

## REVIEW

Vol. 31. No. 2 April-June 2008  
pp 133-138

## Neuraxial ropivacaine in cesarean surgery

Manuel Marrón-Peña, MD;\* Jaime Rivera-Flores, MD\*\*

\* Titular Member Academia Mexicana de Cirugía. Member of the Colegio Mexicano de Anestesiología. Member of the Consejo Consultivo de la SMAGO.

\*\* Vice-President of the Colegio Mexicano de Anestesiología. Member of the Consejo Consultivo de la SMAGO. Anesthesiologist of the Hospital General Balbuena SSDF.

## Reprints request :

Dr. Manuel Marrón Peña  
Sociedad Mexicana de Anestesiología en  
Ginecología y Obstetricia, A.C. (SMAGO).  
Sebastián Lerdo de Tejada Núm. 37  
Col. Del Carmen Coyoacán. Tel. 56589992  
E-mail: smago95@hotmail.com

Received for publication: 21-03-2007

Accepted for publication: 06-08-2007

## SUMMARY

Ropivacaine is the anesthetic premises introduced to the clinical practice in 1996 and its application in neuraxials techniques in obstetrics is ample, mainly for the analgesia of the work of childbirth and for the Caesarean operation. Nevertheless, in Mexico in a revision of the last 10 years of three bibliographical sources of the country, just 20 references indicate their use in this area of the medical knowledge, but none of them with the spinal technique for Caesarean, reason why in this work their main pharmacologic aspects are reviewed, their applications by the routes epidural and spinal in Caesarean and it discusses because it has not been used by this route for the resolution of the pregnancy by the abdominal route. This new anesthetic is a good alternative in the obstetrical surgery by the advantages that offer to the patient, the surgeon and the anesthesia specialist. Its spinal application for Caesarean is recommended now in controlled clinical studies.

**Key words:** Ropivacaine, neuraxial anesthesia, epidural anesthesia, spinal anesthesia, caesarean section.

## RESUMEN

La ropivacaína es un anestésico local introducido a la práctica clínica en 1996 y su aplicación en técnicas neuroaxiales en obstetricia es amplio, principalmente para la analgesia del trabajo de parto y para la operación cesárea. Sin embargo en México, en una revisión de los últimos 10 años de tres fuentes bibliográficas del país, sólo se encontraron 20 referencias que indican su uso en esta área del conocimiento médico, pero ninguna de ellas con la técnica subaracnoidea para cesárea, por lo que en este trabajo se revisan sus principales aspectos farmacológicos, sus aplicaciones por las vías peridural y subaracnoidea en cesárea y se discute el porqué no se ha empleado por esta ruta para la resolución del embarazo por la vía abdominal. Este nuevo anestésico es una buena alternativa en la cirugía obstétrica por las ventajas que ofrece al paciente, al cirujano y al anestesiólogo. Se recomienda su aplicación intratecal para cesárea en estudios clínicos controlados.

**Palabras clave:** Ropivacaína, anestesia neuroaxial, anestesia peridural, anestesia subaracnoidea, cesárea.

## INTRODUCTION

The ropivacaine was introduced into the market about 10 years ago and its intrathecal anesthetic use barely was began in the last five years of the newly initiated millennium.

The clinical experience of the authors in the administration of ropivacaine dates from 2000 to the present, in this period they have used only the peridural route for obstetric anesthesia, elective cesarean section and orthopedic and trauma surgery, with anesthetic-analgesic results that can be de-

scribed as very good and practically with no adverse effect on the patients and their neonates (in the case of cesarean). In the Mexican Republic, on the other hand, reports about this local anesthetic also seem to be limited only to epidural use in anesthesiology practice.

This study is a literature survey about the neuraxial ropivacaine applied by subarachnoid and peridural routes for cesarean section, because there are internationally published works describing the use of these routes. For this purpose, the following three Mexican bibliographic sources were revised in their last 10 years:

