

Ropivacaine versus Bupivacaine for Inter Scalene Block Clinical and Pharmacological Comparative Study

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Abstract :

Introduction : The interscalene approach to the brachial plexus for shoulder surgeries provides excellent anaesthesia with remarkable safety and minimal or no systemic disturbances.

Material and Methods : 60 adult patients ASA I-II undergoing elective shoulder surgery. Patients were randomly allocated into 3 groups. The patients received 20ml of either ropivacaine 1% GI (20 patients), ropivacaine 0.75% GII (20 patients) and bupivacaine 0.5% GIII (20 patients). Onset time of sensory and motor block, duration of analgesia and the need for supplementary analgesics were recorded. Pain was assessed by using VAPS. Haemodynamic parameters, oxygen saturation and respiratory rate were recorded. Unwanted side effects, cardiovascular, neurological, nausea and vomiting etc were recorded. Also, patients satisfaction were noted.

The pharmacological study was done on pentobarbitone cats to determine the effect of different doses of ropivacaine (0.35-2.8mg/kg) versus bupivacaine (0.5-4mg/kg) on arterial blood pressure, ECG and respiratory rate.

Results: The mean onset time of analgesia was faster in ropivacaine groups than bupivacaine group ($p < 0.005$). The studied groups were comparable regarding the duration of analgesia, motor and sensory block, cardiovascular and respiratory effects. The incidence of paraesthesia was more frequent in bupivacaine group than both ropivacaine groups (30% vs 10%) There was more patient satisfaction in ropivacaine groups than bupivacaine groups.

On the other hand the pharmacological study showed that ropivacaine had more less toxic effects on cardiovascular and respiratory systems.

Conclusion : This study concluded that interscalene block performed with either 0.75% or 1% ropivacaine allows for a prolonged postoperative pain relief similar to bupivacaine 0.5% with shorter onset time, more cardiovascular stability and higher patient satisfaction.

Introduction :

Interscalene brachial plexus block (ISB) is used to provide anaesthesia and analgesia for shoulder surgery. Single injection interscalene brachial plexus block is an effective anaesthetic; however it is limited by the duration of action of local anaesthetic. Bupivacaine and ropivacaine have been compared both at different an equal volumes and concentration for ISB. Kinnard and Lirette, (1996).

Bupivacaine is a long-acting local anaesthetic which has been reported to be associated with slower onset time for nerve blockade compared with other intermediate

duration anaesthesia especially when small volumes of anaesthetic are injected. Fanelli *et al.* (1999).

Ropivacaine is a new long acting local anaesthetic with smaller potential for systemic toxicity than bupivacaine. Markham and Faulds (1996), and useful clinical properties when used for peripheral nerve blocks. Fanelli *et al.* (1998).

Because of its long duration of action bupivacaine is frequently the local anaesthetic chosen for regional analgesia techniques. However lethal arrhythmias,

Ropivacaine versus Bupivacaine for.....

including cardiac arrest, can occur after accidental intravascular injection Coyle *et al.* (1994) and Antonio *et al.* (2000).

The new long acting, ropivacaine has been developed as safer alternatives to bupivacaine when large volumes and large concentration are used to establish upper and lower nerve blocks for surgical anaesthesia and during, continuous infusion for pain management. In vitro and vivo studies have demonstrated that ropivacaine has less potential for CNS and cardiovascular toxicity than bupivacaine. Pitkanen *et al.* (1992)

This study was conducted to compare clinical efficacy and safety of interscalene brachial plexus block with ropivacaine 0.75% or 1% versus bupivacaine 0.5% ; Also, some pharmacological studies on different doses of both Ropivacaine and bupivacaine.

Material and Methods :

Experimental Study :

The pharmacological study was done on anaesthetized intact cats to determine the effect of different doses of ropivacaine on mean arterial blood pressure, ECG and respiratory rate in comparison with bupivacaine. The staff of department of pharmacology university of Edinburgh (1970).

Drugs used :

1. Ropivacaine. (Naropin, Astra) ropivacaine hydrochloride
2. Bupivacaine (Marcaine, Astra) bupivacaine hydrochloride

Doses used in this work were calculated according to the method given by (Paget and Barnes, 1964).

Methods :

The Carotid Arterial blood pressure and ECG of phenobarbitone Anaesthetized cats.

Direct arterial blood pressure was recorded Sixteen cats of both sexes (wt 2-3 kg) eight in each group were used. Anaesthesia was induced by halothane inhalation and maintained with pentob-

arbitone (40mg/kg body wt IV). The left common carotid artery was exposed cannulated and connected to a mercury manometer provided with a lever writing on a moving drum of kymograph. The femoral vein on one side was cannulated and connected by means of rubber tube to a burette containing 0.9% saline solution. The drug was injected into the rubber tube as single doses was pushed into the circulation by 1ml saline. Heparin was given in a dose of 500 units/kg to prevent blood clotting. The electrodes of the ECG were connected to the limbs of the cat, Lead II tracing were recorded by Siemens cardiostat. The effect of different doses of ropivacaine (0.35-2.8mg/kg) and bupivacaine (0.5-4mg/kg) on arterial blood pressure and ECG (Lead II) of normal pentobarbitone anaesthetized cats was recorded. Also the respiratory rate was recorded on a drum.

