Original Research Article

DOI: http://dx.doi.org/10.18203/2349-2902.isj20201844

Comparison between two mixtures of lidocaine and bupivacaine for infraclavicular block: a double blind randomized trial

El Kaissi Jaber^{1,3}*, El Moqaddem Amine^{2,3}, Khalil Mounir^{1,3}, Kechna Hicham^{1,3}, Hachimi Moulay Ahmed^{1,3}, Laoutid Jaouad^{1,3}

¹Anesthesiology and Intensive Care Department, ²Department of Emergency, Moulay Ismail Military Hospital, Meknes, Morocco

Received: 16 January 2020 Revised: 15 March 2020 Accepted: 18 March 2020

*Correspondence: Dr. El Kaissi Jaber,

E-mail: dr.jaber109@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: We compare the two mixtures in terms of efficiency, analgesia, and side effects.

Methods: 30 patients scheduled for upper limb surgery were randomized in 2 groups. the group A received a mixture of 50% lidocaine 2% and 50% of bupivacaine 0.5% the group B received a mixture of 75% lidocaine 1% and 25% of bupivacaine 0.5%. Volumes, block onset times, blocks duration times, analgesia, and toxicity were compared.

Results: The volumes were equals in both groups. Sensory block onset was 5.43 min in the group A versus 6.73 min in the group B, motor block onset was 11.93 for the group A versus 13.46 min for the group B. Sensory block duration was 5.48 hours in the group A versus 4.05 hours for the group B (p=0.037), motor block duration was 7.75 hours for group A versus 5.50 hours for group B (p=0.014). Analgesia levels are equals between the two groups, there was no side effects listed.

Conclusions: The use of low concentrated lidocaine and bupivacaine mixture induces an adequate anaesthesia and decreases the duration of motor block with a reduced level of pain and an equal level of analgesia.

Keywords: Analgesia, Local anaesthetics, Nerve block

INTRODUCTION

Peripheral nerve blocks present actually many advantages, they allow to ensure a good management of the airway when used instead of general anesthesia, they also have an action over pain control and inflammatory reaction to the aggression represented by the surgical act.

For a long while, to perform peripheral nerve blocks, bupivacaine was used alone, that arises, in addition of toxicity, a problem of long block onset, and long block duration; we need about 30 to 40 min to have a sensory block and it may last 15 to 20 hours, in the other hand with lidocaine alone analgesia duration doesn't exceed 3 hours and the onset is about 14 to 15 min.^{1,2}

None of all local anesthetics used in daily practice make possible to have both, a rapid block onset and a long block duration; mixtures have been proposed as a solution, but their use has led to a controversy.

Adding lidocaine to bupivacaine allowed to combine fast block onset of lidocaine to long block duration of bupivacaine.³

We compare in this study two mixtures of lidocaine and bupivacaine in infraclavicular block with monostimulation in terms of efficiency and side effects, to demonstrate how realizing the block with low concentrated mixture could be efficient with a safe use.

³Faculty of Medicine, Sidi Mohamed Ben Abdellah University, Fes, Morocco

METHODS

Setting and design

It's about a prospective randomized double blind trial comparing two mixtures of lidocaine and bupivacaine in two groups. The first group has received 50% of lidocaine 2% and 50% of bupivacaine 0.5% mixture. The second has received 75% of lidocaine 1% and 25% of bupivacaine 0.5% mixture.

The trial has been achieved in the military hospital of Meknes, anesthesiology department; in morocco from October 2017 to March 2018.

Patients and procedures

After approval of the ethics committee of hospital and written informed consent from the patients, we have included in present study patients between 18-75 undergoing: hand, forearm, elbow, inferior third of arm surgeries with ASA (drug caution code) physical status from I to III.

Patients refusing regional anesthesia and those undergoing two upper arm thirds, patients with allergy to local anesthetics or with altered coagulation, patients with infection at the site of injection, patients with cardiac conduction troubles, with non-controlled epilepsia or any other neurological disease were excluded. Conversion into general anesthesia automatically excludes the patient.

