Onset Time of 2% Lidocaine and 0.5% Bupivacaine Mixture versus 0.5% Bupivacaine Alone using Ultrasound and Double Nerve Stimulation for Infraclavicular Brachial Plexus Anesthesia in ESRD Patients Undergoing Arteriovenous Fistula Creation

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Objective: *To reduce the onset of 0.5% bupivacaine by adding 2% lidocaine with 0.5% bupivacaine for ultrasound-guided and double stimulation technique at musculocutaneous and radial nerve for infraclavicular brachial plexus block.*
Design: *Prospective randomized double-blinded, controlled trial study.*
Material and Method: *90 patients undergoing creation of arteriovenous fistula under ultrasound-guided infraclavicular brachial plexus block were randomized into 2 groups. Gr. B (46 patients) received 0.5% bupivacaine 30 mL and Gr. BL (44 patients) received mixture of 0.5% bupivacaine 20 mL and 2% lidocaine 10 mL. The onset of sensory block were assessed by response to pinprick (grading: 0 = no sensation, 1 = hypoesthesia, and 2 = normal sensation). Rescue analgesia during the operation, duration of sensory and motor blockade were recorded. Surgeon and patient satisfactions are also evaluated using 6-point scale (0 = dissatisfied to 5 = very satisfied).*
Results: *There were no significant difference in the onset time of either group. Duration of sensory and motor block was not different. Surgeons' and patients' satisfaction were also not significantly different between the groups.*
Conclusion: *Mixing 2% lidocaine with 0.5% bupivacaine to the final concentration of 0.67% for lidocaine and 0.33% for bupivacaine does not reduce the onset of ultrasound-guided infraclavicular brachial plexus block.*

Keywords: *Local anesthetics mixture, Ultrasound-guided infraclavicular brachial plexus block, Onset, Lidocaine, Bupivacaine, ESRD, AV fistula, Nerve stimulation*

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Hemodialysis is the common treatment for end-stage renal disease (ESRD) condition which improves quality of life and survival rate for this group of patients. Arteriovenous fistula (AVF) creation is the vascular access technique that provides long-term vascular access for hemodialysis patients. Pharmacokinetic and pharmacodynamics profile of some anesthetic drugs were changed in this group of patients making anesthesiologist avoid general anesthesia, preferring the brachial plexus block (BPB) for anesthesia in the AVF creation procedure. The BPB provides good analgesia, sympathetic blockade with higher radial artery and AVF blood flow at both the early and late postoperative periods[1].

The onset of the brachial plexus block depends on the technique approach to the brachial plexus and the type of local anesthetics using for the block. Infraclavicular approach BPB provides good analgesia with fewer side effects such as pneumothorax, hemidiaphragm paralysis, Horner's syndrome, etc. Performance time and technique-related pain for infraclavicular BPB under ultrasound guidance were not different from the supraclavicular approach[2]. Ultrasound-guided infraclavicular BPB using double stimulation technique at musculocutaneous and radial nerve achieved the success rate of the block of 96%[3]. Bupivacaine is the local anesthetic that provides long

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duration of action, but the onset time is delayed compare to lidocaine. The present study aims to combine the rapid onset of lidocaine and long duration of bupivacaine by using the mixture of 2% lidocaine 10 mL and 0.5% bupivacaine 20 mL for ultrasound-guided infraclavicular BPB. The authors decided to use ultrasound and double stimulation at musculo cutaneous and radial nerve to have the most successful block.

