Original Article

A randomised trial comparing block characteristics of a mixture versus sequential injections of lignocaine and ropivacaine for supraclavicular brachial plexus nerve block in patients undergoing upper limb surgery

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ABSTRACT

Background and Aim: There is no consensus on the appropriate use of mixtures of local anaesthetic drugs in various combinations for nerve blocks. We intended to compare short-acting lignocaine and long-acting ropivacaine as a mixture versus undiluted sequential injections on block characteristics of ultrasound-guided (USG) supraclavicular brachial plexus block for upper limb surgeries. **Methods:** A double-blinded randomised study was conducted on 64 adult patients scheduled for upper limb surgery who received 15 mL each of 2% lignocaine with adrenaline and 0.75% ropivacaine as a 1:1 mixture in the mixed group (Group M) or sequential injections in the sequential group (Group S) by using a USG technique. The primary outcome was the percentage of participants with complete four nerve sensory blocks at 10 minutes post block injection. Secondary outcomes were sensory and motor block characteristics till 30 minutes, total duration of analgesia, sensory and motor block, and complications. **Results:** Demographic characteristics and time taken for the procedure were similar. The percentage of participants with a complete four-nerve sensory block at 10 minutes was higher in Group S (69%) versus Group M (41%) (P = 0.04). Complete sensory and motor block rates were similar at 30 minutes. The block procedure time, total duration of analgesia, and sensory and motor block were similar in both groups. There were no major complications. **Conclusion:** Sequential lignocaine-ropivacaine, compared to the mixed injection technique, has a higher initial rate of sensory and motor block onset with a similar total block duration.

Keywords: Brachial plexus block, lignocaine, local anaesthetics, ropivacaine, sequential, supraclavicular brachial plexus block, ultrasonography

INTRODUCTION

Lipid-soluble local anaesthetics (LA) such as ropivacaine and bupivacaine are generally more potent and have a significantly longer duration of action as well as a more prolonged onset of action compared to intermediate-potency drugs such as lignocaine, mepivacaine, and prilocaine.[1,2] A combination of two LAs is often used in regional blocks to utilise the different clinical properties of the drugs to achieve a faster onset and longer block duration.[3] The total

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dose, pKa, drug deposition close to the nerve, and use of additives are some factors that influence the onset of nerve blocks, although the volume and concentration of the drug have an unclear role in the onset of the block.[1-4] Although mixing two LAs is relatively common in the clinical practice of such blocks, there is a mixed scientific opinion on such usage.[3,5-7]

When using two LA agents, literature on the use of sequential injections is scarce, more so in the supraclavicular brachial plexus block.[5,7,8] With that background, this study intended to compare the use of a short-acting drug (lignocaine) and a long-acting drug (ropivacaine) as a mixture versus undiluted sequential injections on block characteristics of ultrsonography (USG)-guided supraclavicular brachial plexus block in upper limb surgeries. It was hypothesised that giving sequential undiluted LAs might be more advantageous than providing mixtures of the same drugs to attain a faster block and a longer duration. The primary objective was to compare the percentage of patients with a complete sensory block 10 minutes after block injection of mixture versus sequential injection of lignocaine and ropivacaine. Secondary objectives were to compare the percentage of patients with first sensory and motor block onset and complete block at various time intervals till 30 minutes, block procedure time, total duration of sensory and motor blockade, duration of analgesia, and complications in the two groups.

METHODS

This double-blinded randomised comparative study was conducted on patients scheduled for upper limb surgery under USG-guided supraclavicular brachial plexus block. Patients were recruited into the study after approval from the institutional ethics committee (vide approval number AIIMS/IEC/20/115 dated 08/02/2020). Written informed consent was obtained to participate in the study and use the data for research and educational purposes. The trial was registered before patient enrolment at the Clinical Trials Registry-India (vide registration number CTRI/2020/03/024013; www.ctri.nic.in). The study was carried out according to the principles of the Declaration of Helsinki (2013) and good clinical practice. Inclusion criteria were subjects aged 18–70 years, all genders, weighing 60 kg and above, planned for unilateral upper limb surgery. Exclusion criteria were patient refusal, coagulation or bleeding disorders, local site infection, any nerve injury/neuropraxia/paralysis, history of allergy or anaphylaxis to ropivacaine or lignocaine, pregnant females, difficult or abnormal anatomy, and block failure due to technical reasons.