- A) Thesis of Diploma of Anesthesia and Analgesia in Gynecology and Obstetrics, which organizes annually the Mexican Society of Anesthesiology in Gynecology and Obstetrics (SMAGO from its acronym in Spanish): In 100 captured thesis (1996- 2006), there are only eight works related to this local anesthetic, seven related to epidural analgesia in labor, two of them with the combined spinal-epidural technique and an epidural anesthesia for cesarean section, either by subarachnoid route for this surgery. These works are not published.
- B) Journal Anesthesia in Mexico. In the supplement of November 2005 are the summaries of 88 free works, seven of them described the use of ropivacaine in obstetrics, none by the intrathecal route for a caesarean section and one by this route for general and orthopedic surgery<sup>(1,2)</sup>.
- C) Journal Anesthesia in Mexico. (1999-2007) During these years of publication of the Journal Anesthesia in Mexico; only five works on ropivacaine were found, one of them is the review of Dr. Whiz<sup>(3)</sup>, being the only one mentioning the use of this anesthetic by spinal route for cesarean section based on two articles of the international literature<sup>(4,5)</sup> and in a period when spinal anesthesia still was not using in the world with this local anesthetic, which explains why not in Mexico there are published works on the use of ropivacaine by subarachnoid route for cesarean section.

In summary, over the past 10 years, there are only twenty works on neuroaxial ropivacaine in the consulted national sources, approach was peridural in sixteen of this sources and subarachnoid space was the recipient of this anesthetic in the other four. The results on the anesthetic-analgesic quality were very good and without the presence of complications in patients who received this analgesic<sup>(1-5)</sup>.

World-wide it has become clear over time that subarachnoid, spinal, intrathecal or spinal anesthesia is a safe, inexpensive and easy-to-administer way that also offers a high level of post-anesthesia satisfaction for patients in who is used<sup>(6,7)</sup>.

It is worth mentioning that the method of regional anesthesia, with subarachnoid neuroaxial technique (according to current nomenclature), has more than 100 years of use in daily anesthetic practice around the world. Millions of spinal anesthetics by various approach routes, at single dose, with different types of needle or continuously through microcatheters and with different local anesthetics including cocaine, procaine, lidocaine, mepivacaine, bupivacaine and currently with ropivacaine and levobupivacaine have been applied during this time<sup>(6,7)</sup>. These anesthetics and their subarachnoid adjuvants have been administrated to different patients including pediatric, geriatric, adults and pregnant patients<sup>(3)</sup>. The type of surgeries are located mainly in the abdominal regions and lower extremities, including cesarean section and gynecological and obstetric hysterectomy, demonstrating an excellent anesthetic effectiveness, minimal adverse effects resulting in safety of patients, and favorable risk-benefit and cost-benefit relationships of this technique<sup>(3)</sup>.

Ropivacaine is currently being used for local infiltration in peripheral nerve and epidural blocks by subarachnoid route<sup>(8,9)</sup>.

## PHARMACOLOGY OF ROPIVACAINE

Ropivacaine has been use in neuroaxial, peridural and subarachnoid anesthesia, it has a profile similar to bupivacaine, but with less neuro-and cardiotoxic effect<sup>(10,11)</sup>.

This relatively new local anesthetic belongs to the mepivacaine family and is a member of the amino-amide class. In 1996 it was released in the Anglo-Saxon market for clinical use<sup>(3,12,13)</sup>. It is a white crystalline powder chemically described as S-(-)-1 propyl-2',6'-pipecoloxilidide hydrochloride monohydrate, with a molecular weight of 274 d. The structural difference with bupivacaine is that the butyl group is substituted by a propyl group, other difference is that ropivacaine is prepared as an isomer S (levoisomer) in place of a racemic mixture, these differences make it less fat-soluble and reduced toxicity. Ropivacaine is the first pure enantiomer-type local anesthetic (compound S) (Figure 1).

The R-enantiomer of bupivacaine is more cardiotoxic than the S-isomer, this effect appeared with doses ranging from 0.065% to 0.5% or more. It has similarities in its pharmacokinetics and pharmacodynamics with ropivacaine, only the latter is bound to plasma proteins by 96% and most of this binding is associated with alpha 1-acid glycoprotein, and its elimination is primarily by hepatic metabolism through CP-450, CYP1A2 and CYP3A4 systems, and its main metabolite is 3-hydroxy-ropivacaine. Only 1% is eliminated in urine<sup>(3,12,13)</sup>.