Statistical analysis :

Data were presented as mean (SD) or number of percentage as indicated. Unpaired student's T test and Fisher's test comparison between groups $p < 0.05$ considered significant.

Patients and Methods :

Clinical study :

64 patients classified as ASA I and II physical status, age 23-50 years, scheduled for elective open shoulder surgery with interscalene brachial plexus block (ISB). Patients with history of neurologic pulmonary, moderate to severe, cardiovascular, hepatic, renal, psychiatric disease or failed block and induction of general anaesthesia, were excluded. After obtained an informed consent from patients, an 18 gauge IV cannula was inserted, standard monitors were placed including noninvasive mean arterial blood pressure (MAP), heart rate (HR), ECG, and pulse oximetry (Spo₂). Oxygen (5L/min) was provided for all patients through nasal cannula. Following the original approach described by Winnie, (1970), each patient was placed supine with his head turned away from the side to be blocked. The patient lift his head, the

posterior border of sterno-cleidomastoid muscle was palpated, postero-lateral to that border the interscalene groove was palpated between the anterior and middle scalene muscles. After ordinary sterile precautions and local skin infiltration with xylocaine 1%. The plexus located using a 23G insulated short bevel blunt needle (Braun Medical, Bethlehem, PA) and a nerve stimulator (Stimplex Dig RC) (B/Braun). The needle considered to be placed correctly when a contraction of deltoid and/or biceps muscles in response to stimuli of ≤ 0.5 mA, the metal needle was withdrawn leaving the cannula in place for injection of local anaesthetic. After aspiration to exclude intravascular placement the study drug solution was injected slowly. The patients were randomly allocated to receive ISB using one of the following drug solution:

Group I (20 patients) : 20 ml ropivacaine 1% or Group II (20 patients) : 20 ml ropivacaine 0.75% or Group III (20 patients) : 20 ml bupivacaine 0.5%.

Haemodynamic variable and pulse oximetry were recorded before block placement (base-line), then at 5,10,20 and 30 min after injection was completed. Further measurements were performed at 15min interval until adequate surgical anaesthesia had been achieved. The extent of motor and sensory block was evaluated every 5min until achieving readiness for surgery. Motor function was tested by asking the patient to contract separately the deltoid, biceps and triceps muscles against gravity, while the sensory block was assessed by using the pinprick test. The onset of surgical anaesthesia (readiness for surgery) was defined as the loss of pinprick sensation at the skin dermatomes involved in the surgical field (from C4-C7) with the inability to elevate the operated limb. The adequacy of the block was judged according to the need for supplementary I.V analgesics and sedation : adequate nerve block = no analgesic required to complete surgery; inadequate nerve block = need for additional I.V analgesic (fentanyl 0.1mg) to complete surgery; failed nerve block = general anaesthesia required to complete surgery. The mean onset time of surgical

blocks was recorded from the completion of local anaesthetic injection to surgical anaesthesia.

Postoperative analgesia consisted of ketoprofen 100mg I.V if required. The time lasting from block placement to first pain request was recorded. The occurrence of paresthesia in the tip of the fingers, and other neurological effects was recorded at 24h after ISB. Pain was assessed by using a 10cm VAPS (0cm = no pain; 10cm = worst pain). Unwanted side effects as hypotension and bradycardia (defined as a 20% decrease in relation to base line), neurological complication (pain, dysaesthesia, numbness) or central nervous system toxicity as (ringing in ear, convulsions), nausea, vomiting and respiratory depression (respiratory rate < 10 breaths/min).

At the end of surgery, the patients were transferred to PACU and reassessed to confirm motor and sensory blockade. Data were recorded at 1, 2, 4, 6, 12 and 24 hrs at PACU. and the total consumption of analgesic medication were noted. Patient satisfaction was evaluated 24hrs after surgery with 4 points score (1=poor, 2=moderate, 3=good, 4=excellent).

Statistical analysis: Data are presented as mean (SD) between group comparison were performed using the unpaired student's T test and the Mann-whitney U test for scores. Anova test for inter groups comparison. Categorical data were analyzed with chi-square test. A p value < 0.05 was considered significant.

Pharmacological Results :

I- Effect of different doses of Ropivacaine and bupivacaine on mean arterial blood pressure (MAP) of anaesthetized cats:

Ropivacaine (0.35 - 1.4mg/kg) produced significant rise in MAP. But the dose of 2.8mg/kg showed significant increase of MAP in 6 cats and slight hypotension in 2 cats (table1, Fig.1). On the other hand Bupivacaine 0.5mg/kg produced no significant change in MAP, while 1mg/kg produced no change in MAP in 5 cats and hypotension in the remaining 3 cats. As regards 2mg/kg bupivacaine it developed

hypotension in 5 cats and death of the rest. The survivors died from severe hypotension with a dose of 4mg/kg. (table1, Fig.2)

II- Effect of different doses of ropivacaine and bupivacaine on heart rate (HR) beats/min. of pentobarbitone anaesthetized cats.

