ISSN: 1607-8322, e-ISSN: 2220-5799 Anaesthesia, Pain & Intensive Care
Vol 26(6); December 2022 DOI: 10.35975/apic.v26i6.2055

ORIGINAL RESEARCH REGIONAL ANESTHESIA

Comparative study between bupivacaine 0.5% vs. bupivacaine 0.5% plus lidocaine 2% vs. lidocaine 1.5% in ultrasound guided axillary brachial plexus block for brachiocephalic fistula formation in chronic renal failure patients

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Abstract

Background: Patients with chronic renal insufficiency need to have arteriovenous fistula (AVF) for hemodialysis. Ultrasound guided axillary brachial plexus block is a good substitute to general anesthesia or local anesthesia as it causes vasodilatation and minimum hemodynamic derangement, besides offering prolonged postoperative analgesia. We compared three types of local anesthetic solutions; bupivacaine 0.5%, bupivacaine 0.5% plus lidocaine 2% and lidocaine 1.5% for onset and duration when used for axillary brachial plexus block.

Methodology: Sixty-six patients were randomly allocated to one of the three different groups: Group B: patients received 30 ml of bupivacaine 0.5% for the block; Group BL: received 15 ml of bupivacaine 0.5% with 15 ml lidocaine 2% and Group L: received 30 ml of lidocaine 1.5% for the block under US guidance. Onset of sensory and motor anesthesia were registered, and the time to first analgesic demand postoperatively was noted. Statistical analysis of the results was undertaken.

Results: Results showed that regarding the onset of sensory anesthesia, lidocaine group had the shortest time and the results were statistically significant compared to the other two groups. A statistically non-significant difference was found between Group B and Group BL, where Group BL had shorter time of onset than Group B, e.g., 9.05 ± 1.36 vs. 9.77 ± 0.97 min. The onset of motor block was the earliest in Group BL and the result was considered non-significant between Group L and Group B being shorter in Group L; the difference in results was also non-significant between Group BL and Group L. Significantly longer duration of motor and sensory blocks was noted in Group B and compared to the BL and L groups. As regards the timing of first analgesic need, there was statistically significant difference between all groups being longest in Group B (608.68 ± 21.74 min)

Conclusion: This study revealed that using 30 ml of bupivacaine 0.5% in axillary brachial plexus block with ultrasound guidance in ESRD patients for AVF creation gives much better results than 30 ml of lidocaine 1.5% or a mixture of

bupivacaine 0.5% with lidocaine 2% as regards to onset of anesthesia, postoperative analgesia and patient satisfaction.

Trial Registry: PACTR202208582938205

Abbreviations: AVF: arteriovenous fistula; BPB: Brachial plexus block; ESRD: End stage renal disease; GA: General anesthesia; NRS: Numeric rating scale; RA: Regional anesthesia

Key words: Bupivacaine; Lidocaine; Hemodialysis; Brachial plexus block

Citation: Abdelhady ISM, Ghallab MAA, Zaki MSM, Abdelrahman KAS, Soliman AFH. Comparative study between bupivacaine 0.5% vs. bupivacaine 0.5% plus lidocaine 2% vs. lidocaine 1.5% in ultrasound guided axillary brachial plexus block for brachiocephalic fistula formation in chronic renal failure patients. Anaesth. pain intensive care 2022;26(6):743−748; **DOI:** 10.35975/apic.v26i6.2055

Received: September 14, 2022; **Reviewed:** October 28, 2022; **Accepted:** October 31, 2022

1. Introduction

The arteriovenous fistula (AVF) construction is a routine procedure for patients with chronic renal dysfunction. The primary failure rate for AVF construction under local anesthesia infiltration is very high; approximately one-third of AVFs fail at an early stage so regional anesthesia is a good alternative with better results.[1]

The three acceptable anesthetic techniques used for the surgical construction of AVF are general anesthesia (GA), regional anesthesia (RA), and local anesthetic infiltration; however, the choice of anesthetic methodology may significantly affect early patency or long-term AVF outcomes. Brachial plexus block (BPB) is thought to improve local circulatory parameters when compared to local anesthesia (LA).[1]