Patients were randomized by random draw with boxes containing sealed envelopes. Mixtures were prepared by anesthesiologist not participating neither in realization of block nor in data collection.

Two mixtures were prepared i.e., mixture A with 20 ml of lidocaine 2% added to 20 ml of bupivacaine 0.5% and mixture B with 30 ml of lidocaine 1% added to 10 ml of bupivacaine 0.5%

The collect of data was realized by anesthesiologist not participating neither in realization neither in randomization.

All the patients received after routine monitoring a premedication with midazolam 0.05 mg/kg.

The infraclavicular block was realized in supine position, head turned to the opposite side of injection, elbow flexed to 90°, forearm in pronation, hand posed on the chest.

After sterilization and local anesthesia, the injection site was selected in the deltopectoral groove 2 cm inside, 2 cm down the coracoid process.

The injection was realized after distal radial response in 0.3-0.5 mA after aspiration test.

Duration of realization was noted. Sensitive blockade was evaluated with cold test and motor blockade was evaluated in different distal nerves territories: radial, ulnar, median, and musculocutaneous nerve.

Blocks onset time, complications, blocks duration, pain level evaluated by visual analog scale were noted.

All data were collected in a report sheet and analyzed using SPSS statistical program, the significance level was determined as p=0.05.

Quality variables are expressed with rates and quantity variables are reported with means±standard deviation.

RESULTS

30 patients were enrolled in the trial and randomized in two groups A (n=15) and B (n=15). The anthropometric data, the ASA (drug caution code) status were comparable in both groups (Table 1).

Table 1: Anthropometric data of patients (n=15).

	Group A	Group B	
Age (years)	33.33±18.37	34.93±17.82	
Height (cm)	170.66±11.13	172±11.34	
Weight (kg)	76.80±17.07	75.86±17.80	
Sex (M/F)	11/4	10/5	
ASA statute	ASA I=86%	ASA I=80%	
	ASA II=14%	ASA II=20%	

Table 2: Block characteristics.

	Group A	Group B	P value
Realization time (min)	12.53±4.61	12.13±6.16	0.45
Injected volume (ml)	25.33±7.18	24.66±6.11	0.878
Sensory block onset (min)	5.43±2.43	6.73±3.17	0.24
Motor block onset (min)	11 .93±13.87	13.46±6	0.11
Duration of sensory block	5.84±2.40	4.05±2.06	0.037
Duration of motor block (hours)	7.57±2.59	5.50±1.84	0.014

Injected volume was 25.33 ± 7.18 in group A, 24.66 ± 6.11 in group B (p=0,878). Sensory bloc onset was 5.43 ± 2.43 min in group A and 6.73 ± 3.16 min in group B (p=0.24). Motor block onset was 11.93 ± 13.87 min in group A, and 13.46 ± 6 min in group B (p=0.11). The sensory block lasts 5.84 ± 2.40 hours in group A and 4.05 ± 2.06 hours in group B (p=0.037). Motor block offset happens after 7.57 ± 2.59 hours in group A and after 5.50 ± 1.84 hours in group B (p=0.014) (Table 2). There was no side effects and pain levels were comparable in both groups with visual analog

scale level not exceeding 4 in both groups, only paracetamol and non-steroidal anti-inflammatory drugs were necessary to control pain.

DISCUSSION

The rise that has known regional anesthesia was accompanied by an alarming observation. Many cardiac and neurological effects were reported and published; the potential toxicity of local anesthetic drugs was clear shortly after the first use of cocaine.⁴

Interest over local anesthetics toxicity increased with bupivacaine that has an elevated cardiac toxic potential and a narrow therapeutic window that may led to devastating consequences. Facing this situation, a need to develop safer regional anesthesia practices was evident; developing first recommendations about good use: slow and fractioned injections, aspiration test, use of adrenaline, then to limit doses of drugs, in this context had appeared the mixtures ideas. The theoretical benefit of use of local anesthetics is to decrease toxicity by reducing the dose of each local anesthetic used. However those associations harmlessness have never been demonstrated. In fact there is an addictive toxicity of each drug in the mixture. Many studies bring new items about that.⁵