No abnormality in ECG pattern was observed with ropivacaine in dose (0.35-0.70mg/kg). But slight bradycardia occur in a dose of 1.4mg/kg and significant bradycardia (2.8mg/kg). Table (2) Fig. (3).

Concerning the effect of bupivacaine on ECG, significant bradycardia occurred with 1-2mg/kg. The ECG changes were seen after 5min. from injection of 2mg/kg bupivacaine (Fig.4). These changes included depression of S-T segment widening of QRS, prolongation of PR interval and Finally cardiac arrest and death of 3 cats. The last dose 4mg/kg of bupivacaine was fatal to the remaining survivors cats. (Table2 ,Fig.4)

III- Effect of different doses of ropivacaine and bupivacaine on respiratory rate of pentobarbitone anaesthetized cats.

No abnormality in respiratory pattern was observed with ropivacaine apart from the decrease in respiratory rate occurring with the bigger doses of ropivacaine (1.4-2.8mg/kg). (Table3, Fig.5)

On the other hand bupivacaine showed decrease in respiratory rate with dose of 1 and 2mg/kg and respiration became deep and slow and finally ended by arrest and death of 3 cats. The bigger dose 4mg/kg was fatal to the rest of cats.(Table3, Fig.6).

Clinical Results :

4 patients were excluded from the study 2 patients in bupivacaine group and 2 patients in ropivacaine groups for failed to achieve surgical block and were given general anaesthesia. The success rate of interscalene was (60 of 64) 93.75%. there were no differences in age, weight, sex and duration of surgery, table (4).

The mean onset time of surgical block was more slowly significantly with bupiv-

acaine 0.5% (25±15min) than ropivacaine 0.75% (15±8min) (p=0.005) or ropivacaine 1% (10±5min) (p=0.0005). But there was no significant change in the onset time between the two ropivacaine groups (p>0.05) There was no intra-operative difference in the quality of blockade. Pain scores using VAPS were similar in the 3 groups (VAPS ≤ 3cm). The need for intra-operative analgesic supplementation (Fentanyl 0.1mg I.V) was noted in one patient in ropivacaine 1%, two patients in ropivacaine 0.75% and four patients in bupivacaine 0.5% group. No differences in the degree of pain measured at the 1st requirement for post-operative analgesic medication (6.2±1.5cm, 7.2±1.8 cm, and 7.3±1.6 cm after ropivacaine 1%, 0.75% and bupivacaine 0.5% respectively. The time from block placement to the 1st request for medication (block duration) was (11.7±2.5h, 10.7±2h, 10.9±3.6h) after ropivacaine 1%, 0.75% and bupivacaine 0.5%, respectively) Table (5). The amount of ketoprofen needed was similar between groups. As regard haemodynamic changes the study showed no differences between groups, except one patient developed bradycardia treated with atropine and another one patient developed hypotension treated with ephedrine and I.V fluids in bupivacaine group, but no cardio-vascular changes occurred in ropivacaine groups. Comparing these changes between the 3 groups revealed no significant differences. No clinically relevant changes was observed between groups as regard to respiratory rate and oxygen saturation throughout the study.

Specific side effects of interscalene block in the 3 groups were similar in the studied groups. But, the incidence of paraesthesia in the fingers was more frequent in bupivacaine group than both ropivacaine groups (30% vs 10%) (p<0.05). paraesthesia disappeared within 3 days. The incidence of other side effects were similar in the three groups. Table (6). patient satisfaction was high in both groups, but more significantly higher in ropivacaine groups than bupivacaine group. (p<0.05) (Table 7.)

Table (1): percent change in MAP (mm Hg) of anaesthetized cats in response to different doses of Ropivacaine and bupivacaine

	Ropivacaine mg/kg				Bupivacaine mg/kg			
	0.35	0.70	1.4	2.8	0.5	1.0	2.0	4.0
	% increase	% increase	% increase	% increase	% change	% change	% decrees	% decrees
Mean	3.28	6.86	9.73	10.82	2.36	2.16	20.11	
SD	0.63	0.80	0.92	0.95	0.91	1.39	0.73	
P	> 0.05	< 0.01	< 0.001	< 0.001	> 0.05	> 0.05	< 0.001	< 0.0001

P <0.05 = significant

Table (2) Percentage reduction in heart rate (HR) (beats/min) of pentobarbitone anaesthetized cats in response to different doses of ropivacaine and bupivacaine.