After the recruitment of subjects, they were randomly assigned to one of the two study groups using a computer-generated random sequence. Allocation concealment was done using opaque sealed envelopes, which were sequentially numbered. The patient and outcome assessor were blinded to group allocation. The sequential group (Group S) received a sequential injection of 15 mL of 2% lignocaine with adrenaline (1:2,00,000), followed by 15 mL of 0.75% ropivacaine. The mixed group (Group M) received a 1:1 mixture of 2% lignocaine with adrenaline (1:2,00,000) (15 mL) and 0.75% ropivacaine (15 mL), a total volume of 30 mL. All patients underwent a thorough pre-anaesthetic evaluation before the planned surgery.

On the day of surgery, after obtaining consent for surgery and anaesthesia, intravenous (IV) access was secured, and anxiolysis was given in the form of IV midazolam 1 mg. The block was performed in a block room adjoining the operation theatre (OT) with appropriate monitoring and resuscitation equipment. The anaesthesiologist and the assistant performing the intervention opened the envelope to prepare drugs and equipment for the block. After explaining the procedure again to the patient, a USG-guided supraclavicular brachial plexus block was performed, following which the patient was taken into the OT, and routine monitoring was applied (electrocardiogram, non-invasive blood pressure, and pulse oximetry) for the surgery.

USG scanning of the area was done before injection to achieve an optimal view of the supraclavicular brachial plexus and identify the subclavian artery, first rib, and pleura. A high-frequency 13-6 MHz linear USG probe (Edge-II, Fujifilm Sonosite Inc., Bothell, WA, USA) was used. Cleaning and draping of the area of injection were performed. Next, 1 mL of lignocaine (2%) with adrenaline (1:2,00,000) was injected at the needle insertion area. The needle insertion direction was from lateral to medial (a 22-G block needle of appropriate length) with an in-plane technique. The drug was injected into the lower and upper part of the nerve cluster by using a two-point injection technique. In Group S, 15 mL of 2% lignocaine with adrenaline was injected first (7.5 mL each at the two points of the plexus), followed by an injection of 15 mL of 0.75%

ropivacaine with the intent to surround the lignocaine drug already deposited. In Group M, 30 mL of the mixture of both LAs was directly deposited in the lower part of the cluster, followed by the upper part, with 15 mL in both areas. Based on previous literature and our departmental practice, a total volume of 30 ml LA was used in both groups.[9,10] An anaesthesiologist performed USG scanning and block with at least 3 years of work experience after post-graduation and experience performing at least 50 USG-guided supraclavicular nerve blocks. The study subject and the person recording the observations were blinded to the group allocation.

Demographic data such as age, gender, weight, height, and the type of surgery were recorded. The duration of the block procedure and the duration of surgery were also recorded. Sensory blockade was evaluated in the innervated area of the four nerves: musculocutaneous (lateral forearm), median (the palmar aspect of the second finger), radial (dorsum of the hand between the thumb and second finger), and ulnar (fifth finger). Motor blockade was assessed by elbow flexion (musculocutaneous), wrist flexion (median nerve), wrist extension (radial nerve), and flexion of the fourth and fifth fingers (ulnar nerve). A three-point evaluation scale assessed sensory and motor blocks for each muscle supplied by the four nerves, where sensory is 1 = no sensation, 2 = hypoesthesia, and 3 = normal sensation (to pinprick). For motor, 1 = complete paralysis, 2 = decreased motor function, and 3 = normal motor function.[11]

