Singapore Med J 2014; 55(4): 229-232
doi:10.11622/smedj.2014057

Addition of clonidine or lignocaine to ropivacaine for supraclavicular brachial plexus block: a comparative study

Bhatia Rohan[1], MBBS, MD, *Payal Yashwant Singh*[1], MBBS, MD, *Khurana Gurjeet*[1], MBBS, MD

INTRODUCTION Clonidine is used with local anaesthetics to improve analgesia. However, the improvement conferred when clonidine is used together with ropivacaine is controversial. Thus, the present study aimed to evaluate the improvement in analgesia when clonidine is used together with ropivacaine for supraclavicular brachial plexus block.

METHODS This was a prospective, randomised, double-blind controlled study. A total of 75 patients who were scheduled to undergo supraclavicular block were randomly assigned into three groups (i.e. clonidine, lignocaine and control groups) of 25. Patients in all three groups received 20 mL of 0.75% ropivacaine. In addition to that, patients in the clonidine group received 1 mL of clonidine (150 µg) plus 9 mL of saline, patients in the lignocaine group received 10 mL of 2% lignocaine with adrenaline (1:200,000), and patients in the control group received 10 mL of saline. The characteristics of anaesthesia and analgesia for these three groups were assessed.

RESULTS The addition of 2% lignocaine with adrenaline to ropivacaine led to earlier onset of the sensory block (by 4.88 mins), but no increase in the duration of analgesia when compared to analgesia using ropivacaine alone. The addition of clonidine to ropivacaine led to earlier onset of sensory and motor blocks (by 2.88 mins and 3.28 mins, respectively), as well as an increased duration of sensory and motor blocks (by 222.64 mins and 192.92 mins, respectively) when compared to analgesia using ropivacaine alone. The total duration of analgesia was increased by 208.24 mins with clonidine when compared to analgesia using ropivacaine alone. There were no significant differences in sedation score and no side effects in all three groups.

CONCLUSION When compared to the use of ropivacaine alone, the addition of 150 µg clonidine to ropivacaine for brachial plexus block achieved earlier analgesic onset and improved duration of analgesia, without unwanted side effects.

Keywords: anaesthetic technique, clonidine, duration of analgesia, ropivacaine, supraclavicular brachial plexus block

INTRODUCTION

Brachial plexus blocks remain a well-accepted anaesthetic technique for surgical procedures on the upper limbs. Clonidine, when used as an adjuvant to intermediate or long-acting local anaesthetics, improves the duration of analgesia and anaesthesia in brachial plexus or peripheral nerve blocks.[1,2] Although ropivacaine is a chemical congener of bupivacaine, the effect of clonidine when added to ropivacaine for brachial plexus block remains controversial, with some studies not supporting the analgesia-enhancing effects of clonidine as an adjuvant to ropivacaine.[3-5] However, in these studies, the blocks were performed using an axillary approach. To the best of our knowledge, no previous study has combined the use of clonidine and ropivacaine for supraclavicular blocks. As the supraclavicular approach may have many advantages over the axillary approach (e.g. early onset, and complete and predictable anaesthesia for the entire upper extremity),[6] the present study was designed to evaluate the onset and duration of anaesthesia, analgesia and sensory/motor blockade following supraclavicular brachial plexus blocks in which clonidine was used as an adjuvant to ropivacaine.

METHODS

Following approval from the local ethics committee, a prospective, randomised, double-blind controlled trial was designed. Written informed consent was obtained from all patients selected for inclusion in the present study. The study included a total of 75 patients, who were aged ≥ 18 years, weighed ≥ 40 kg, had ASA (American Society of Anesthesiologists) physical status I–III, and were scheduled to undergo elective surgery on the upper extremity. Patients who refused to participate in the present study, had neurological diseases of the upper extremities, had contraindications to regional anaesthesia and any of the study drugs (i.e. clonidine, ropivacaine or lignocaine), and/or were pregnant or lactating, were excluded from the study.