	Ropivacaine mg/kg				Bupivacaine mg/kg			
	0.35	0.70	1.40	2.80	0.5	1.0	2.0	4.0
Mean	2.02	3.12	8.92	10.67	4.89	9.48	15.82	
SD	1.82	1.95	2.35	2.67	2.08	4.62	5.92	
P value	>0.05	>0.05	<0.05	<0.01	<0.05	<0.01	<0.001*	**

* 3 cats out of 8 developed Cardiac arrest. ** All remaining 5 cats died. (bupivacaine group)

Table (3): Percentage reduction in respiratory rate (breaths/min) of pentobarbitone anaesthetized cats in response to different doses of Ropivacaine and Bupivacaine.

	Ropivacaine mg/kg				Bupivacaine mg/kg			
	0.35	0.70	1.4	2.8	0.5	1.0	2.0	4.0
Mean	3.02	4.16	8.86	12.76	6.14	13.72	20.12	
SD	1.15	1.18	2.42	2.25	1.21	1.83	2.73	
P value	>0.05	<0.05	<0.01	<0.001	<0.05	<0.01	<0.001*	**

* 3 cats out of 8 developed respiratory arrest and died.

** All remaining 5 cats died. In (bupivacaine group)

Table (4) : Demographic Data.

	G I	G II	GIII
	Ropivacaine 1%	Ropivacaine 0.75%	Bupivacaine 0.5%
Number	20	20	20
Age	31(±11)	33(±12)	35(±10)
Sex(M/f)	13/7	12/8	11/9
Duration (min.)	156 (±17)	146(±18)	150(±16)

Values as Mean (SD)

F=Female

M=Male

Ropivacaine versus Bupivacaine for.....

Table (5) : Onset time,Block duration and VAPS at 1st analgesic request..

	Ropivacaine 1% G 1	Ropivacaine 0.75% G11	Bupivacaine 0.5% G111
Mean onset time (min)	10 (± 5)	15 (± 8)	* 25 (± 15)
Block duration (h)	11.7 (± 2.5)	10.7 (± 2)	10.9 (± 3.6)
VAPS at 1 st analgesic request (cn)	6.2 (± 1.5)	7.2 (± 108)	7.3 (± 1.6)

Values as mean (± SD)
h= hours

*P<0.005 = significant
VAPS = Visual analogue painscale.

Table (6) : Side effects in the studied groups.

	Ropivacaine 1%	Ropivacaine 0.75%	Bupivacaine 0.5%
Paraesthesia of fingers	1(5%)	1(5%)	6(30%)
Cardiovascular	0(0%)	0(0%)	2(10%)
Nausea	1(5%)	1(5%)	2(10%)
Vomiting	1(5%)	1(5%)	1(5%)
Dizziness	1(5%)	1(5%)	1(5%)
Respiratory	0(0%)	0(0%)	0(0%)

Data are presented as a number (%)

Table (7) patient satisfaction.

	Ropivacaine 1%	Ropivacaine 0.75%	Bupivacaine 0.5%
Excellent	16(80%)	15(75%)	10(50%)
Good	3(15%)	3(15%)	5(25%)
Moderate	1(5%)	2(10%)	5(25%)
Poor	0	0	0

Data are presented as a number (%)

p<0.05= significant

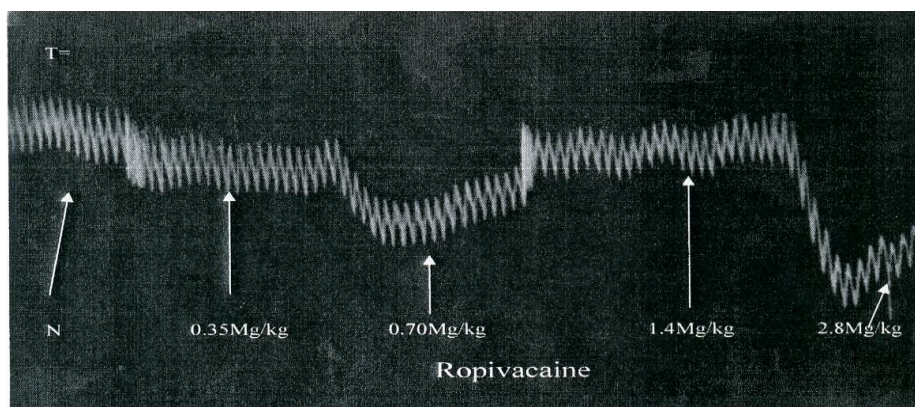


Fig.(1) Effect of ropivacaine on mean arterial blood pressure of normal anaesthetized cats