Sensory scores were noted at intervals of 3, 5, 7, 10, 15, and 30 minutes post block injection using a pinprick. Motor scores were recorded at 4, 8, 12, 16, and 30 minutes. The primary outcome was the percentage of patients with a complete sensory block (score 1) in all four nerve areas at 10 minutes post injection. Secondary outcomes were assessment of the onset of sensory and motor block and complete sensory and motor block at the time mentioned above. Other outcomes included duration of analgesia, duration of sensory block, duration of motor block, block failures, and complications (patients were monitored in the post-anaesthesia care unit every one hour and in the ward every 2 hours by the outcome assessor). Any additional requirements of IV fentanyl, LA supplementation via local infiltration (at any time during the surgery), or sedation (IV midazolam) were also noted during the surgery. No other systemic analgesics were given during or after surgery unless the patient complained of pain. At that time, injection/oral paracetamol 1000 mg was given, and the time was noted.

In some cases, with dressing or plaster *in situ* postoperatively, the complete return of sensory block was estimated by corroborating with the duration of analgesia and checking the sensation in the nearest available sensory area as a surrogate. Similarly, for the motor block, the nearest free joint was checked for power to estimate the duration of the block. Patients were also requested to note the time they perceived the return of motor power and convey it to the nursing staff so that the durations could be emphasised more precisely.

Outcomes were defined as follows. Onset of sensory block: the percentage of patients with a sensory score of 1 in any of the four nerves. Onset of motor block: the percentage of patients with a motor score of 1 in any of the four nerves. Complete sensory block: the percentage of patients with a sensory score of 1 in all four nerves. Complete motor block: the percentage of patients with a motor score of 1 in all four nerves. Block procedure time: time from insertion to removal of the needle. Duration of analgesia: time from completion of block procedure to first request for an analgesic. Duration of sensory block: time from completion of block procedure to complete return of sensation (score 3) in all four nerves. Duration of motor block: time from completion of block procedure to complete return of motor power (score 3) in all four nerves. A failed block was when conversion to general anaesthesia or a supplement block was required (these cases were not considered in the final analysis). Duration of surgery: from skin incision to completion of final dressing. Complications: LA toxicity, Horner's syndrome, phrenic nerve palsy, pneumothorax, and other block-related issues were noted.

The sample size was calculated based on a study where the percentage of subjects with a complete sensory block was 57% at 10 minutes post injection of a mixture of lignocaine and ropivacaine with supraclavicular brachial plexus block.[11] To be able to detect an increase in this rate to 90% at 10 minutes by using the sequential technique, we required 27 participants in each group to be able to reject the null hypothesis that there is no difference between the two techniques with a 5% alpha error and 80% power. Thirty-three people in each group were finally

required, assuming 20% block failures due to technical reasons and drop-outs.

Data were recorded in an Excel spreadsheet (MS Office Home, 2019). Instat version 3.05 (Graphpad Inc., Boston, MA, USA) was used for data analysis. Numerical data were expressed as mean [standard deviation (SD)], and categorical data in percentages. Parametric variables (all normally distributed continuous numerical data) were compared using unpaired *t*-test, non-parametric data by the Wilcoxon rank sum test, and categorical data (all proportions including the percentage of participants with sensory or motor nerve block at various time intervals) by the Fisher's exact test. $P \leq 0.05$ were considered significant.

RESULTS

A total of 70 initial participants were considered for participation, and after exclusion at various stages, a final of 64 (32 in each group) were analysed [Figure 1]. Demographic variables, including age, gender, height, and weight, were similar in both groups. The proportion of patients requiring LA, analgesic, or sedation supplementation and the duration and type of surgery were comparable [Table 1]. Block procedure time, the total duration of analgesia, and sensory and motor block were comparable in both groups [Table 2]. There was one case of Horner's syndrome in the sequential group, which was resolved by the end of the surgery. There were no other block-related complications in any of the patients.