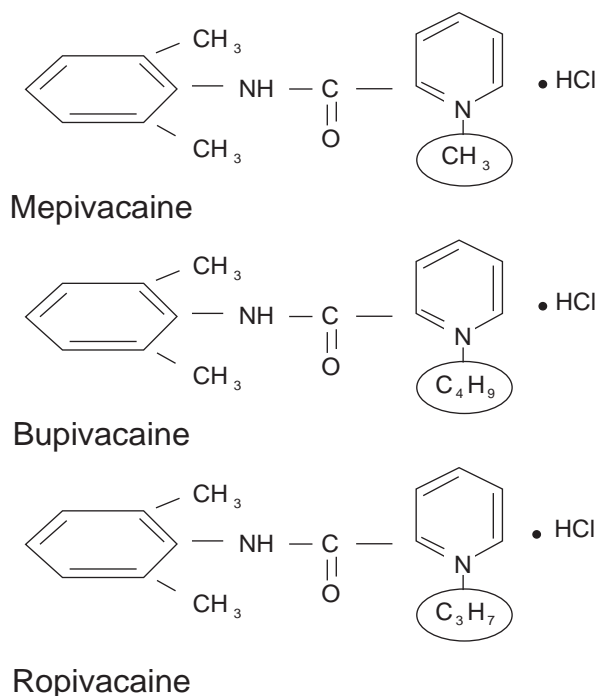
Documented most frequent adverse events and with an incidence of <5% are hypotension, bradycardia, nausea, vomiting, paresthesia and urinary retention, although all are considered mild and transient<sup>(3,12-15)</sup>.

Ropivacaine, like other local anesthetics of amide type, if accidentally placed in the subarachnoid space at a dose calculated for the epidural space, it will cause a massive anesthesia shock which shall receive of immediate treat-

ment with breathing and administering IV vasopressors and fast loads of colloids and crystalloids<sup>(15)</sup>.

The main contraindications of ropivacaine are obstetric emergencies and the hypersensitivity of local anesthetics<sup>(3,13-15)</sup>, the latter aspect is self-explanatory and is an absolute contraindication for this type of anesthetic. With regard to obstetric emergencies, we refer mainly to the type of hemorrhagic (Abruptio placenta and total bleeding central anterior placenta) where concomitant hypovolemia, anemia and placenta accreta requiring required general anesthesia to resolve the problem that is endangering the live of the maternal-fetal binomial. Therefore the ropivacaine and any other local anesthetic as well as the neuroaxial anesthesia are contraindicated. This same situation occur when there is a severe fetal distress or when the fetus is in dying, as they are obstetric emergencies requiring immediate resolution<sup>(3,13-15)</sup>.

The physicochemical characteristics of some amide type local anesthetics used in neuroaxial anesthesia/analgesia in obstetrics are shown in the Table I. Clinical doses and toxicity thresholds of ropivacaine compared with bupivacaine, lidocaine and mepivacaine are also shown in this table.



**Figure 1.** Chemical structure of ropivacaine and its similarity with bupivacaine and mepivacaine.

## EPIDURAL ROPIVACINE FOR CESAREAN SECTION

The half-life of ropivacaine after epidural administration is 5-7 hours. There are studies demonstrating that ropivacaine, as compared to bupivacaine, causes a less profound motor block of shorter duration having a higher neurotoxic and cardiotoxic threshold, ie higher doses are needed and the neurological and cardiovascular manifestations take longer to appear<sup>(10,11,13,14)</sup>.

**Table I.** Physico-chemical characteristics of amide type local anesthetics. (Elaborated by authors with date of the bibliographical citations 3, 18, 19, 25-27).

Name	Lidocaine	Mepivacaine	Bupivacaine	Ropivacaine
Molecular weight	234	246	288	274
Union proteins (%)	70	77	96	94 - 96
PK	7.9	7.6	8.1	8.1
Power (Procaine = 1)	4	2	10-16	8 -12
Latency (min)	5-10	10-15	20-30	10 -15
Duration (min)	60-100	90-180	180-360	180 - 300
Maximum dose (mg/kg)	4	5	2	2 - 2.5
Dose with adrenaline	7	7	2.5	2 - 2.5 It does not need adrenaline
Threshold toxic plasma (µg/mL)	5-6	5-6	1.6	2 - 3
Convulsions (mg/kg)	14	19	4.5	5
Peridural concentration (%)	1-2	1-2	0.25 - 0.75	0.5 - 0.75
Spinal concentration (%)	2.5 -5	5	0.5 - 0.75	0.5 - 0.75