Regional blocks result in significant venous distention with a 25% increase in venous radius after the onset of BPB. In a prospective study, re-evaluating vasculature immediately after RA to avoid graft construction increased the success rate of fistula from 61.7% to 79.8%.[2]

As an alternative to infraclavicular nerve block, ultrasound-guided axillary block can be used to create radial cephalic and brachial cephalic fistulas with less motor blockade.[3] It was demonstrated that a BPB dramatically improves flow through the fistula compared to local anesthesia alone up to 8 weeks after surgery, but there was no difference in fistula patency.[2]

The primary outcome of our study was to figure out the local anesthetic agent, or agents, the concentration, and the volume to be used during axillary approach of BRB by ultrasound guidance, that will be the most suitable to fit the anesthetic and surgical requirements for the successful creation of brachiocephalic fistula taking into consideration the start of anesthesia, the duration of the intra-operative anesthesia and the duration of the postoperative analgesia. The secondary outcome of this study was to enhance the patient satisfaction and decreasing the cost of postoperative stay.

2. Methodology

This prospective randomized comparative single blinded trial was done at El Demerdash Hospitals over 18 months starting from June 2020 to January 2022. The study was designed for ESRD patients aged from 25−75 y.

Patients who had a history of neuromuscular disorder, severe liver impairment, or heart disease were excluded from the research. Also candidates who had localized infection at axilla, opioid dependence, a contraindication to regional anesthesia, or who refused the consent, were excluded from this study.

Based on the outcomes of an earlier study with an alpha value of 0.05 and a power of 95%, the sample size was estimated to be 60. In order to account for the potential dropout cases, we included 22 cases in each category.

All cases received information on the advantages and risks of axillary block as well as the drugs to be utilized before participation in the trial. Informed consent was obtained from all patients.

Following computer-generated randomization, the sealed envelope was opened. The sixty-six patients were equally distributed into three categories: Group B: 30 ml of bupivacaine 0.5% was injected for the axillary block; Group BL: 15 ml of bupivacaine 0.5% plus 15 ml lidocaine 2% was used and Group L: 30 ml of lidocaine 1.5% was injected for the axillary block. All patients were operated by one surgical team to avoid variations in duration of the operation.

In the operating room, monitoring with ECG, non-invasive automated blood pressure monitor, and pulse oximeter was established. Intravenous normal saline was given after inserting an intravenous cannula in the arm that wasn't operated upon. Through a nasal cannula, oxygen 2 L/min was given. The elbow was flexed to ninety degree while the arm was externally rotated and abducted.

The axilla and upper part of the arm were disinfected with povidone iodine. A 38-mm high frequency (912 MHz)

Table 1: Basic demographics and clinical data of patients

Patient Characteristics	Group B	Group BL	Group L	P value
Age (y)	44.78 ± 8.33	48.95 ± 10.08	46.82 ± 7.08	0.78
Sex [n (%)]				
• Male	3 (13.6)	4 (18.18)	5 (22.72)	0.737
• Female	19 (86.36)	18 (81.82)	17 (77.28)	
BMI (kg/m^2)	27.58 ± 3.06	27.58 ± 2.62	27.31 ± 2.71	0.94
Diabetes (%)	18	17	19	0.74
History of hypertension (%)	16	16	19	0.46
History of CAD (%)	18	19	18	0.89
LVEF	48.36 ± 8.2	47.36 ± 7.49	48.18 ± 8.2	0.91

Data presented as Mean ± SD or n (%).

linear probe was used and an in-plane technique was utilized to specifically identify each nerve.

Patients received inj. midazolam 1−2 mg in the established IV line. All blocks were performed by one of the authors, according to the group allocation.

