivacaine may still have a role in the operations that need more muscle relaxation. For this reason, it may be useful for painless labor, caudal block and postoperative continuous epidural infusion. Its lower toxicity compared with bupivacaine, allows ropivacaine to be used for surgical anesthesia at concentrations up to 1 %, and it may therefore constitute an alternative for IVRA. Nowadays ropivacaine is used in painless labor, PCEA and lower abdominal surgery. Dosage recommendation of ropivacaine is presented in table 5. Future clinical use of ropivacaine will depend on the further clinical trial and more experience in practical use.

**Table 5.** Dosage Recommendation of Ropivacaine.

Procedure	Concentration (mg/ml)	Volume (ml)	Dosage (mg)
Epidural <sup>(7,31)</sup>			
■ Surgery	7.5 -10	15 - 25	113 - 200
■ Cesarean section	5 - 7.5	15 - 20	113 - 150
■ Painless labor	2.0 - 2.5	10 - 20 , 6 - 8 ml/hr	20 - 40
■ PCEA	2.0	6 - 14 ml/hr	12 - 28 mg/hr
Caudal <sup>(67-71)</sup>	2 - 5	-	0.7 - 1 ml/hr
Peripheral nerve block <sup>(72-75,77)</sup>	5 - 7.5	1 - 30	5 - 225
IV regional anesthesia <sup>(84,85)</sup>	2 - 3.5	-	1.2 mg/kg

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## กิจกรรมการศึกษาต่อเนื่องสำหรับแพทย์

ท่านสามารถได้รับการรับรองกิจกรรมการศึกษาต่อเนื่องสำหรับแพทย์ประเภทที่ 3 (ศึกษาด้วยตนเอง) ได้ จากการอ่านบทความเรื่อง "Ropivacaine: ที่ใช้ในทางคลินิกในปัจจุบัน" โดยตอบคำถามข้างล่างนี้ พร้อมกับส่งคำตอบที่ท่านคิดว่าถูกต้องโดยใช้แบบฟอร์มคำตอบท้ายคำถามแล้วใส่ชื่อพร้อมของเปล่าติดแสตมป์เจ้าหน้าที่ของถึงตัวท่าน ส่งถึง

ศ. นพ. สุทธิพร จิตต์มิตรภาพ  
บรรณาธิการจุฬาลงกรณ์เวชสาร  
และประธานคณะกรรมการการศึกษาต่อเนื่อง  
คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย  
หน่วยจุฬาลงกรณ์เวชสาร  
ตึกอบรมวิชาการ ชั้นล่าง  
เขตปทุมวัน กทม. 10330

ท่านจะได้รับเฉลยคำตอบพร้อมหนังสือรับรองกิจกรรมการศึกษาต่อเนื่อง

### คำถาม - คำตอบ

- ยาชาเฉพาะที่ต่อไปนี้ไม่ได้อยู่ใน Pipicolyl xylidides family?
  - Ropivacaine
  - Mepivacaine
  - Bupivacaine
  - Xylocaine
- ข้อแตกต่างระหว่างยา Ropivacaine และ Bupivacaine ข้อใดผิด?
  - pKa ของ Ropivacaine เท่ากับ Bupivacaine
  - เวลาที่เริ่มออกฤทธิ์ (Onset of action) เท่ากัน
  - ร้อยละของการจับกับโปรตีนของ Bupivacaine มากกว่า Ropivacaine เล็กน้อย
  - ระยะเวลาของการออกฤทธิ์ (Duration of action) ของ Ropivacaine นานกว่า Bupivacaine

คำตอบ สำหรับบทความเรื่อง "Ropivacaine: ที่ใช้ในทางคลินิกในปัจจุบัน" จุฬาลงกรณ์เวชสาร  
ปีที่ 45 ฉบับที่ 4 เดือน เมษายน พ.ศ. 2544

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3. ข้อดีของการใช้ Ropivacaine ใน Epidural analgesia ระหว่างการคลอด เปรียบเทียบกับ Bupivacaine?
- ก. Intensity ของ Motor block ใน Ropivacaine น้อยกว่า
  - ข. การคลอดปกติทางช่องคลอดใน Ropivacaine พบได้มากกว่า
  - ค. NACS ของเด็กที่ 24 ชั่วโมงหลังคลอดในกลุ่ม Ropivacaine ดีกว่า
  - ง. ถูกทุกข้อ
4. ผลข้างเคียงของยา Ropivacaine ได้แก่ข้อใด?
- ก. มีพิษต่อหัวใจมาก
  - ข. เกิดอาการชักได้ ถ้าฉีดยาเข้าหลอดเลือด
  - ค. ตับล้มเหลว
  - ง. ไตวาย
5. ที่ใช้ในทางคลินิกของยา Ropivacaine ที่ไม่พบข้อดีเหนือกว่ายา Bupivacaine?
- ก. Intrathecal anesthesia
  - ข. Epidural anesthesia in cesarean section
  - ค. Brachial plexus block
  - ง. Epidural analgesia in labor

ท่านที่ประสงค์จะได้รับเครดิตการศึกษาต่อเนื่อง (CME credit) กรุณาส่งคำตอบ

ศาสตราจารย์นายแพทย์สุทธิพร จิตต์มิตรภาพ  
ประธานคณะกรรมการการศึกษาต่อเนื่อง  
คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย  
หน่วยจุฬาลงกรณ์เวชสาร  
ตึกอบรมวิวิชาการ ชั้นล่าง  
คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย  
เขตปทุมวัน กทม. 10330