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SCIENTIFIC ARTICLE

Efficiency of levobupivacaine and bupivacaine for supraclavicular block: a randomized double-blind comparative study

Cenk Ilham, Elif Bombaci, Serhan Yurtlu*, Serhan Çolakoğlu

Dr. Lütfi Kırdar Research and Education Hospital, Istanbul, Turkey

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Abstract
Background and objectives: Success rate of catheter applications is low in supraclavicular block. Thus, bupivacaine and levobupivacaine become important with their long effect time in single injection practices. In this study, we aimed to compare the effectiveness, side effects and complications of bupivacaine and levobupivacaine in supraclavicular block.
Methods: Sixty patients aged between 20 and 65, with body weight between 50 and 100 kg, in the ASA I-II-III group who were scheduled for hand, forearm and arm surgery using supraclavicular block were randomized into two groups of 30. The patients received 30 ml 0.5% bupivacaine (Group B) or 30 ml 0.5% levobupivacaine (Group L). Motor and sensory blocks were evaluated. Motor and sensory block onset times, total block durations, postoperative pain, amount of postoperative analgesic used and patient satisfaction were recorded.
Results: Demographic data, distribution of surgical area and hemodynamic data were similar between the two groups. Surgery, motor and sensory block durations of Group B and L patients did not vary statistically significantly. However, motor and sensory block onset times in Group B were significantly shorter than Group L ($p < 0.05$). The mean time for first postoperative analgesic demand were 16.6 ± 8.0 h in Group B and 14.4 ± 7.3 h in Group L ($p > 0.05$).
Conclusion: 30 ml 0.5% bupivacaine and levobupivacaine provide similar block characteristics for supraclavicular block. Bupivacaine leads to faster motor and sensory block onset compared to levobupivacaine however similar duration of postoperative analgesia.

Introduction

Currently bupivacaine is one of the most commonly used local anesthetic for central and peripheral nerve blocks. However, it has a potential to cause serious cardiovascular side effects and the new local anesthetic levobupivacaine is reported to be safer in this respect.[1,2] The experience with levobupivacaine is limited in peripheral blocks when compared to bupivacaine.

Supraclavicular block enables a complete anesthesia to the arm, elbow and hand. Postoperative analgesia requires a catheter insertion perineurally, however success rate of

* Corresponding author.
E-mail: syurtlu68@gmail.com (S. Yurtlu).

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catheter applications in supraclavicular block is lower than other brachial plexus nerve block sites. An another way of providing postoperative analgesia is to use local anesthetics with long duration of action. Long term postoperative analgesia with a single application is possible with the use of bupivacaine, levobupivacaine or ropivacaine. Thus we aimed to compare bupivacaine with its S(+) enantiomer, levobupivacaine in terms of their effectiveness, side effects and complications in supraclavicular block.

Methods

Prior to the study, approval of the hospital ethics committee (Dr Lütfi Kırdar Research and Education Ethics Committee, Date: 29-03-2007, Number: 3) has been obtained.

Sixty patients aged between 20 and 65 years, weighing between 50 and 100 kg and at ASA I-II-III physical condition who were scheduled for elective hand, forearm or arm surgery were included in this study. A written informed consent of participating patients were obtained.

Exclusion criteria included being classified as ASA risk classification of IV or above, analgesic drug intake in the last 24 h, coagulation anormalities, having infection or previous surgery in the operative site, anatomic deformations on block site, presence of neurological deficiencies on the operative extremity, uncooperable patients, suffering a peripheral nerve disorder, undergoing psychiatric treatment, alcohol and/or drug abuse, known allergy to study medications, and having diaphragm paralysis and/or pneumothorax on the contralateral side to be operated.

Patients who participated in the study were randomly divided into two groups of 30 individuals in each with a computer generated randomization list (Group B: 30 ml 0.5%, 5 mg/ml bupivacaine; Group L: 30 ml 0.5%, 5 mg/ml levobupivacaine). Patients were taken to the regional anesthesia section within the operating theater 1 h prior to surgery. They were laid in supine position on the block table. Baseline hemodynamic parameters [systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturations (SpO_2)] and electrocardiograms were monitorized. All values were measured prior to the block and recorded as control values. Venous access was obtained by using a 20 G branula and crystalloid infusion was initiated. As a premedication, 0.03 mg/kg iv midazolam was administered.