Local anesthetics are weak bases present in plasma in 2 forms: freely circulating, which is the toxic form or bound to plasmatic proteins, albumin and more preferentially alpha acid glycoprotein which is rapidly saturated, so consequently the free fraction is increasing and leads to toxicity.⁶

Moreover, Cuvillon affirms that this saturation mechanism is amplified with mixture. Local anesthetics have a different affinity levels to alpha acid glycoprotein; this one fixes bupivacaine and ropivacaine more than lidocaine so practically free fraction of lidocaine would be more important and more toxic in consequence.⁷

Animal studies show some opposing results. Clarckson et al have demonstrated that there is a dose-dependent and stimulation frequency dependent competition of local anesthetics about cardiac sodium channels; lidocaine has a more rapid fixation kinetics than bupivacaine, in consequence lidocaine would fix more to sodium channels for low concentrations an low stimulations, this effect is not seen with bupivacaine even with increasing concentrations, so adding lidocaine to bupivacaine would minimize bupivacaine, which is more cardiotoxic than lidocaine, block of heart sodium channels; the mixture would be much safer according to this.⁸

Daos et al have demonstrated the opposite, they have compared impact of mixtures on cardiac toxicity, they found that mixing tetracaine with procaine, chloroprocain, mepivacaine or lidocaine reduces time to have cardiac arrest; a reduction that may arrive to 75 per cent.9

Lefrant et al have analyzed effects of increasing doses of lidocaine, bupivacaine, and mixture of both in the same posology on pigs. This study have revealed that mixture would have a protector effect concerning electrophysiological parameters (QRS interval, AH interval, HV interval), in the opposite it has a deleterious effect on hemodynamic parameters (inotropism, heart flow). Those authors have demonstrated in the same model a double effect that would make difficult to recommend to use mixtures or not.

Concerning neurological effects, studies have found opposite results, Munson and al have realized electroencephalographs while injecting, slowly then in bolus, mixtures of lidocaine-etidocaine and lidocaine-tetracaine to monkeys. They found that in the same posology mixture have the same epileptic potential as the anesthetics used alone.¹¹

De Jong et al have determined the convulsive dose and the lethal dose of lidocaine, chloroprocaine and bupivacaine and their mixtures, they found that mixtures are not more convulsivant that drugs used alone.¹²

Spiegel et al concluded the same thing, by injecting lidocaine, bupivacaine, and mixture of both to mice. 13

Cuvillon reconsidered the interest of mixture in his double blind randomized trial. He realized femoral and sciatic block with bupivacaine, ropivacaine, and mixture of both in 50:50 proportion with lidocaine, then he has determined C_{max} and T_{max} of the two drugs when used alone and in mixture. ¹⁴

If in this study the mixture shows real advantage in block onset and offset comparing to pure solutions, the potential toxicity leads to controversy.

Cuvillon has found that bupivacaine C_{max} was higher in group bupivacaine alone (1095 ng/l) compared to mixture group (450 ng/l) but addition of a lidocaine concentration with C_{max} =2650 ng/l in this group with a comparable T_{max} between lidocaine and bupivacaine leads to more toxicity.

Reniken reported a sudden cardiac arrest of 97 kg young adult patient who received 360 mg of lidocaine with adrenaline and 150 mg ropivacaine in a mixture for interscalenic block realization with neurostimulation. Those posologies represent respectively 53% and 52% of the maximal recommended posology for the first injection which are 3 mg/kg for ropivacaine and 7 mg/kg for lidocaine. We note here that the use of adrenaline didn't prevent this incident.¹⁵

The use of mixtures stays polemical and in this passionate debate we have to mark that in present study

we didn't note any side effect neither in the concentrate mixture nor in the low concentrated one.