Material and Method

After ethical approval by the Siriraj ethical committee review board (SIRB, COA Si433/2009) and registered in the Clinical Trials.gov (NCT00993746). Ninety ESRD patients for creation of AVF were enrolled in the study. Inclusion criteria were age more than 18 year old, BMI between 20-35 kg/m^2, consent for BPB, cooperated, communicable and, able to read and write Thai language. Exclusion criteria were body weight less than 35 kg, allergy to local anesthetics, pre-operative neurological deficit, neuromuscular disorder or old CVA, psychiatric disorder, coagulation disorder, congestive heart failure, pregnancy, and infection at the site of block. All patients provided informed consent were randomized using the sealed envelope to group B (Gr. B) received 0.5% bupivacaine 30 mL and group BL (Gr. BL) received 0.5% bupivacaine 20 mL plus 2% lidocaine 10 mL for ultrasound-guided infraclavicular BPB using double stimulation at musculocutaneous and radial nerve. After insertion of an IV catheter in the contralateral arm fentanyl 50 mcg and midazolam 1 mg were given, standard monitoring was applied. All patients were placed supine with the head turn away from the arm to be blocked and the arm abducted to 90 degree and the elbow flexed. One experienced anesthesiologist (1st author) who blinded to the drug prepared performed the block by placing the ultrasound probe 13-6 MHz linear transducer (Sono Site, Bothell, WA, USA) just medial to coracoid process in parasagittal plane and scanned the deltopectoral area under the sterile technique. A transverse image of the axillary vessels and the 3 nerve cords posterior to the pectoralis minor muscle was obtained and 2 mL of 2% lidocaine was local infiltrate. The insulated 22-gauge, 100 mm needle (Stimuplex®, B Braun, Germany) was inserted in-plane from the cephalad aspect, with the insertion point just inferior to the clavicle. The nerve stimulator (B Braun, Stimuplex®, HNS 11) was set at 100 μs, 1.5 mA, and 1 Hz. The needle was directed to the lateral cord when a motor response of the biceps at a current output ranging between 0.3 and 0.5 mA was obtained 8 mL of local anesthetic solution was injected. The needle was then redirected to posterior cord which is posterior to the axillary artery when supination of forearm, wrist or finger extension at a current output ranging between 0.3 and 0.5 mA was obtained 22 mL of local anesthetic solution was injected.

The sensory response to pinprick was assessed by well-trained nurse anesthetist who was blinded to the local anesthetic(s) used in that patient every 1 min. for 10 min, every 2 min for 10 min, and every 5 min. for 10 min or until no response to pinprick on 4 major nerves distributions (radial, ulnar, median, and musculocutaneous) compared with the response to pinprick on the contralateral arm. Grading for the sensory block was undertaken using the following scale: 0 = no sensation, 1 = hypoesthesia, and 2 = normal sensation. A successful block was defined as the absence of pinprick response. The primary outcome was the difference in onset of sensory block by the different types of local anesthetic(s) so the authors would not wait until the onset of the 4 major nerves, which was the definition for successful block. The present study defines the onset of sensory block as the time from injection of local anesthetic(s) to hypoesthesia or no sensation in 1 of the 4 major nerves as in the study by Ozmen et al[4]. The duration of the sensory block was the time from injection of local anesthetic until the first pain or the request for paracetamol.

The motor response was assessed every 5 minute for 30 minute on 4 major nerves: the radial (thumb abduction), median (third finger flexion), ulnar (fifth finger flexion), musculocutaneous (elbow flexion). Grading for motor block was undertaken using the following scale: 0 = complete paralysis, 1 = partial weakness, 2 = normal motor power. The onset of motor block was the time from injection to partial weakness in 1 of the 4 major nerves. The duration of the motor block was the time from injection of local anesthetic until the full recovery of the 4 nerve distributions.

If the patient had pain sensation at the operative site during the operation, the surgeon would ask to local infiltrate 2% lidocaine not more than 10 mL. If the patient needed more than 10 mL of lidocaine, the anesthetic technique would turn to general anesthesia and the block was considered a failed block. Surgeon satisfaction (6 point scale: 0 = dissatisfied to 5 = very satisfied) and decision whether to choose the same technique and drug(s) was recorded at the end of the operation. The surgeons were blinded to the drug, which the patient received. Patient satisfaction (6 point

scale: 0 = dissatisfied to 5 = very satisfied) was recorded at 24 hours after the operation. Patients were questioned as to which anesthetic method (same regional anesthesia technique or general anesthesia) they would choose for future surgery at the same period.

During postoperative period numeric rating pain scale (NRS: 0 = no pain to 10 = worst pain) was recorded by the ward nurse every 2 hours for 6 hours, every 4 hours for 24 hours. Paracetamol 500 mg was given on request for pain score ≥5 and Tramadol 50 mg was given on request for pain score ≥7. The time of first analgesic requested, types, and total dose were recorded. Immediate and late complications (vascular puncture, pneumothorax, local anesthetic systemic toxicity, residual paresthesia) were noted.