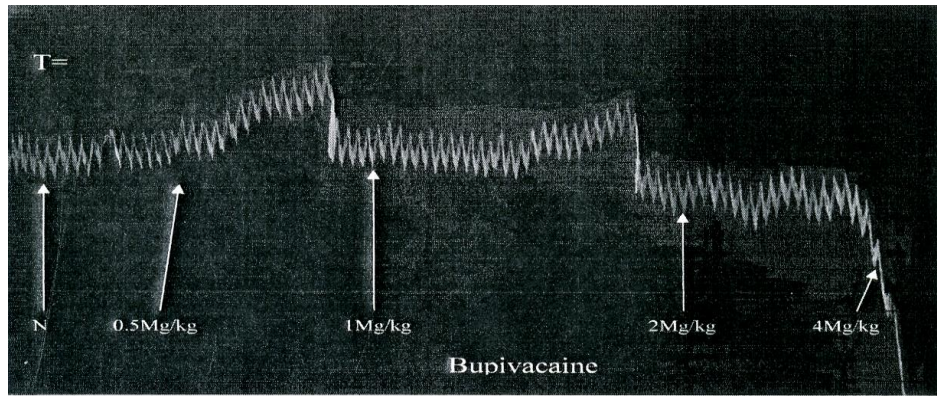


Fig.(2) Effect of bupivacaine on mean arterial blood pressure of normal anaesthetized cats

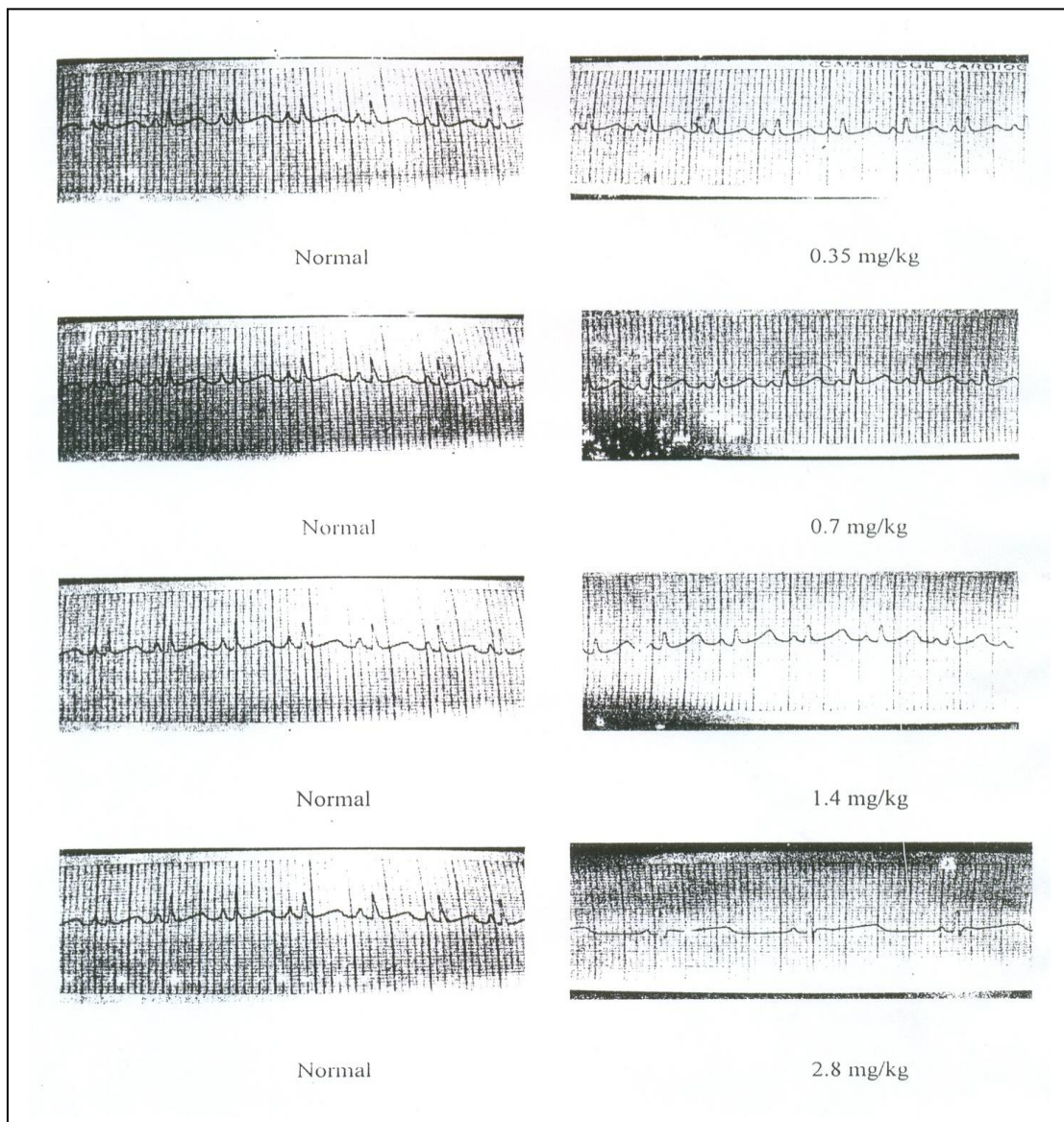


Fig.(3) Effect of ropivacaine on ECG rate and pattern of anaesthetized cats .