If the mixture allows us to decrease concentrations with a potential additional toxicity which needs to be demonstrated on more representive samples, it gives us the advantage of using a short-term action Local anesthetic with a long-term action one in the reduced onset and the extended duration of block.

In term of efficiency, the two mixtures have allowed realization on an adequate anesthesia for all patients.

In present study sensory block onset was about 5.43 ± 2.43 min in the A group and 6.73 ± 3.17 in B group (p=0.24), and the offset was about 5.84 ± 2.40 hours in the A group and 4.05 ± 2.06 in B group (p=0.037).

Ozmen et al have mixed equal proportions of lidocaine 2% and bupivacaine 0.5% for sagittal infraclavicular block which was the same mixture used in our A group; sensory block onset time was about 4.4 min and a the block duration was 6.1 hours with an injected volume of 20 ml instead of 25 ml used in our trial those results are nearly equals to ours, then they have compared the results to lidocaine and bupivacaine used alone. They concluded that mixture may be a good alternative because it decreases block onset time: 4.4 min for lidocaine alone and 9.7 min for bupvacaine; and it prolongs postoperative analgesia requirement time 2.6 hours for lidocaine alone and 4.2 hours for bupivacaine alone. ¹⁶

Nishiyama has compared the realization of the intescalenic block with mixtures of bupivacaine 0.5% and bupivacaine 0.25% with lidocaine 1% in equal proportions with an injected volume of 30 ml, he found that the sensory block onset was about 11 min in bupivacaine 0.25% group and 10 min in the bupivacaine 0.5% group and the block duration was 4.5 hours in bupivacaine 0.25% group to 6 hours in bupivacaine 0.5% group. Decreasing concentration of bupivacaine reduced the sensory block duration. To in present study we have decreased both bupivacaine and lidocaine doses, the duration of sensory block decreased but we still had an adequate anesthesia.

Duncan et al have used equal proportions mixture of lidocaine 2% and bupivacaine 0.5% for supraclavicular block realization, posologies were determined by weight and toxic limits were respected; sensory block onset was 5.90 min and lasts 6.68 hours.¹⁸

In present study sensory block onset time was comparable between the two groups but the block duration was reduced in the B group; and this with a comparable pain levels which was not important. This observation joins the result of Cuvillon in his study, in fact he found a comparable pain levels between all groups.

So using low concentrated local anesthetics solutions allowed us to have an adequate anesthesia with reduced analgesia time without real impact on pain level which stays satisfying.

Literature hasn't given the same importance to motor blockade as the sensory one, nevertheless a long lasting motor blockade would be unwanted by patients. In present study motor block lasts 7.57 ± 2.59 hours in the A group and lasts 5.50 hours in the B group (p=0.011); by decreasing concentrations we reduced the duration of motor block which would be source of discomfort for our patients.

In total we have decreased the concentration of lidocaine by quarter and bupivacaine by half between groups A and B, with comparable volumes injected, low concentration mixture allowed the realization of satisfying surgery without any problems and with efficient analgesia and with reduced motor blockade duration; the security on the use would be an argument but leads to controversy and needs to be demonstrated on more important samples.

CONCLUSION

Local anesthetics systemic toxicity may be fatal, so the prevention is the key word, precautions and good practice rules should be respected to avoid such tragic events. Mixtures decreased administrated posologies and gives advantages in block onset time and duration but additional toxicity make this choice polemical. Low concentrated mixture allowed us to have adequate anesthesia with no side effect, the security of use must be demonstrated on more important samples.

ACKNOWLEDGEMENTS

I want to express my deepest gratitude to Professor Laoutid Jaouad for being a constant source of encouragement and for his perpetual support, and I want to express my highest respect to Professor Hachimi in recognition of his valuable guidance.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

Institutional Ethics Committee

REFERENCES

- 1. Bromage PR, Gertel M. improved brachial plexus blockade with bupivacaine hydrochloride and carbonated lidocaine. Anesthesiology. 1972;36(5):479-87.
- Cuvillon P, Zoric L, Ripart J. Comment je gère la durée d'un bloc (dose, concentration, cathéter). Mise au point en anesthésie réanimation. 2011: 83-92.