Statistical analysis

Sample size was calculated based on the studies of Misiolek et al[5]. Median time of sensory onset was 22.4±7.3 minute. We assumed 25% reduction in onset time to 16.8 minute. A power calculation for a 25% difference in the onset time with a probability level of 0.05 and power of 0.80 yielded a sample size of 36 patients for each group. We enrolled 45 patients (20% add up) to allow for dropouts and failed block. Kolmogorov-Smirnov test was used to verify normal distribution of continuous variables. Continuous variables are expressed as mean ± standard deviation. Statistical analysis was done using Statistica version 6 (Stat Soft Inc.; Tulsa, OK, USA; 2001) and Graph Pad Prism version 4 (Graph Pad Software Inc.; San Diego, CA, USA; 2005) software. Distributed continuous variables were compared using Student's unpaired t-test, whereas Mann-Whitney U test was used for comparison of NRS pain scores. Categorical variables were compared by Chi-square test or Fisher's exact test, as appropriate. All analyses were two-tailed and $p<0.05$ was considered statistically significant.

Results

Demographic and surgical data of the 90 patients enrolled are shown in Table 1. Duration of surgery was not significant difference. No statistically significant differences were determined between Gr. B and Gr. BL in term of sensory and motor onset (Table 2). Onset of sensory block to hypoesthesia and anesthesia in Gr. B and Gr. BL were 2.0±0.29 minute vs. 2.07±3 minute and 6.68±0.94 minute vs. 6.84±0.96

Table 1. Patients' characteristics and duration of surgery (mean ± SD)

	Gr. B (n = 46)	Gr. BL (n = 44)	*p*-value
Gender (male/female)	18/28	22/22	0.300
Age (year)	65±13	58±15	0.970
Weight (kg)	59±14	59±13	0.775
Height (cms)	158±9	160±9	0.294
BMI (kg/m^2)	23±4.5	23±4.2	0.810
Underlying disease			
DM, m (%)	26 (56.5)	21 (47.7)	N/A
Hypertension, n (%)	43 (93.5)	44 (90.9)	
IHD, n (%)	10 (21.7)	32 (72.7)	
Duration of surgery (minute)	119±38	128±44	0.348

BMI = body mass index; DM = diabetes mellitus; IHD = ischemic heart disease

Table 2. Onset and duration of sensory block and motor block (mean ± SD)

Variables	Gr. B	Gr. BL	*p*-value
Onset of sensory block to hypoesthesia (minute)	2.00±0.29	2.07±3.0	0.852
Onset of sensory block to no sensation (minute)	6.68±0.94	6.84±0.96	0.845
Onset of motor block (minute)	6.40±3.31	7.70±5.64	0.192
Duration of sensory block (hours)	11.23±7.07	13.48±7.27	0.142
Duration of motor block (hours)	9.57±5.67	11.50±6.15	0.125

minute, respectively. Duration of sensory and motor blockade was not different between groups. None of the patients necessitated conversion to general anesthesia. About one fourth of patients in Gr. B and Gr. BL needed additional 2% lidocaine local infiltration. The mean volume of 2% lidocaine supplementation was 0.55 mL in Gr. B and 0.74 mL in Gr. BL. Surgeon were satisfied with the drugs used in both groups as the answer for choosing the same technique and drug(s) were "yes" for 100%. Surgeons' satisfaction as shown in Fig. 1 were not different between groups (p = 0.902). Patients'satisfaction was also not different between groups (p = 0.244) (Fig. 2). One patient in Gr. B said that she would go for general anesthesia if she is going to have the same operation in the future because of anxiety for being awaked even without pain. Postoperative pain by NRS was not significantly different between groups at any point in time (Fig. 3).

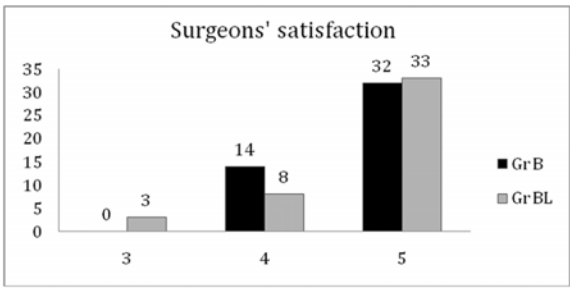

Fig. 1 Surgeons' satisfaction (6 point scale: 0 = dissatisfied to 5 = very satisfied) (p = 0.9).