On the other hand, 0.75% or 7.5 mg/mL concentration levels of ropivacaine are the most recommended 15-25 mL (113-188 mg) dose for epidural caesarean administrated by peridural route. This dose must be administrated fractionally. There are reports describing the administration of doses of up to 200 mg (30 mL). These doses have been used cumulatively up to 770 mg in 24 hours with well tolerance, producing satisfactory analgesia and anesthesia as well as adequate muscle relaxation<sup>(13,14)</sup>. Latency obtained by peridural route is 10-20 with an average of 14 minutes, although it is ideal to wait 30 minutes for the lock is of high quality. The average duration of sensory block at T6 varies from 1.7 to 3.2 hours, whereas motor block is from 1.4 to 2.9 hours. In summary, as compared to bupivacaine, the anesthetic potency of ropivacaine is from 1.3 to 1 respectively, the sensory block duration is slightly higher, producing less intense motor block and a differential lock more appropriate and therefore more sensitive than motor, thus by facilitating a more rapid recovery, while maintaining analgesia and the outpatient aspect, especially in patients receiving postoperative epidural or obstetric analgesia with this anesthetic at concentrations of 0.2%<sup>(3,8,9,13,14)</sup>.

In order to improve analgesia, epidural opioids can be added to ropivacaine utilizing the same doses used commonly when they are used with lidocaine or bupivacaine, 50 to 100 micrograms of fentanyl or 5 to 10 micrograms of sufentanyl mixed in a single syringe with local anesthetic for caesarean section. It is not necessary to add sodium bicarbonate or epinephrine to this local anesthetic for the reasons discussed below.

The Apgar and neurobehavioral evaluations of newborns whose mothers received epidural ropivacaine or bupivacaine had no significant difference in elective surgery where there is a severe fetal distress, scores were always high<sup>(3,8,9)</sup>.

The use of ropivacaine during pregnancy before term does not affect the development and growth of the fetus *in utero*. If it is used for obstetric anesthesia and analgesia in pregnancy at term does not produce negative effects on the future neonate. The excretion of ropivacaine in human breast milk has not been studied, however it is considered that the newborn, breastfed by a mother receiving ropivacaine in neuroaxial anesthesia, receives less local anesthetic as compared to anesthetic previously received *in utero* and therefore has no adverse effects<sup>(8,9)</sup>.

### SUBARACHNOID ROPIVACAINE FOR CESAREAN SECTION

This drug is one safe anesthetic due to the absence of preservatives in the commercial solution of ropivacaine and its physicochemical characteristics when it is injected into the

subarachnoid space. Moreover, it does not require that you add epinephrine, as produces a mild vasoconstrictor effect even in high concentrations<sup>(3,16)</sup>, the absence of epinephrine clearly distinguishes it from other local anesthetics because they cause vasodilation<sup>(3,17)</sup>. The acceptance of its use for intrathecal route was delayed by this somewhat unusual effect, causing decreased medullary blood flow without clinical repercussions, for fear that neurological damage is present. When it was shown that there is no reasons for concern and it has an even less neurotoxicity than other local anesthetics having an added vasoconstrictor, its approval was authorized.

In international literature reports presented here and which subarachnoid ropivacaine has been used for cesarean section, the used technique is the combined spinal-epidural anesthesia, by administering local anesthetics alone or with adjuvants first by intrathecal route through a No. 25 to 27 "pen tip" needle, leaving the epidural catheter only for administering booster doses or for postoperative analgesia.

The Khaw K.S. et al<sup>(18)</sup> study seems to be the first clinical report in which subarachnoid ropivacaine was administrated to pregnant women for caesarean section.

In another study by the same author, the dose of intrathecal local anesthetic was 25 mg (3.3 mL) isobarically as compared to 25 mg hyperbaric dose by adding 8.3% glucose.

The results obtained in this report<sup>(19)</sup> are shown in Table II, where it can be observed that hyperbaric subarachnoid ropivacaine has a lower latency and spread up to T4 was also faster, like the complete motor block, recovery up to L1 and full recovery. It also provides deeper and safe

**Table II.** Effects of subarachnoid isobaric and hyperbaric one for caesarean. (Elaborated by the authors with data taken from bibliographical citation 19).

Farmacologic effect	Hyperbaric ropivacaine	Isobaric ropivacaine
Dose	25 mg	25 mg
Latency	5 – 10 min.	10 – 15 min.
Diffusion even T4	7.7 min.	16.4 min.
Blockade motor complete	9.9 min.	13.8 min.
Recovery even L1	189 min.	215 min.
Complete recovery	190 min.	218 min.
Neurological toxicity	None	None
Apgar to the 5 minutes	≥ 7	≥ 7
Hemodynamic changes	Minimum	Minimum
Satisfactory anesthesia	100%	*75%

\* In 25% of cases there was insufficient analgesia.

anesthesia for this type of surgery in 100% of patients, while the isobaric ropivacaine requests booster doses of the epidural catheter in 25% of patients because there is less rostral spread. There are no neurologic complications in any case and Apgar levels in the neonates were equal to or greater than 7 with no difference between the two studied types of ropivacaine. In summary, hyperbaric ropivacaine produces a faster neuroaxial block with quicker recovery and no need for supplementation through peridural route as compared to isobaric ropivacaine which in some cases provides inadequate analgesia.