Ropivacaine versus Bupivacaine for.....

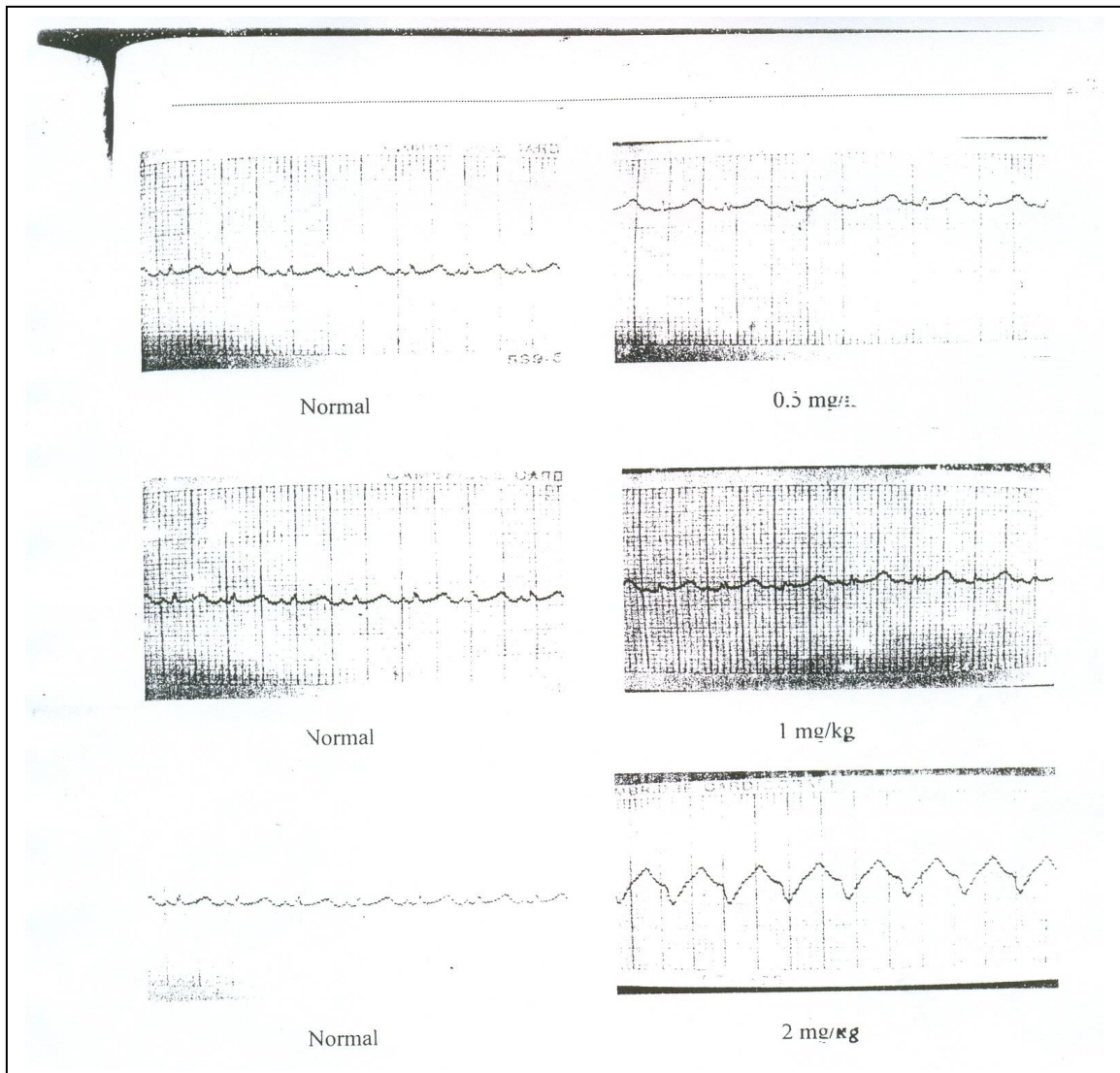


Fig.(4) Effect of bupivacaine on ECG rate and pattern of anesthetized cats .