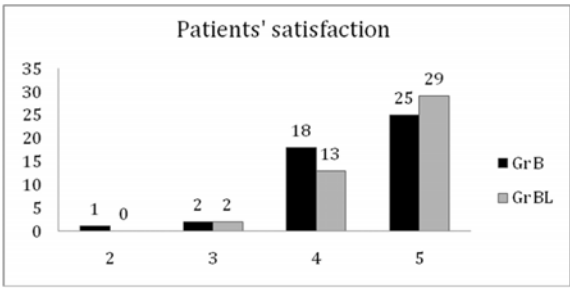

Fig. 2 Patients' satisfaction (6 point scale: 0 = dissatisfied to 5 = very satisfied) (p = 0.24).

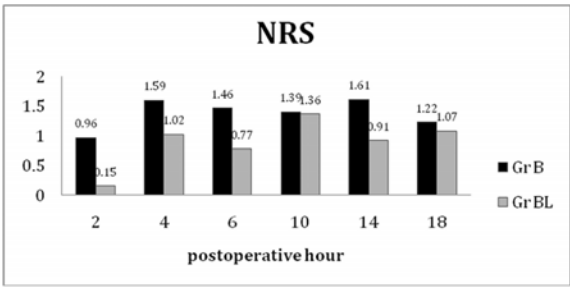

Fig. 3 Numeric rating pain score during postoperative hour period (mean) (NRS: 0 = no pain to 10 = worst pain).

Discussion

General anesthesia in ESRD patient during early post-dialysis period may increase the risk of hypotension from systemic vasodilatation. Brachial plexus block provides sympathetic block with regional vasodilatation and higher AVF blood flow compared to local infiltration[1]. The present study aims to evaluate the onset of different types of local anesthetics for infraclavicular BPB. The authors decided to improve the success rate by using the double stimulation technique with ultrasound guidance as described by Minville et al[3]. To improve the optimal outcome of the AVF creation by increasing blood flow to AVF, long duration of sympathetic blockade is very important. Bupivacaine provides long duration of action when using for BPB. High failure rate of BPB was reported when using 0.25% bupivacaine[6] so the authors decided to mix only 10 mL of 2% lidocaine to 20 mL of 0.5% bupivacaine to keep the concentration of bupivacaine higher than 0.25%. The present study could not demonstrate the reduction of onset time of infraclavicular BPB by adding 2% lidocaine 10 mL to 0.5% bupivacaine 20 mL. The mixing of 2% lidocaine 10 mL and 0.5% bupivacaine 20 mL may cause the dilution effect on both local anesthetics. The final concentration for lidocaine is 0.67% and final concentration for bupivacaine is 0.33%. The minimal effective anesthetic concentration in 90% ($MEAC_{90}$) of patients for ultrasound-guided femoral nerve block using lidocaine was 0.93%[7] and $MEAC_{90}$ of patients for ultrasound-guided axillary BPB using bupivacaine was 0.241%[8]. The 0.67% final concentration of lidocaine in this study may be too low to show the benefit of rapid onset. The profile of the block pattern in both groups such as duration of sensory and motor block are similar to bupivacaine alone which demonstrate the adequate concentration for both 0.33% and 0.5% bupivacaine in Gr. B and Gr. BL, respectively. Possible methods to increase concentration of lidocaine to at least 0.93% could be done by adding 2% lidocaine with 0.5% bupivacaine in the ratio of 1:1, sequential injection of 2% lidocaine 10 ml follow by 0.5% bupivacaine without mixing both drugs in the same syringe, etc. Ozmen et al[4] compared