In other studies<sup>(20,21)</sup>, ropivacaine was compared with hyperbaric bupivacaine and levobupivacaine applied intrathecally for cesarean section with combined technique. In these studies was found that the minimum dose is 10.58 mg for the latter anesthetic, whereas for ropivacaine is 14.22 mg and that the power is from 1.34 to 1 for levobupivacaine. It is also accepted that the best concentration of ropivacaine by this route is 0.75% and the anesthetic/ analgesic effects are dose dependent with an ideal average between 15 and 22.5 mg (2 to 3 mL), in where the motor block is more intense if the concentration and dose used of the drug are higher. In the above dose and concentration, the latency is from 5 to 10 minutes with duration from 2 to 3 hours, and with postoperative analgesia it is up to 9 hours as compared to 5 hours provided by bupivacaine and levobupivacaine. Finally, in the following studies<sup>(2,21-23)</sup> it is concluded that the addition to the anesthetic solution of 10 µg of fentanyl or 2.5 to 5 µg of sufentanyl or 150 µg of morphine or dexmedetomidine, improves the quality of transoperative analgesia and prolongs it in the postoperative period without affecting the duration of motor block, as has been said, it has

a faster recovery as compared to preparations of 0.5% levobupivacaine and bupivacaine, which makes deambulation, urination, and oral fluid intake are more quickly initiated, these effects make it very attractive in obstetric-gynecologic surgery, particularly in the caesarean section and also in the short hospital stay.

## CONCLUSIONS

Ropivacaine is the first pure enantiomer-type local anesthetic, this characteristic gives it reduced cardiotoxicity and neurotoxicity as compared to bupivacaine. The advantages of not requiring vasopressors or preservatives and ability of combination with opioids make it highly recommended in obstetric analgesia and anesthesia. Thus it is suggested to begin clinical researches in Mexico; they must be applied neuroaxially primarily by subarachnoid route for caesarean section because there are not many reports on this aspect.

In the subarachnoid regional anesthesia for cesarean section is very important to use local anesthesia providing a longer duration of analgesic effect with minimal side effects and a low risk of toxicity for maternal-fetal binomial, ropivacaine seems to have this profile<sup>(18-24)</sup>.

In the reviewed studies, 0.75% or 7.5 mg / mL hyperbaric ropivacaine was more effective as intrathecal local anesthetic for cesarean section as compared to 0.5% levobupivacaine and bupivacaine and the same 0.75% isobaric ropivacaine, as hyperbaric ropivacaine provides most lasting residual analgesia and faster recovery of motor block and without significant hemodynamic or other disturbances.

## REFERENCES

1. Mexican Federation of Anesthesiology. Mexican Magazine of Anesthesiology. Free Papers from the XXXIX Mexican Congress of Anesthesiology. Puerto Vallarta City, Jalisco State. Mexico. (Supl) 2005;263-451.
2. Ávila LA, Chavéz JR. Spine anesthesia through 0.75% dexmedetomidine plus ropivacaine vs. 0.75% ropivacaine. *Rev Anest Méx (Supl)* 2005;439.
3. Whizar LVM, Carrada PS. Ropivacaine. A novel alternative in regional anesthesia. *Rev Mex Anest* 1999;22:122-52.
4. Wahedi W, Nolte H. Ropivacaine for spinal anaesthesia. *Reg Anaesth* 1993;18(Suppl):62.
5. Van Kleef JW, Veering B, Burm AG. Spinal anesthesia with ropivacaine: A double blind study on the efficacy and safety of 0.5% and 0.75% solution in patients undergoing minor lower limb surgery. *Anesth Analg* 1994;78:1125-30.
6. Marrón PM, Rivera FJ. Subarachnoid ropivacaine in caesarean section. *SMAGO Bulletin*. 2006;3:4-5
7. Gautier C, de Kock M, Van Steenberghe A, Poth N, Lahaye-Goffart B, Farnard L, Hody JL. Intrathecal ropivacaine for ambulatory surgery. A comparison between intrathecal ropivacaine for knee arthroscopy. *Anesthesiology* 1999;91:1239-1245.
8. Willie M. Intrathecal use of ropivacaine: A review. *Acta Anaesthesiol Belg* 2004;55:251-59.
9. Milligan KR. Recent advances in local anaesthetics for spinal anaesthesia. *Eur J Anaesthesiol* 2004;21:837-47.
10. Pitkanen M, Covino BG, Feldman HS, Arthur GR. Chronotropic and inotropic effects of ropivacaine, bupivacaine and lidocaine in the spontaneously beating and electrically paced isolated perfused rabbit heart. *Reg Anesth* 1992;17:183-192.
11. Scott DB, Lee AL, Fagan D, Bowler GMR, Bloomfield P, Lundh R. Acute toxicity of ropivacaine compared with that of bupivacaine. *Anesth Analg* 1989;69:563-569.
12. Silva-Ortiz H, Opalin-Guzmán L, Silva-Jiménez A, Castillo-Becerril G, Tenorio-Marañón R, Martínez-Segura T. Comparison between 0.75% intrathecal ropivacaine and 0.5% intrathecal bupivacaine in lower-extremity orthopedic surgery. *Rev Mex Anest* 2002;25:252-56.
13. González SJM, Cedillo MA, Cárdenas JJ, Gómez O. Ropivacaine vs. bupivacaine through spinal route. *Rev Mex Anest* 2001;24:217-20.