Patients were randomly assigned to any one of three groups (i.e. either the clonidine, lignocaine or control group); each group had a total of 25 patients. The anaesthetist who performed the randomisation also prepared the drug solutions, but was otherwise not involved in the study. In the preoperative area, an intravenous (IV) line was established and IV midazolam 1–2 mg was administered to all 75 patients. The

[1]Department of Anaesthesiology, Himalayan Institute of Medical Sciences, Uttarakhand, India
Correspondence: Dr Y S Payal, Associate Professor, Department of Anaesthesiology, Himalayan Institute of Medical Sciences, Swami Ram Nagar, Dehradun, Uttarakhand 248140, India. dryspayal05@gmail.com

patients were then moved to the operating room, where their heart rate, respiratory rate, oxygen saturation and noninvasive blood pressure were monitored. The supraclavicular blocks were performed by an anaesthetist who was unaware of the composition of the local anaesthetic solution administered, as per the method described by Franco.[7] A 22-gauge 50-mm needle (Stimuplex®A 50; B.Braun, Melsungen, Germany) connected to a nerve stimulator (NM-20®; INMED Equipments Pvt Ltd, Vadodara, India) was inserted at an initial current output of 1.0 mA, 0.1 ms and 2 Hz frequency, which was gradually reduced to 0.2–0.5 mA. The local anaesthetic solution (30 mL) was injected into all patients following negative aspiration, while maintaining the visible twitch of muscle groups in the forearm.

Patients in the clonidine group (R_C) received 20 mL 0.75% ropivacaine with 9 mL 0.9% saline and 1 mL clonidine (150 µg). The patients in the lignocaine group (R_L) received 20 mL 0.75% ropivacaine with 10 mL 2% lignocaine with adrenaline (1:200,000). Patients in the control group (R_O) were given 20 mL 0.75% ropivacaine with 10 mL 0.9% saline. The final concentration of ropivacaine in the local anaesthetic solution was maintained at 0.5%.

Completion of injection was considered as time-0, and the sensory block was evaluated using the pin prick method[8] (score 0: sharp pain; score 1: touch sensation only; score 2: no sensation) at 2-min intervals from time-0 until complete sensory block was achieved. Onset time of sensory block (OTSB) was defined as the time interval (in mins) from time-0 to the time the sensory block started to be detected (i.e. score = 1). Time for complete sensory block (TCSB) was the time interval (in mins) from time-0 to the time complete sensory block was achieved (i.e. score = 2). Total duration of sensory block (TDSB) was the time interval (in mins) from the time complete sensory block was achieved to the time the score was < 2. Total duration of analgesia (TDA) was taken as the time interval (in mins) between the time complete sensory block was achieved and the time of first analgesic request.

Motor block was evaluated using the Modified Bromage Scale[9] (score 0: able to raise the extended arm at 90° for a full 2 s; score 1: able to flex the elbow and move the fingers, but unable to raise the extended arm; score 2: unable to flex the elbow, but able to move the fingers; score 3: unable to move the arm, elbow and fingers). Findings were recorded every 2 mins from time-0 until the complete loss of motor power. As with the sensory block, the onset time of motor block (OTMB) was defined as the time interval (in mins) from time-0 to the time the motor block started to be detected (i.e. score ≥ 1). Time for complete motor block (TCMB) was the time interval (in mins) from time-0 to the time complete motor block was achieved (score = 3). Total duration of motor block (TDMB) was the time interval (in mins) between the time complete motor block was achieved and the time when the score was < 3. Adequacy of the block was evaluated using the Allis clamp test.[9]

Heart rate, arterial blood pressure (systolic, diastolic and mean measurements) and arterial oxygen saturation were recorded every 5 mins from time-0 until the completion of surgery, and thereafter every 30 mins until recovery. Hypotension, which was defined as a decrease in mean arterial pressure of more than 25% from baseline, was treated with ephedrine 5 mg IV bolus. Clinically significant bradycardia (< 45 bpm) was treated with IV atropine 0.6 mg. Mild postoperative pain was treated with six-hourly IV paracetamol 1 g, while fentanyl 100 µg was added for moderate-to-severe pain. All patients were monitored until complete recession of motor and sensory blocks; the time to first analgesic requirement and the total analgesic dose administered were noted.

Sedation was assessed every 5 mins from time-0 until the end of surgery, and every 30 mins thereafter, with the use of the Sedation Scale[10] (1: awakened and alert; 2: sedated, but responding to verbal stimulus; 3: sedated, but responding to mild physical stimulus; 4: sedated, but responding to moderate or strong physical stimulus; 5: not arousable).

The sample size of the present study was determined according to the methodology described in previous studies.[11,12] Results were presented as mean ± standard deviation for parametric data and as percentages for nonparametric data. Data was analysed using standard statistical test softwares such as Microsoft Office Excel 2007 (Microsoft, Redmond, WA, USA) and IBM SPSS Statistics version 19.0 (IBM Corp, Armonk, NY, USA). Kruskal-Wallis H test was used to compare the data among the three patient groups and unpaired *t*-test was used to determine significant differences between the groups. A p-value of < 0.05 was considered statistically significant and a p-value of < 0.001 was taken to be highly significant.