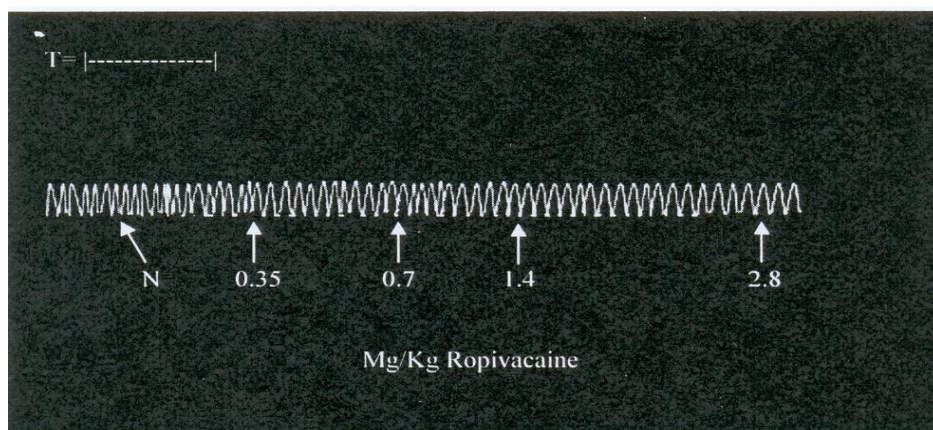


Fig.(5) Effect of ropivacaine on respiratory rate of normal anaesthetized cats

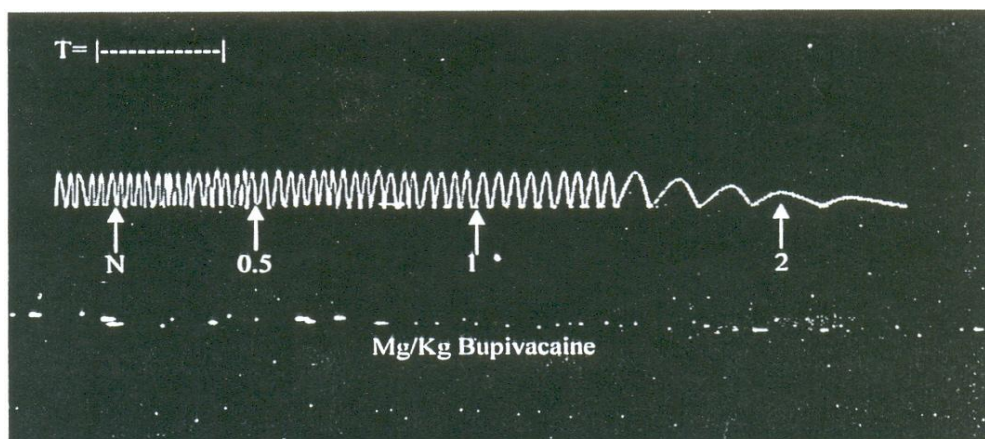


Fig.(6) Effect of bupivacaine on respiratory rate of normal anesthetized cats

Discussion

Interscalene brachial plexus block (ISB) is used to provide anaesthesia and analgesia for shoulder surgery. Casti *et al.* (2003). Bupivacaine and ropivacaine have been compared both at equal volumes and different concentrations for ISB. (Hofmann-kiefer *et al.*, 2002).

The experimental study: On mean arterial blood pressure (MAP) and ECG of pentobarbitone-anaesthetized cats ropivacaine (0.35-2.8mg/kg) exerted a significant increase in MAP. ECG records showed no change in HR and rhythm in low ropivacaine doses but higher doses (1.4-2.8mg/kg) showed slight decrease in HR. without abnormalities in ECG pattern. In contrast, bupivacaine elicited varied pattern of MAP. 0.5-1mg/kg of the drug had no significant change on MAP. But, 2mg/kg of bupivacaine exerted significant hypotension in 5 cats and death of the remaining cats. All survivors died after a dose of 4mg/kg of bupivacaine. Also, the ECG study revealed that bupivacaine at dose of 0.5mg/kg had no significant change. While, the other doses (1-2 and 4mg/kg) showed significant decrease in HR. The ECG change in the form of prolongation of PR interval, widening of QRS, flattening ST segment appeared 5min from injection of large dose of bupivacaine (2-4mg/kg) these changes ended by heart block and cardiac arrest.

In conformity with the previous results, the result of Bariskaner *et al.* (2003) who indicated that ropivacaine produced vasoconstriction of human umbilical artery

while bupivacaine produced vasodilation. The rate of injection and rapidity with which a particular blood level is achieved will influence the toxicity of local anaesthetics (Dony *et al.*, 2000). If the blood level of local anaesthetic is excessively elevated cardiovascular depression occurs that is related to its depressant effect on myocardial contractility, heart rate and conductivity as well as vasodilator action. (Mc Cartney *et al.*, 2003).

Ohmura *et al.* (2001) revealed that the occurrence of cardiovascular toxicity and changes in ECG pattern is mostly less in ropivacaine compared with bupivacaine. Also, Groban *et al.* (2001) stated that bupivacaine is less vasoconstrictor than ropivacaine.

Also, our study showed no abnormality in respiratory pattern was observed with ropivacaine apart from decrease in rate with bigger doses. But, bupivacaine produced more decrease in respiratory rate, then respiration became deep and slow and finally arrested with bigger doses. This is similar to the results of Ohmura *et al.* (2001). Who stated that bupivacaine had more toxic effect on respiration than ropivacaine in bigger doses.

In this clinical study the success rate of ISB was 93.75%. This result is similar to the result of Fanelli *et al.* (1999) who reported that the success rate of ISB was 94% for shoulder surgery and Hofmann-Kieferk *et al.* (2002) who reported effective ISB in 85% of blocks using either

Ropivacaine versus Bupivacaine for.....

ropivacaine 0.75% or bupivacaine 0.5% for shoulder surgery.