The point where block would be administered was identified by using the classical technique.[3] Stimuplex HNS 12® (B. Braun, Melsungen, Germany) was used as nerve stimulator and Stimuplex A® (B. Braun, Melsungen, Germany; 22 G, 50 mm) was used as a block needle. After administering local anesthesia at the marked point of entry, a block needle was used to search for movement of muscles innervated by the nerves of the brachial plexus Two of these nerves (median, ulnar, radial or .musculocutaneous nerve) were localized and an equal amount of local anesthetic (15 ml) was administered to each one. Aspiration test was repeated once in every 5 ml during the injections. An anesthesiologist who did not take part in the rest of the study prepared the local anesthetic solutions according to randomization and another anesthesiologist (CI) who was unaware of the syringe content has performed all the block procedures. Group B was administered 30 ml 0.5% bupivacaine and Group L 30 ml 0.5% levobupivacaine. Five minutes after the end of injections, the surgical area started to be checked with the pin-prick test with 5 min intervals. Sensory block was assesed with 3 point scale (0 = No sensory loss, 1 = Loss of sensation to pin-prick, 2 = Loss of sensation to touch) and motor block was evaluated with Modified Bromage Scale (MBS; 0 = Normal muscle function, 1 = Elbow flexion, 2 = Wrist flexion, 3 = Full motor block) and recorded.

Motor block onset time was taken as the time between injection of local anesthetic and appearance of MBS 1, while sensory block onset time was taken as the time between injection of local anesthetic and the loss of pain sensation with pin-prick stimuli. Surgery was allowed when ''pin-prick'' was positive in the surgery area.

Sensory block duration was defined as the duration between sensory block onset and first feeling of pain, while motor block duration was the time between motor block onset and full arm mobility. These durations were determined based on patient reports at postoperative 4th, 8th and 24th hour.

SAP, DAP, MAP, HR, SpO_2 of patients were recorded at the beginning of surgery, at minutes 5, 10 and 15 of block administration, and thereafter with 10 min intervals.

In case of pain sensation at the beginning of or during the surgery, local anesthetic infiltration (prilocaine, 5–10 ml in 2% concentration) to the surgical site was planned. Administration 50 mcg fentanyl and/or 1 mg midazolam was also planned in cases of pain or stress despite local infiltration. The doses would be recorded if administered.

All patient complaints during and after block, all block-related complications and side effects of drugs were recorded.

Postoperative pain complaints were assessed on a ''verbal rating scale'' (VRS) (0: no pain, 1: mild pain, 2: moderate pain, 3: severe pain and 4: unbearable pain), and patient satisfaction was assessed at postoperative hour 24 as ''not satisfied, slightly satisfied, and satisfied''. The first analgesic (diclofenac iv) dose was planned in case of VRS >2. When patients were visited in the clinic at hours 4–8 and 24, complaints of pain and total amount of analgesics taken were recorded.

Statistical analysis

As a result of the power analysis we performed, it was decided that each group should have at least a minimum of 26 cases (80% power and 0.05% α error). Considering possible data loss due to technical reasons, both groups were admitted 30 patients.

Statistical analyses in the study were performed by using the NCSS 2007 package. Descriptive statistical methods were used as well as repeated analysis of variance for continuous data of multiple groups, Newman Keuls multiple comparison test for subgroup comparisons, independent t test for the comparison of paired groups, chi-square test for the comparison of qualitative data, and McNemar's test for the time interval measurements of qualitative data. The results were evaluated at a significance level of $p < 0.05$.

Table 1 Distribution of patients with respect to demographics (mean ± SD).

	Group B	Group L	*t*	*p*
Age (years)	40.3 ± 14.88	38.2 ± 11.44	0.96	0.643
Body weight (kg)	73.8 ± 12.59	73.9 ± 13.81	−0.03	0.977
Height (cm)	171.43 ± 8.34	173.1 ± 7.98	−0.79	0.432

Table 2 Distribution of patients with respect to gender and ASA classification.