RESULTS

Among the patients in the R_C, R_L and R_O groups, no significant differences were observed with respect to the following factors: age, gender, height, weight and duration of surgery (Table I). No instances of failed blocks necessitating the administration of general anaesthesia were noted in any of the three patient groups.

The onset of sensory and motor blocks was earliest in the R_L group (OTSB 3.84 ± 0.80 mins; OTMB 5.76 ± 1.05 mins) followed by the R_C group (OTSB 5.84 ± 0.55 mins; OTMB 6.80 ± 1.00 mins); onset was significantly delayed in the R_O group (i.e. the control group; OTSB 8.72 ± 1.13 mins; OTMB 10.08 ± 0.90 mins) ($p < 0.001$). Similarly, sensory and motor blocks were achieved in a shorter duration of time in the R_L group (TCSB 9.52 ± 1.33 mins; TCMB 14.32 ± 0.94 mins) compared to the R_C group (TCSB 11.80 ± 1.28 mins; TCMB 17.12 ± 1.30 mins). The achievement of sensory and motor blocks was significantly delayed in the R_O group (TCSB 15.12 ± 1.42 mins; TCMB 19.52 ± 0.87 mins) ($p < 0.001$). The total durations of the sensory and motor blocks were significantly longer in the R_C group (TDSB 450.08 ± 54.45 mins;

Table I. Characteristics of the patients who underwent elective surgery of the upper extremity (n = 75).

Variable	Mean ± SD			p-value
	R_O group (n = 25)	R_L group (n = 25)	R_C group (n = 25)	
Age (yrs)	38.20 ± 15.74	42.64 ± 16.39	39.04 ± 16.47	0.589
Gender*				0.803
Male	20 (80.0)	18 (72.0)	19 (76.0)	
Female	5 (20.0)	7 (28.0)	6 (24.0)	
Height (cm)	161.02 ± 5.95	162.78 ± 7.42	164.42 ± 7.41	0.265
Weight (kg)	60.10 ± 7.58	60.56 ± 10.49	62.96 ± 11.00	0.651
Duration of surgery (mins)	46.32 ± 38.03	58.52 ± 34.18	83.88 ± 51.08	0.052
Duration of block (mins)				
OTSB	8.72 ± 1.13	3.84 ± 0.80	5.84 ± 0.55	< 0.001†
OTMB	10.08 ± 0.90	5.76 ± 1.05	6.80 ± 1.00	< 0.001†
TCSB	15.12 ± 1.42	9.52 ± 1.33	11.80 ± 1.28	< 0.001†
TCMB	19.52 ± 0.87	14.32 ± 0.94	17.12 ± 1.30	< 0.001†
TDSB	227.44 ± 36.27	238.04 ± 35.10	450.08 ± 54.45	< 0.001†
TDMB	172.64 ± 40.86	183.76 ± 26.73	368.56 ± 59.68	< 0.001†
TDA	297.04 ± 24.80	298.04 ± 27.06	505.28 ± 48.39	< 0.001†

*Data is presented as no. (%). †Highly significant (i.e. p < 0.001).
OTMB: onset time of motor block; OTSB: onset time of sensory block; R_C group: group administered ropivacaine + clonidine; R_L group: group administered ropivacaine + lignocaine; R_O group: group administered ropivacaine + saline (i.e. control group); SD: standard deviation; TCMB: time for complete motor block; TCSB: time for complete sensory block; TDA: total duration of analgesia; TDMB: total duration of motor block; TDSB: total duration of sensory block

TDMB 365.56 ± 59.68 mins) than in the R_L group (TDSB 238.04 ± 35.10 mins; TDMB 183.76 ± 26.73 mins) and R^O group (TDSB 227.44 ± 36.27 mins; TDMB 172.64 ± 40.86 mins) (p < 0.001). TDA was also significantly longer (over 1.5 times) in the R_C group (505.28 ± 48.39 mins) than in the R_L group (298.04 ± 27.06 mins) and R_O group (297.04 ± 24.80 mins) (p < 0.001).

In the present study, the addition of clonidine to ropivacaine was not found to cause any significant increase in the incidences of hypotension or bradycardia. Sedation, a major side effect with the use of clonidine, was not seen in any of our patients. Three patients (two from the R_O group and one from the R_C group) had vessel injury, which was managed with pressure application. No haematoma formation was noted postoperatively.