The current study showed faster onset time of surgical block in both ropivacaine groups (1% and 0.75%) than bupivacaine 0.5% group. This is in agreement with Casati *et al.* (1999) and Wang *et al.* (2001). On the other hand Casati *et al.* (2000) Found that both ropivacaine and bupivacaine at different volumes had similar onset time to surgical anaesthesia.

The need for intra-operative analgesic supplementation, and the amount of ketoprofen rescue were similar in the 3 groups. These results are in accordance with the result of Klein *et al.* (1998) who compared bupivacaine 0.5% and ropivacaine 0.5%, 0.75%.

Pain scores were similar in ropivacaine 1%, 0.75% and bupivacaine 0.5% groups. Also, no differences in pain scores at 1st request for post operative analgesic medication and block duration time in the 3 groups. Similar results were reported by Ekatothramis *et al.* (2003) when they compared ropivacaine and bupivacaine for analgesia with ISB after shoulder surgery.

The haemodynamic changes were comparable in the 3 groups. Only one patient developed bradycardia and another one developed hypotension in bupivacaine group. This result is in agreement with Kampe *et al.* (2004) who noted that both ropivacaine and bupivacaine had similar cardiovascular effects. Also, the study showed no abnormality in respiratory rate or oxygen saturation between the studied groups, as reported by De Negri *et al.* (2004) who revealed that there was no difference as regard respiratory rate, tidal volume or oxygen saturation after they compared 1%, 0.75% ropivacaine with 0.5% bupivacaine.

Ropivacaine seems to be superior over bupivacaine for regional blocks in which the risk for inadvertent intravascular injection exists due to its lower potential for cardiovascular and central nervous system toxicity. Wang *et al.* (2001).

The incidence of paraesthesia was frequent in the bupivacaine group than both ropivacaine groups (30% vs 10%). This

results is coincide with Borgeat *et al.* (2001), who noted that paraesthesia was more frequent in bupivacaine than ropivacaine. The other side effects were similar and low in the studied groups, as reported by Eroglu *et al.* (2004).

As regard to patient satisfaction the study showed that patients in ropivacaine groups more satisfied than in bupivacaine group (80% vs 50%) ($p < 0.05$). Similar results showed by Rawal *et al.*, (2002) and Eroglu *et al.* (2004).

In conclusion this study demonstrated that 20ml of ropivacaine 1% or 0.75% are suitable for interscalene block for shoulder surgery providing intra and post operative pain relief similar to that produced by bupivacaine 0.5% but with faster onset time, less paraesthesia and high patient satisfaction.

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التخدير الموضعي للضفيرة العصبية لجراحات الكتف باستخدام عقار
الروببفاكين مقارنة بالبيوببفاكين دراسة إكلينيكية وفارماكولوجية
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**

إن التخدير الموضعي للضفيرة العصبية للطرف العلوي لإجراء جراحات الكتف
يوفر تخدير ممتاز مع درجة عالية من الأمان للمريض مع تلاشي احتمال حدوث أعراض
جانبيه.

أجري هذا البحث على 60 من المرضى الأصحاء من الجنسين تم تقسيمهم عشوائياً
إلى ثلاث مجموعات 20 مريض في كل مجموعة.
في المجموعة الأولى تم حقن 20 ملل روببفاكين 1% في المجموعة الثانية تم حقن
20 ملل روببفاكين 0.75% أما في المجموعة الثالثة تم حقن 20 ملل بيوببفاكين 0.5% قمنا
بقياس وتسجيل الوقت اللازم لبدء التأثير الحركي والحسي على بدء الجراحة ومدة التخدير
ومدى الاحتياج لمسكنات اضافية أو الحاجة إلى مخدر عام, وكذلك تم ملاحظة وتسجيل أي
تغييرات في الدورة الدموية والتنفس وأي مضاعفات ودرجة ارتياح المريض في كل
مجموعة.

أما الدراسة الفارماكولوجية أجريت على 16 قطة مخدرة بالبنتوباربيتون لتحديد
الآثار الجانبية للجرعات المختلفة من الروببفاكين (0.35 - 2.8 مجم لكل كجم) بالمقارنة
مع البيوببفاكين (0.5 - 4 مجم لكل كجم) وتأثيرهم على ضغط الدم ورسم القلب الكهربائي
ومعدل التنفس.

ولقد أثبتت الدراسة أن الروببفاكين أعطى تأثيراً أسرع وحقق درجة ارتياح أعلى بين
المرضى أكثر من البيوببفاكين الذي سبب تنميل في أطراف الأصابع أعلى من الروببفاكين
وأوضحت الدراسة أيضاً قلة تأثير عقار الروببفاكين على الدورة الدموية والتنفس مقارنة
بعقار البيوببفاكين.