- 3. pour la Pratique Clinique R. Blocs périphériques des membres chez l'adulte. Paris, SFAR. 2003;22:567-81.
- 4. Vasques F, Behr AU, Weinberg G, Ori C, Di Gregorio G. A review of local anesthetic systemic toxicity cases since publication of the American society of regional anaesthesia recommendations: to whom it may concern. Reg Anesth Pain Med. 2015;40:698-705.
- Choi J, Gadsden J. Local anaesthetic mixtures for peripheral nerve blocks. In: Hadzic A, ed. Hadzic's textbook of regional anaesthesia and acute pain management. Mcgraw hill; 2017.
- Beloeil H, Mazoit JX. Pharmacologie des anesthésiques locaux. EMC (Elsevier Masson SAS, Paris), Anesthésie-Réanimation. 2010;36:320-A-10.
- 7. Cuvillon P, Boisson C, Ripart J. Il ne faut plus mélanger les anesthésiques locaux pour faire des blocs. Le praticien en anesthésie réanimation: 2012;16(2):71-3.
- 8. Clarkson CW, Hondeghem LM. Evidence for a specific receptor site for lidocaine, quinidine, and bupivacaine associated with cardiac sodium channels in guinea pig ventricular myocardium. Circ Res 1985;56:496-506.
- 9. Daos F, Lopez L, Virtue R. Local anaesthetic toxicity modified by oxygen- and by combination of agents. Anesthesiology. 1962;23:755-61.
- Lefrant JY, Muller L, de La Coussaye JE, Lalourcey L, Ripart J, Peray PA, et al. Hemodynamic and cardiac electrophysiologic effects of lidocainebupivacaine mixture in anesthetized and ventilated piglets. Anesthesiology. 2003;98:96-103.
- 11. Munson E, Paul W, Embro W. Central nervous toxicity of local anesthesic mixtures in monkeys. Anesthesiology. 1977,46:179-83.
- 12. De Jong R, Bonin J. Mixtures of local anaesthetics are no more toxic than the parent drugs. Anesthesiology. 1981;54:177-81.

- 13. Spiegel D, Dexter F, Warner DS, Baker MT, Todd MM. Central nervous system toxicity of local anesthetic mixtures in the rat. Anesth Analg. 1992;75:922-8.
- 14. Cuvillon P, Nouvellon E, Ripart J, Boyer JC, Dehour L, Mahamat A, et al. A comparison of the pharmacodynamics and pharmacokinetics of bupivacaine, ropivacaine (with epinephrine) and their equal volume mixtures with lidocaine used for femoral and sciatic nerve blocks: a double-blind randomized study. Anesth Analg. 2009;108:641-9.
- Reinikainen M, Hedman A, Pelkonen O, Ruokonen E. Cardiac arrest after interscalene brachial plexus block with ropivacaine and lidocaine. Acta Anaesthesiol Scandinav. 2003;47:904-6.
- Ozmen O, Alici HA, CeLiK M, Dostbil A, Cesur M. Effect of addition of lidocaine to bupivacaine on anaesthesia beginning time, block time, and block quality in lateral sagittal infraclavicular block. Turk J Med Sci. 2013;43:542-7.
- 17. Nishiyama T. Comparison of the motor and sensory block by ropivacaine and bupivacaine in combination with lidocaine in interscalene block. Med Arch. 2012;66(5):315-7.
- 18. Duncan M, Shetti AN, Tripathy DK, Roshansingh D, Krishnaveni N. A comparative study of nerve stimulator versus ultrasound-guided supraclavicular brachial plexus block. Anesth Essays Res. 2013;7:359-64.

Cite this article as: Jaber EK, Amine EM, Mounir K, Hicham K, Ahmed HM, Jaouad L. Comparison between two mixtures of lidocaine and bupivacaine for infraclavicular block: a double blind randomized trial. Int Surg J 2020;7:1342-6.