DISCUSSION

In the present study, we found that the addition of 150 µg clonidine to 30 mL of 0.5% ropivacaine (R_C group) led to an earlier onset of sensory and motor blocks, as well as an increased duration of analgesia, when compared to the use of 0.5% ropivacaine alone (R_O/control group). The addition of 2% lignocaine with adrenaline to 0.5% ropivacaine (R_L group) led to the earliest onset of sensory and motor blocks among the three groups; however, this was without a significant improvement in the duration of analgesia. Our findings are in agreement with previous systematic reviews, which demonstrated that clonidine, when used as an adjuvant to local anaesthetics, improves anaesthesia and the analgesic duration of the local anaesthetic block.[1,2]

The early onset of sensory and motor blocks in the R_L group of the present study is likely related to the pharmacological properties of lignocaine. In the R_C group, the combined vasoconstrictive property of clonidine[13] and ropivacaine[14] may have led to the greater availability of these drugs at the vicinity of the nerve plexus; this may possibly account for the earlier onset of sensory and motor blocks seen in the R_C group, as compared to the R_O group. Studies have also reported that clonidine is effective in blocking the conduction of Aδ-fibres and C-fibres, and that it intensifies the conduction block of local anaesthetics.[15,16] Although a faster onset could have been achieved with the use of higher concentrations of ropivacaine, the concentration of ropivacaine was restricted to 0.5% in the present study because increasing concentrations of ropivacaine were not found to affect the duration of post-operative analgesia in previous studies.[17]

In the present study, the blocks were performed via the supraclavicular approach instead of the axillary approach, as the former was associated with faster onset[11] and many other advantages.[6] It should be noted that the brachial plexus is not surrounded by a 'sheath', instead it lies in a tissue plane closely surrounded by the clavicle, scapula, chest wall and humerus.[18] Elements of the brachial plexus (i.e. its trunks, divisions and cords) interlace and interlink at the supraclavicular level. As these elements are closer to each other at the supraclavicular level, the plexus is more compact at this level than at the axillary level. This means that, at the supraclavicular level, the connective tissues containing these nerves allow a more even spread of the drug solution,[19] making the use of 30-mL drug solutions sufficient and as effective as 40-mL drug solutions, which has been used in other studies for axillary blocks.[11,12,20,22]

Improvement in the duration of analgesia following the addition of clonidine to local anaesthetics has been reported in earlier studies.[11,12,20-22] Antinociception due to the action of adrenoceptors (e.g. clonidine on α2 receptors) is well documented in clinical trials conducted on animals and humans.[23] The analgesic property of clonidine is attributed

to its greater affinity for the α2 receptors that are located on the brainstem nuclei, including those on the locus ceruleus and those on the neurons in the superficial laminae of the spinal cord and primary afferent terminals. A decrease in the activity of these nuclei by α2 agonists supports the possibility of analgesic action at the spinal and supraspinal sites.[3,24] Although it is unlikely that the spinal and supraspinal effect is the mechanism that prolongs the analgesic effect of clonidine deposited at peripheral sites,[3] a central analgesic effect that results from the systemic absorption of clonidine cannot be excluded. Sia and Lepri demonstrated that clonidine does not provide postoperative analgesia when administered as the sole analgesic agent,[25] suggesting that synergistic activity is more likely the mechanism for the prolonged analgesic duration observed with the use of clonidine. The direct action of clonidine, independent of its action on α2 receptor nerve fibre conduction, has been demonstrated in some studies,[16,26,27] indicating another possible mechanism for its action as a local anaesthetic additive. Hutschala et al have postulated that the effect of clonidine is local.[28]

The mechanism of action for the prolonged duration of analgesia observed when clonidine is used as an adjuvant to ropivacaine has been reported to be multifactorial and complex.[11] While the synergistic effects of clonidine, or lignocaine, with ropivacaine were evident in the R_C and R_L groups in our study, we were unable to draw meaningful inferences regarding the underlying mechanisms involved from the available data, as the present study was not designed to elucidate the mechanism for prolongation of analgesia.

In the present study, the addition of 2% lignocaine with adrenaline to 0.5% ropivacaine was not found to improve the duration of analgesia, as ropivacaine is known to have intrinsic vasoconstrictive properties.[14] The prolonged duration of the motor block in the R_C group in our study is in agreement with the findings of a study by El Saied et al.[11] We did not observe any adverse effects such as sedation, arterial hypotension or bradycardia in our patients. The dose of clonidine (150 μg) used appeared to have minimal or no adverse effects among our patients, similar to the findings of El Saied et al.[11]

To conclude, the addition of clonidine to ropivacaine for analgesia was found to be safe and effective in the present study. In the clinical setting, the addition of clonidine to ropivacaine during supraclavicular brachial plexus block would achieve early operating conditions and prolonged analgesia. In contrast, the addition of lignocaine to ropivacaine resulted only in earlier onset of sensory and motor blocks, without improvement in the duration of analgesia.

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