14. Torres GV, Torres HM. Epidural anesthesia by ropivacaine vs. bupivacaine for abdominal surgery in gynecological patients. *Rev Mex Anest* 2002;25:29-33.
15. Marrón PM. Neuraxial anesthesia adverse events. What should we do when they are present? *Rev Mex Anest* 2007;30 Supl. 1:S357-S375.
16. Lida H, Watanabe Y, Dori S, Ishiyama T. Direct effects of ropivacaine and bupivacaine on spinal pial vessels in canine. *Anesthesiology* 1997;87:5-81.
17. Dahl JB, Simonsen L, Mogensen T, Henriksen JH, Keheler H. The effect of 0.5% ropivacaine on epidural blood flow. *Acta Anaesthesiol Scand* 1990;34:308-310.
18. Khaw KS, Ngan Kee WO, Wong M, Liu JY, Chung R. Spinal ropivacaine for cesarean section: a dose finding study. *Anesthesiology* 2001;95:1346-50.
19. Khaw KS, Ngan Kee WO, Wong M, Ng F, Lee A. Spinal ropivacaine for cesarean delivery: a comparison of hyperbaric and plain solutions. *Anesth Analg* 2002;94:680-85.
20. Parpaglioni R, Frigo MG, Lemma A, Sebastiani M, Barbati G, Celleno D. Minimum local anaesthetic dose (MLAD) of intrathecal levobupivacaine and ropivacaine for caesarean section. *Anaesthesia* 2006;61:110-15.
21. Coppejans HC, Vercauteren MP. Low-dose combined spinal-epidural anesthesia for caesarean delivery: a comparison of three plain local anesthetics. *Acta Anaesthesiol Belg* 2006;57:39-43.
22. Sanli S, Yegin A, Kayacan N, Yilmaz M, Coskunfirat N, Karsli B. Effects of hyperbaric spinal ropivacaine for caesarean section: with or without fentanyl. *Eur J Anaesthesiol* 2005;22:457-61.
23. Ogun CO, Kirguiz EN, Duman A, Okesli A, Akyurek S. Comparison of intratecal isobaric bupivacaine-morphine and ropivacaine-morphine for caesarean delivery. *Br J Anaesth* 2003;90:659-64.
24. Puón GAMG, Torres AB, Gómez MJC. Effectiveness and safety of subarachnoid ropivacaine at different densities in caesarean section. *Rev. Anestesia en México* (Mexican Magazine of Anesthesiology). Memories from the XL Mexican Congress of Anesthesiology. Mérida City, Yucatán State, Mexico. 2006:158.
25. Villarejo DM. Pharmacology of local anesthetics. *Obstetric Anesthesia. El Manual Moderno* Ed. 2001;7:97-106.
26. Domech GA, García GGL. Ropivacaine vs. bupivacaine in epidural anesthesia for abdominal hysterectomy. *Cuban Magazine of Anesthesiology and Reanimation (Revista Cubana de Anestesiología y Reanimación)*. 2004;3:13-25.
27. Wiedemann D, Muhlrichel B, Staroske E, Neumann W, Rose W. Plasmatic ropivacaine concentrations during 120 hours of epidural infusion. *British Journal of Anaesthesia* 2000;85: 830-835.