the effect to mixing 0.5% bupivacaine and 2% lidocaine in 1:1 ratio with bupivacaine and lidocaine 20 mL alone for infraclavicular BPB using peripheral nerve stimulator. The onset of sensory block defined as the time from injection of local anesthetic(s) to no sensation in 1 of the 4 major nerves. The sensory onset time in bupivacaine group was 9.7±1.86 minute, which is longer than the present study at 6.68 minute but the onset time in mixing group was 4.0±1.31 minute comparable to 4.4±1.03 minute in lidocaine group. The present study did not have 2% lidocaine group as a control group because the short duration of sympathetic block by lidocaine would not benefit for AVF creation procedure. The definition of sensory onset for infraclavicular brachial plexus block may influence the difference in sensory onset time. The sensory onset time of 0.5% bupivacaine for infraclavicular BPB using ultrasound and triple nerve stimulation at posterior, medial, and lateral cord was 6 minute[9], which was comparable to the present study. The definition of onset was complete loss of sensation in all distribution of the nerves. The time for first analgesia requirement in the mixing of bupivacaine and lidocaine group were 6.1±2.21 hours, which were longer than 4.4±1.21 hours and 2.6±0.62 hours in bupivacaine and lidocaine group, respectively[4]. In this study, the duration of the block was not different between the groups. Duration of sensory block for BPB was 10.7 hours in ESRD patient in the study by Tawfic et al[10], which was comparable to 11.23 hours in the present study. Theoretically, sequential injection of local anesthetics would not have dilutional effect. Sequential injection of 1.5% mepivacaine15 mL followed 90 sec later by 0.5% ropivacaine 15 mL provides no advantage of shortening the onset time compared with injection of the same doses mixing in the same syringe for ultrasound-guided supraclavicular BPB[11]. Local anesthetic systemic toxicity (LAST) is another concern when using the combination of local anesthetics in ESRD patient. When two local anesthetic are used together in mice, the toxicities were additive[12]. Reduced clearance, faster absorption of local anesthetics from hyperdynamic circulation in ESRD patients lead to rapid elevation in plasma concentration[13]. None of the patients in the present study had signs or symptoms of local anesthetic systemic toxicity. One limitation of the present study was the dilution of lidocaine to the concentration lower than $MEAC_{90}$ in the 2% lidocaine and 0.5% bupivacaine mixture in the ratio of 1:2. Increasing concentration of lidocaine by mixing of both local anesthetics in 1:1 ratio or sequential injection of 2% lidocaine follow by 0.5% bupivacaine may accelerate the onset of brachial plexus block.

Conclusion

Mixing 10 mL of 2% lidocaine with 20 mL 0.5% bupivacaine does not shorten the onset of ultrasound-guided infraclavicular BPB using double stimulation technique at musculocutaneous and radial nerve in ESRD patients for AVF creation. Final concentration of lidocaine at 0.67% in this present study may be too low to show the rapid onset of lidocaine. The patterns of the block in mixing local anesthetics group are similar to bupivacaine alone. Clinical Trials.gov Register: NCT00993746.

What is already known on this topic?

Onset of 0.5% bupivacaine for ultrasound-guided infraclavicular BPB is longer than 2% lidocaine.

What this study adds?

Mixing 2% lidocaine 10 mL with 0.5% bupivacaine 20 mL to final concentration of lidocaine at 0.67% for ultrasound-guided infraclavicular BPB could not demonstrate the rapid onset of lidocaine. The block pattern in the mixture group was similar to bupivacaine alone group.

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Potential conflicts of interest

None.

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การศึกษาเปรียบเทียบระยะเวลาเริ่มออกฤทธิ์ของยา lidocaine 2% ผสมกับ bupivacaine 0.5% และการใช้ bupivacaine 0.5% อย่างเดียวในการทำ infraclavicular brachial plexus block โดยใช้อัลตราซาวด์สำหรับการผ่าตัด arteriovenous fistula ในผู้ป่วย โรคไตวายระยะสุดท้าย

อรวรรณ พงศ์รวีวรรณ, นิภา อินเชื้อ, ชณัฐี กิจศิริพันธ์, เบ็ญจวรรณ์ คงเมือง, วรรณภา ติวิรัช