Following the infiltrative injection of 2 mL of lidocaine (10 mg/mL) to the puncture site, each of the three terminal nerves (medial, ulnar, and radial) was targeted with a 50-mm 18G insulated needle using ultrasound guidance. To facilitate circumferential LA distribution around the nerve, the needle was moved to various sites all the way around each nerve. The injection of a total of 30 mL of LA solution was done as 7.5 ml for each nerve of the four main nerves followed by observation to ensure that each nerve was completely encircled. Every five min for 30 min, or until the block effect was terminated, the sensory and motor blocks were assessed. A motor score of 2 or below, as well as the lack of cold and pinprick sensations in the vicinity of all three terminal nerves, were considered adequate for surgical anesthesia.

The time-point at which the LA injection was finished, was considered zero point to calculate onset of sensory and motor blocks. The pinprick test was used to assess sensory block.

The period between injection and full recovery of the block was used to characterize the total duration of anesthesia. Additionally, analgesia time-the period of time between the injection of local anesthetic solution and the onset of discomfort at the incision was noted. The numeric rating scale (NRS) was used to measure pain (from zero to ten). The typical analgesic for the initial discomfort was 500 mg acetaminophen given when NRS score of four or more was noticed. The time to first analgesic needed was noted; and then at NRS scores at 2, 4, 8 and 12 h postoperatively were noted.

Patients, who required further nerve blocks were excluded from the trial.

Adverse effects, e.g., nausea, vomiting, bradycardia and sedation etc., were noted.

At the same time-points, the level of sedation was assessed in each patient at 4-point scale, e.g., 1- awake and aware; 2 - sedated but responding to verbal stimulation; 3 - deeply sedated, 4 - unable to arouse.

Statistical analysis

The collected data was coded, analyzed using a Social Science Statistical Package (SPSS 15.0.1) for windows (SPSS, inc, Chicago, IL, 2001). Data is presented as mean ± SD for quantitative parametric data and medial and inter-quartile range for quantitative non-parametric data. Student's t-test analyzed quantitative data, while chi square test and fisher exact test were used to analyze qualitative data. $P < 0.05$ was considered statistically significant.

3. Results

Sixty-six ESRD patients aged from 25−75 y who were scheduled for brachiocephalic AVF, were included in this prospective randomized comparative single blinded research study.

There was no significant difference between the three categories regarding the patient demographic criteria, e.g., age, sex, diabetes, hypertension, body mass index, coronary artery disease and left ventricular function, as shown in Table 1.

As regard onset of the sensory block, the results were considered significant between Group B vs. Group L, and also between Group BL vs. Group L but non-significant between Group B vs. Group BL.

Regarding the onset of sensory block, lidocaine group had the shortest onset time of sensory block and the results

Table 2: Comparison between the three groups regarding the onset of sensory and motor blocks and duration of sensory and motor blocks

	Group B (n = 22)	Group BL (n = 22)	Group L (n = 22)	Post hoc Tukey's test			P-value (ANOVA)
				B vs. BL	B vs. L	BL vs. L	
Onset of sensory block (min)	8.59 ± 0.8	7.8 ± 1.3	5.59 ± 1.18	0.06	< 0.001	< 0.001	< 0.001
Onset of motor block (min)	9.77 ± 0.97	9.05 ± 1.36	9.64 ± 1.26	0.12	0.93	0.24	0.11
Duration of sensory block (min)	593.64 ± 22.3	442.14 ± 11.54	286.5 ± 17.24	< 0.001	< 0.001	< 0.001	< 0.001
Duration of motor block (min)	562.68 ± 23.72	405.36 ± 46.4	265.05 ± 15.87	< 0.001	< 0.001	< 0.001	< 0.001
Time to 1st analgesic request (min)	608.68 ± 21.74	439.02 ± 18.27	296.22 ± 70.13	< 0.001	< 0.001	< 0.001	< 0.001

Table 3: Comparison between the three categories regarding duration of operation (min)

	Group B (n = 22)	Group BL (n = 22)	Group L (n = 22)	P value
Duration of Surgery (min)	50.5 ± 6.27	53.32 ± 5.02	51.64 ± 4	0.2

were statistically significant compared to the other two groups. There was statistically significant difference between Group B and Group BL where Group BL has shorter time of onset (7.8 ± 1.3 min) than group B (11.68 ± 2.19) as shown in Table 2.