	Group B		Group L		
Gender					
Male	22	73.30%	22	73.30%	χ^2: 0
Female	8	26.70%	8	26.70%	$p = 1$
ASA					
I	19	63.30%	22	73.30%	
II	9	30.00%	8	26.70%	χ^2: 2.27
III	2	6.70%		0.00%	$p = 0.32$

Table 3 Comparison of groups with respect to peroperative fentanyl use, VRS at postoperative hour 24 and satisfaction.

	Group B		Group L		
Perop. fentanyl					
No fentanyl use	23	76.70%	22	73.30%	
50 mcg	4	13.30%	3	4.00%	χ^2: 2.18
>50 mcg	3	10.00%	5	16.70%	$p = 0.534$
Postop. VRS (Hour 24)					
No pain	5	16.70%	2	6.70%	
Mild pain	20	66.70%	13	43.30%	
Moderate pain	3	10.00%	13	43.30%	χ^2: 9.02
Severe pain	2	6.70%	2	6.70%	$p = 0.029$
Postop satisfaction (Hour 24)					
Not satisfied	3	10.00%	3	10.00%	
Slightly satisfied	–	0.00%	1	3.30%	χ^2: 1.01
Satisfied	27	90.00%	26	86.70%	$p = 0.601$

Results

The study was implemented on 60 patients and no data loss occurred. No statistically significant difference existed between the demographic data and ASA distributions of the patients (Tables 1 and 2). HR, SAP, DAP, MAP and SpO_2 values were similar at all measurement times in comparisons within and between the groups.

The patients in Groups B and L had similar peroperative opioid use and postoperative satisfaction rate (Table 3). Mean postoperative VRS scores of Group L patients was higher than that of Group B patients ($p < 0.05$). Thirteen patients (43.3%) in Group L and 3 patients (10%) in Group B had moderate pain (Table 3).

The operation duration, motor and sensory block times of patients in Group B and Group L did not vary significantly. The sensory and motor block onset times in Group B patients were shorter than Group L ($p < 0.05$) (Table 4).

Motor block scores of Group B and Group L patients at minutes 1, 5, 10, 15, 20, 30, 45 and 60 were not statistically

Table 4 Surgery, motor and sensory block durations (mean hour ± SD).

	Group B	Group L	*t*	*p*
Surgery duration	1.48 ± 0.61	1.52 ± 0.66	−0.20	0.84
Motor block duration	14.55 ± 5.55	13.8 ± 2.95	0.73	0.468
Sensory block duration	14.25 ± 5.81	12.81 ± 3.32	1.12	0.268

Table 5 Motor and sensory block onset times (mean minute ± SD).

	Group B	Group L	*p*
Motor block onset time	5.07 ± 4.07	9.2 ± 7.9	0.0041
Sensory block onset time	19.64 ± 10.70	25.66 ± 10.72	0.036

different at shoulder level. The rate of full motor block (MBS 3) at minutes 1, 5 and 10 in the shoulder region of Group B patients was higher than that in Group L patients. However, a statistically meaningful difference was not found in the comparison of all time intervals including these. No statistical difference was observed between motor block distribution of Group B and L patients at elbow level at all measurement times.

While partial block in the fingers was seen in 12 patients in Group L (40%), it was seen in 7 patients (23.3%) in Group B. The difference was not statistically significant (Table 5).

Patient assessment according to MBS showed that there were more patients in Group B who had higher block quality at minutes 5, 10, 15 and 20 than in Group L (Table 6).

No statistical difference existed between the sensory block assessment of Group B and L patients at minutes 1, 15, 20, 30, 45 and 60. Sensory block ratio in Group B patients was statistically higher than those in Group L at minutes 5 and 10 ($p < 0.05$) (Table 7).

Among both groups of patients, the distribution of surgery areas was similar (Table 8).

Table 6 Distribution of mean motor block score by time in groups with respect to MBS and patient ratio.

Minute	Group B	Group L
1	0	0
5	1 (33.3%)*	1 (13.3%)
10	2 (26.7%)*	2 (16.7%)
15	3 (20.0%)*	3 (3.3%)
20	3 (36.7%)*	3 (10.0%)
30	3 (53.3%)	3 (40.0%)
45	3 (63.3%)	3 (46.7%)
60	3 (66.7%)	3 (56.7%)

* $p < 0.05$.

Partial block occurred in 4 patients in Group B. All four were given peroperative 50 mcg fentanyl due to pain. Additional local anesthetics were administered to one patient by the surgery team due to mild pain at the beginning of surgery. General anesthesia was initiated in three patients (10%) due to blockage failure.