Onset of sensory block: the proportion of patients with a sensory score of 1 in any of the four nerves at 3, 5, 7, and 10 minutes was higher in Group S but was statistically similar in both groups [Figure 2]. The

Table 1: Demographic and operative data

Characteristics	Group S (*n*=32)	Group M (*n*=32)
Age (years)	31.86 (14.69)	32.88 (14.94)
Height (cm)	162.28 (7.91)	163.16 (9.68)
Weight (kg)	66.13 (7.44)	65.25 (6.49)
Male	22	24
Female	10	8
Fentanyl/LA/sedation supplementation	1	2
Duration of surgery (min)	136.43 (82.46)	126.25 (48.72)
Type of surgery		
Elbow surgery	1	2
Forearm surgery	9	6
Wrist surgery	10	8
Hand/finger surgery	12	16

Data expressed as mean (standard deviation) or numbers. LA=local anaesthesia, *n*=number of patients

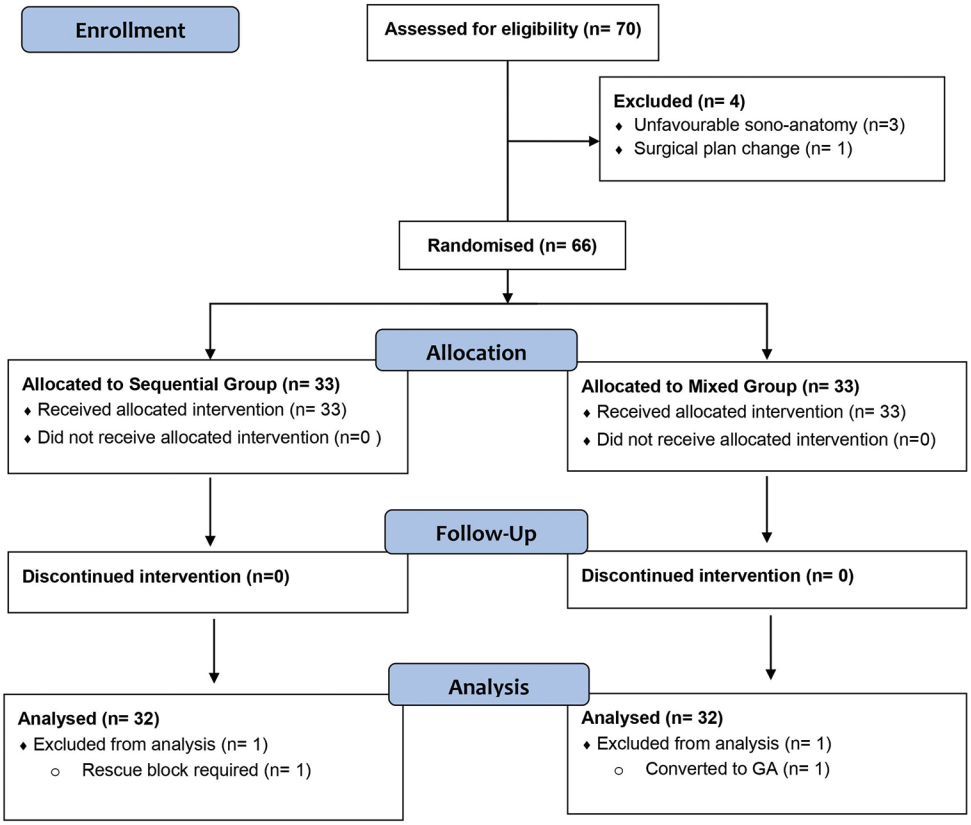

Figure 1: Consolidated standards of reporting trials (CONSORT) flow chart for patient recruitment. GA=General anaesthesia

onset of motor block: the proportion of patients with a motor score of 1 in any of the four nerves at 4, 8, and 12 minutes was similar in both groups [Figure 2].