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบระยะเวลาเริ่มออกฤทธิ์ของ bupivacaine 0.5% 20 mL ผสมกับ lidocaine 2% 10 mL หรือ bupivacaine 0.5% เพียงอย่างเดียวในการออกฤทธิ์สกัดกั้นเส้นประสาทที่รับรู้ความรู้สึกในผู้ป่วย end stage renal disease ที่มารับการผ่าตัด arteriovenous fistula ภายใต้เทคนิคการให้ยาระงับความรู้สึก infraclavicular approach brachial plexus block โดยใช้อัลตราซาวด์ร่วมกับการกระตุ้นเส้นประสาท musculocutaneous และเส้นประสาท radial

วัสดุและวิธีการ: เป็นการศึกษาแบบไปข้างหน้าในผู้ป่วย 90 ราย อายุมากกว่า 18 ปีที่มารับการผ่าตัด arteriovenous fistula ภายใต้การระงับความรู้สึก infraclavicular approach brachial plexus block โดยใช้อัลตราซาวด์ร่วมกับการกระตุ้นเส้นประสาท musculocutaneous และเส้นประสาท radial ผู้ป่วยได้รับการสุ่มออกเป็น 2 กลุ่ม คือ กลุ่ม B (46 คน) ผู้ป่วยจะได้รับ bupivacaine 0.5% 30 mL เพียงอย่างเดียว กลุ่ม BL (44 คน) ผู้ป่วยจะได้รับ Bupivacaine 0.5% 20 mL ผสมกับ Lidocaine 2% 10 mL ยาผสมที่ได้คือ bupivacaine 0.33% และ lidocaine 0.67% วิสัญญีพยาบาลผู้ได้รับการฝึกอบรมการทดสอบการทำงานของเส้นประสาทและไม่ทราบชนิดของยาชาที่ผู้ป่วยได้รับทดสอบความรู้สึกโดยใช้ pinprick แบ่งออกเป็น 3 ระดับ คือ 0 หมายถึง ไม่มีความรู้สึกอะไรเลย 1 หมายถึง มีความรู้สึกลดลง 2 หมายถึงมีความรู้สึกปกติ ระยะเวลาการเริ่มออกฤทธิ์ของยาชา นับจากเวลาที่ฉีดยาชาเสร็จจนมีความรู้สึกระดับ 1 หรือ 0 บริเวณผิวหนังที่เลี้ยงโดยเส้นประสาทเส้นใดเส้นหนึ่งของ brachial plexus ตามลำดับ วิสัญญีพยาบาลทำการบันทึกปริมาณยาชาที่ผู้ป่วยได้รับเพิ่มเติมระหว่างการผ่าตัด ระยะเวลาการออกฤทธิ์ระงับความรู้สึกและระยะเวลาการหย่อนตัวของกล้ามเนื้อ ความพึงพอใจของศัลยแพทย์ผู้ทำผ่าตัดจะถูกถามเมื่อเสร็จสิ้นการผ่าตัด และความพึงพอใจของผู้ป่วยจะถูกถามเมื่อ 24 ชั่วโมงหลังการผ่าตัด โดยแบ่งความพึงพอใจออกเป็น 6 ระดับ คือ 0 หมายถึงไม่พึงพอใจจนถึงระดับที่ 5 คือ พึงพอใจมากที่สุด

ผลการศึกษา: ไม่พบความแตกต่างของระยะเวลาการเริ่มออกฤทธิ์ของยาชา ระยะเวลาการออกฤทธิ์ของยาชา และความพึงพอใจของศัลยแพทย์และผู้ป่วยในกลุ่มที่ใช้ยาผสมระหว่าง lidocaine 2% กับ bupivacaine 0.5% เมื่อเปรียบเทียบกับการใช้ bupivacaine 0.5% เพียงอย่างเดียว

สรุป: การใช้ยาผสมระหว่าง lidocaine 2% 10 mL กับ 0.5% bupivacaine 20 mL ในการให้ยาระงับความรู้สึก infraclavicular approach brachial plexus block โดยใช้อัลตราซาวด์ร่วมกับการกระตุ้นเส้นประสาท musculocutaneous และเส้นประสาท radial สำหรับการผ่าตัด arteriovenous fistula ในผู้ป่วยไตวายระยะสุดท้ายไม่ช่วยให้ระยะเวลาการเริ่มออกฤทธิ์ของยาชาสั้นลง เมื่อเปรียบเทียบกับการใช้ bupivacaine เพียงอย่างเดียว