As regards the onset of motor block, all results were considered non-significant. The onset of motor block was the shortest in Group BL and the result was considered significant between Group L and Group B being shorter in Group L. But the result was non-significant between Group BL and L. Significantly longer duration of motor and sensory block was seen in both groups and Group BL compared to the Group L. There was no statistically significant difference between groups B and BL. Time to first analgesic request was longer in both Group B and Group BL compared to Group L (Table 2).

As regards the duration of operation, there was no significant difference between the three categories as shown in Table 3.

NRS was checked at 2, 4, 8 and 12 h postoperatively. As regard to scores at 2 and 4 h, there was no significant difference between the three group while NRS scores at 8 h showed significant difference ($P < 0.001$) giving higher scores in Group L as duration of sensory block was shorter and time to first analgesic request was shorter in comparison to Groups B and BL. As regard to NRS at 12 h there was no statistically significant difference between the three groups as shown in Table 4.

Two patients suffered from bradycardia in Group L, and one patient in Group B, which was managed by 1 mg atropine; while in Group BL no patient suffered from bradycardia.

In Group L no patient had nausea or vomiting, while in Group BL three patient experienced nausea and vomiting, and in Group B two patients had nausea / vomiting which was managed by 8 mg of inj. ondansetron slow IV. No patient experienced sedation or disturbance in conscious level and all of them had a sedation score 1.

4. Discussion

In this present research we compared three groups of patients undergoing AV fistula formation in patients with

Table 4: Comparison between B, BL and L regarding NRS scores

NRS	Group B		Group BL		Group L		P-value
	Median	IQR	Median	IQR	Median	IQR	
NRS 2	0	(1−0)	0	(1−0)	0	(1−0)	0.93
NRS 4	1	(2−0)	1	(2−1)	1	(2−0)	0.97
NRS 8	1	(2−1)	2	(3−1)	2.5	(3−2)	**< 0.001**
NRS 12	2	(2−1)	2	(2−2)	2	(2−1)	0.85

ESRD under axillary approach of BPB under ultrasound guidance in El Demerdash University hospitals.

The demographic data and clinical history in all three groups were similar with no significant differences between the groups ($P > 0.05$). Most of the patients had ESRD, hypertension, diabetes and coronary artery disease.

We compared the three different groups, so the result of the study was (as regard duration of surgery) statistically non-significant $P < 0.05$.

Results of this study illustrated that the time of onset of sensory block in Group L was the most rapid (5.59 ± 1.18 min) in comparison to Group BL (7.8 ± 1.3 min) and Group B (8.59 ± 0.8 min). The onset of motor block was most rapid in Group BL (9.05 ± 1.36) min in comparison to Group L (9.64 ± 1.26) min and Group B (9.77 ± 0.97). So, the result of this present study as regard to sensory block onset time was statistically highly significant $P < 0.001$. but when comparing Group B and BL, P was 0.06 which was statistically non-significant.

In the trial done in 2013, Ozmen and his colleagues compared the effect of adding lidocaine to bupivacaine on the duration of anesthesia, the length of the block, and the quality of the block in lateral sagittal infraclavicular block, and showed that the block onset time was the most rapid in bupivacaine lidocaine group which was 4.0 ± 1.31 min in comparison to Group Lidocaine which was 4.4 ± 1.03 min and group bupivacaine which was 9.7 ± 1.86 min and this result was not in agreement with our trial.[4]

In our study the duration of sensory block was the longest in Group B (593.64 ± 22.3 min) in comparison to Group BL which was 442.14 ± 11.54 min and Group L which was 286.5 ± 17.24 min and this was significant result.

Orawan et al. compared infraclavicular brachial plexus anesthesia with 2% lidocaine and 0.5% bupivacaine mixture vs. 0.5% bupivacaine alone, and showed that the duration of sensory block in Group BL (13.48 ± 7.27 h) was longer than the duration of sensory block in Group B which was 11.23 ± 7.07 h. This result was in not concordance with our present study.[5]

In our study the duration of motor block was the longest in Group B which was 562.68 ± 23.72 min in comparison to Group BL which was 405.36 ± 46.4 min and Group L which was 265.05 ± 15.87 min and this result was statistically significant.