Table 7 Sensory block assessment in groups with respect to time.

Sensory	Group B		Group L		
Min. 1					
None	30	100.00%	30	100.00%	
Min. 5					
None	26	86.70%	30	100.00%	χ^2: 4.28
Full	4	13.30%*		0.00%	$p = 0.038$
Min. 10					
None	20	66.70%	29	96.70%	χ^2: 9.01
Full	10	33.30%*	1	3.30%	$p = 0.003$
Min. 15					
None	16	53.30%	21	70.00%	χ^2: 1.76
Full	14	46.70%	9	30.00%	$p = 0.184$
Min. 20					
None	9	30.00%	12	40.00%	χ^2: 0.659
Full	21	70.00%	18	60.00%	$p = 0.417$
Min. 30					
None	3	10.00%	6	20.00%	χ^2: 1.17
Full	27	90.00%	24	80.00%	$p = 0.278$
Min. 45					
None	2	6.70%	0	0.00%	χ^2: 2.06
Full	28	93.30%	30	100.00%	$p = 0.15$
Min. 60					
None	1	3.30%	0	0.00%	χ^2: 1.01
Full	29	96.70%	30	100.00%	$p = 0.313$

* $p < 0.05$.

Table 8 Distribution of surgical areas in the groups.

AREA	Group B	Group L
ARM	1 (3.3%)	2 (6.6%)
ELBOW	2 (6.6%)	1 (3.3%)
FOREARM	7 (23.3%)	7 (23.3%)
WRIST – HAND	20 (66.8%)	20 (66.8%)

Eleven patients in Group L experienced partial block. As there was mild pain during surgery in 2 patients, the surgery team administered local anesthesia. Two others needed 50 mcg peroperative fentanyl due to pain. Six patients (20%) required general anesthesia.

Motor and sensory block recovery times of patients who required general anesthesia were also recorded at the end of surgery.

In the postoperative stage, 16 patients in Group B and 17 in Group L were administered analgesic drugs due to VRS >3. Other patients did not need postoperative analgesic drugs within the first 24 h. The mean time before the need for first postoperative analgesia was 16.61 ± 8.05 h in Group B and 14.37 ± 7.27 h in Group L. The difference was not statistically significant.

Side effects

Group B patients experienced significantly more side effects than Group L. Four patients in Group B (13.3%) suffered from side effects, while none in Group L did.

Two patients in Group B had Horner's syndrome and the other 2 had prolonged motor blockage (longer than 24 h). These side effects were not seen in any of the patients in Group L. Full recovery was observed at 8th hr visit of patients who suffered Horner's syndrome.

Discussion

An advantage of supraclavicular block is that the upper extremity position does not affect application negatively during the procedure.[4,5] Even though blocks with ultrasound are known to yield more successful outcomes, the importance of experience is also mentioned in previous studies.[6,7] We therefore preferred nerve stimulator (NS) in our study as we had more experience with it. Our successful block rate with NS was 90% in Group B and 80% in Group L.

Despite the high doses of bupivacaine and levobupivacaine used in peripheral blocks, serious cardiovascular, pulmonary or neurological complications are rare.[8–13] Our results are also similar.

Cox et al.[14] compared bupivacaine and levobupivacaine in brachial plexus block. They found no difference between the dose-dependent effects of 0.25% and 0.5% levobupivacaine; however, they found that 0.25% levobupivacaine had slower onset, shorter maintenance and a lower overall success rate than the other two groups (0.5% levobupivacaine, 0.5% bupivacaine). They reported a general success rate of 65–80% in relation to the anesthesia technique. This study found levobupivacaine to be appropriate for brachial plexus block. Its lower toxic potential than bupivacaine also supports this, and levobupivacaine is expected to increase the safety margin in regional anesthesia. No statistically meaningful difference was found between the sensory and motor block onset times of the two drugs.

In our study, the motor and sensory block onset times were meaningfully shorter in Group B than Group L ($p < 0.05$). Mean motor block onset time was 5 min in Group B and 9 min in Group L, while mean sensory block onset time was 19 min in Group B and 25 min in Group L. Even though there is a statistical difference between the two drugs, we are of the opinion that a 6 min difference is not of significance in clinical application.