Gadsden et al. compared the effect of mixing 1.5% mepivacaine and 0.5% bupivacaine on the duration of analgesia and latency of block onset in ultrasound-guided interscalene block, the study showed that the duration of motor anesthesia for the combination group (11.5 ± 4.7 h) was between that of the bupivacaine (16.4 ± 9.4 h) and mepivacaine (6.04 ± .2 h) groups. Duration of analgesia was the shortest with mepivacaine (4.9 ± 2.4 h), longest with bupivacaine (14.0 ± 6.2 h), and intermediate with the combination group (10.3 ± 4.9 h) ($P = 0.001$ for mepivacaine vs. combination group; $P = 0.01$ for bupivacaine vs. combination group) and this result was in agreement with our study.[6]

Orawan et al. showed that the duration of motor block in Group BL which was 11.50 ± 6.15 h was longer than the duration of motor block in Group B which was 9.57 ± 5.67 h and this result was not in agreement with our present study.

In this present study time to first analgesic request was the longest in Group B which was 608.68 ± 21.74 min in comparison to BL Group which was 439.02 ± 18.27 min, and Group L which was 296.22 ± 70.13 min and this can be considered statistically significant as $P < 0.001$. The explanation of this result may be due to the rate of return of sensation and Group B was much slower in comparison to Group BL, which made the patients ask for analgesia little bit earlier in Group BL.

Ozmen and his colleagues showed that the analgesia requirement time was the longest in bupivacaine-lidocaine group which was 6.1 ± 2.21 h in comparison to Group L which was 2.6 ± 0.62 h and Group B which was 4.4 ± 1.21 h, and this result was against our study and it may be due to injection of 20 ml only of bupivacaine in Ozmen study, but we used larger volume of 30 ml bupivacaine which made delayed the first analgesic request.

Robert et al. studied the onset and duration of the analgesic effect of various concentrations of local anesthetic solutions, illustrated that the total duration of the block in group of patients who received 30 ml of bupivacaine 0.33% was 546.4 ± 14.9 min, which was shorter than duration in our study may be due to the usage of higher concentration of bupivacaine which was 0.5% in our trial.[7]

Nestor et al. concluded in a review article that mixing drugs of varying pH can change their ionized and non-ionized percentages. The greater the proportion of non-ionized local anesthetic, the higher the pH; conversely. Lidocaine has the lowest acidity of the commonly mixed agents, with a pH of 6. As a result, combining lidocaine (fast onset) with other agents like bupivacaine (slower onset) lowers the pH, resulting in a lower proportion of non-ionized lidocaine. As a result, the justification for combining local anesthetics to accelerate onset was flawed and not supported by pharmacological principles or clinical research.[8]

When used for axillary block, the addition of lidocaine reduced the duration of sensory and motor block when compared to bupivacaine or plain ropivacaine, which was consistent with our findings.[9]

5. Conclusion

The results of our study reveal that using 30 ml of bupivacaine 0.5% in ultrasound guided axillary brachial plexus block in ESRD patients undergoing AVF creation gives much better results than 30 ml of lidocaine 1.5% alone or a mixture of 15 ml bupivacaine 0.5% with 15 ml lidocaine 2% as regard onset of anesthesia, postoperative analgesia and patient satisfaction. However, these results must be confirmed with further multicentre studies with larger patient populations.

6. Limitations

There were no obvious limitations to our study.

7. Ethical clearance

The research ethical committee at the medical school at Ain Shams University gave its approval to this study. (FMASU MD 259a/ 2018/2019 / 2020 / 2021) with Pan African Clinical Trial Registry, identifier PACTR202208582938205.

8. Availability of data

All the data generated in this study are available upon reasonable request from the main author.

9. Competing interests

The authors declare that there were no competing interests involved.

10. Funding

There was no funding involved in any from any funding agency.

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