Another noteworthy finding from Cox et al.'s[14] study is that 0.5% levobupivacaine had the longest effect duration. They found that sensory block duration was 892 min (approximately 14 h) with 0.25% levobupivacaine; 1.039 min (approximately 17 h) with 0.5% levobupivacaine; and 896 min (approximately 15 h) with 0.5% bupivacaine. As on sensory block, 0.5% levobupivacaine had the longest effect duration on motor block as well (approximately 17.5 h). However, the difference between groups regarding sensory and motor block maintenance duration and block level was not statistically meaningful. Our results also corroborate these findings.

Lisanantti et al.[13] found no meaningful difference with respect to sensory block quality between (45 ml and 0.5% concentration) ropivacaine, levobupivacaine and bupivacaine at minutes 5, 10 and 15. There was a higher rate of achieving anesthesia at a desired level at min 45 with ropivacaine and bupivacaine than in comparison with levobupivacaine. The frequency of obtaining sensory and motor block at min 45 was similar across all 3 groups. Mean total sensory block duration was 17.1 ± 6.5 h in the levobupivacaine group, 17.8 ± 7.2 h in the bupivacaine group and 15.0 ± 5.4 h in the ropivacaine group. The difference was not statistically significant. Mean total motor block durations were 19.5 ± 8.0 h with levobupivacaine, 19.3 ± 7.7 h with bupivacaine, and 17.3 ± 6.6 h with ropivacaine. D'Ambrosio et al.[15] compared 0.5% concentrations of ropivacaine, bupivacaine and levobupivacaine in two different blocks (brachial and femoral), and found that ropivacaine provided faster block but had a shorter analgesia duration than the other two. They did not observe a difference between levobupivacaine and bupivacaine. No drug induced side effects arose in the study and, considering the potential cardiotoxic and neurotoxic side effects of bupivacaine, the authors concluded that ropivacaine or levobupivacaine could be used depending on the need for anesthetic.

In our study, we did not found a statistical difference between the total motor and sensory block durations of the two groups. Compared to similar studies, sensory block duration with levobupivacaine was similar while that of motor block was shorter. This difference may be attributed to differences in technique and methods.

Postoperative VRS values in the study by D'Ambrosio et al.[15] were higher in the ropivacaine group than the other two (levobupivacaine and bupivacaine). No difference existed between the levobupivacaine and bupivacaine groups.

In our study, VRS at postoperative hour 24 in Group B was 1 in 20 patients, 2 in three patients, and 3 in two patients. In Group L, it was 1 in 13 patients, 2 in 13, and 3 in 2. This shows that VRS values were better in Group B than in Group L. Even though postoperative pain levels were lower in Group

B patients than those in Group L, we are of the opinion that the difference is not significant in clinical practice since the scores are below 3.

Regarding postoperative analgesia, Liisanantti et al.[13] found that first postoperative analgesia was needed at 17.8 ± 7.2 h in the bupivacaine group, 17.1 ± 6.5 h in the levobupivacaine group, and 15.0 ± 5.4 h in the ropivacaine group. The difference was not statistically meaningful. D'Ambrosio et al.[15] did not find any difference regarding postoperative analgesia need with levobupivacaine and bupivacaine. Our results corroborate this finding.Cox[14] states that a sharp decline from 0.2% to 0.01% has been observed in the last 30 years in incidences of systemic toxicity with local anesthetics, and that even though the incidence of systemic toxicity is highest in peripheral nerve blocks with 7.5 in 10,000, the incidence of neural damage is lowest at 1.9 in 10,000. In our study, Horner's syndrome occurred in 2 patients and prolonged paresthesia occurred in another 2 in Group B. No complications were noted in Group L. No toxicity findings related to bupivacaine or levobupivacaine was present in either group. On follow-up, a permanent neurological disorder was not detected in any of the patients who developed complications.

In sum, we found that 30 ml 0.5% bupivacaine and levobupivacaine was enough to obtain motor and sensory supraclavicular block. Considering the higher side effect rate of bupivacaine and its potential cardotoxic side effects, we are of the opinion that levobupivacaine may be the preferred drug for brachial plexus blocks with the supraclavicular approach.

Conflicts of interest

The authors declare no conflicts of interest.

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