Complete sensory block: the proportion of patients with a sensory score of 1 in all four nerves was higher in Group S at all time points and, at 10 minutes, was significantly higher in Group S (69%) compared to Group M (41%), ($P = 0.044$). At the end of 30 minutes in Group M, 12% of patients had failed to achieve a score of 1 in all four nerves. In Group S, a complete block was achieved in 100% of patients at 30 minutes. Complete motor block: the proportion of patients with a motor score of 1 in all four nerves was statistically similar in both groups at all time points. At the end of 30 minutes, in Group M, 19% of patients had failed to achieve a motor score of 1 in all four nerves compared to 6% in Group S [Figure 3].

DISCUSSION

We observed that the percentage of patients with complete four nerve sensory blocks at 10 minutes post injection was significantly higher in Group S compared to Group M. This difference decreased over time and remained till 30 minutes post block. Similar findings were observed for the motor block as well.

Most of the research on using LA mixtures in regional nerve blocks has been conducted on lignocaine and bupivacaine.[12,13] Following the use of two different LA agents in regional nerve blocks, the question of how to use the drugs arose, which has led to some recent research on the use of sequential injections. Jafari *et al.*[5] utilised a sequential technique while comparing two different mixture combinations of LAs for interscalene blocks. Gadsden *et al.*[8] tested the sequence of a short -acting followed by a long-acting LA in inter-scalene blocks versus vice versa and found no difference in outcomes due to the order of the sequence. Roberman *et al.*[7] compared mixed versus sequential injections in supraclavicular brachial plexus block by using a combination of ropivacaine (0.5%) and mepivacaine (1.5%), similar to the current study.

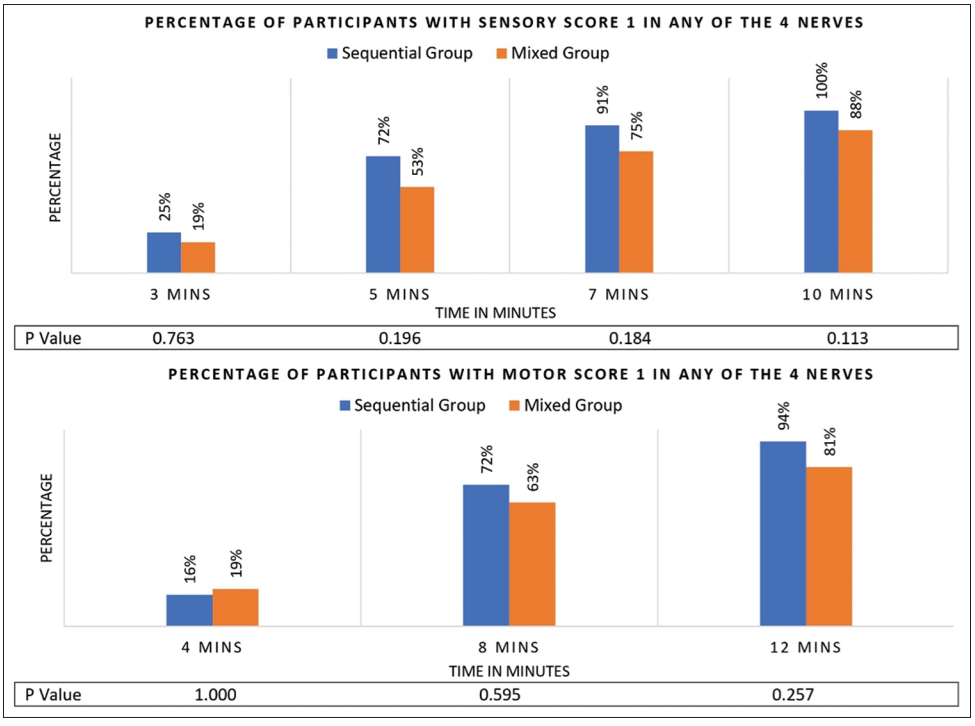

Figure 2: Block characteristics of the first onset of sensory and motor block. MINS = minutes

Table 2: Comparison of duration of block and block procedure time

Characteristics	Group S (*n*=32)	Group M (*n*=32)	*P*
Duration of analgesia (min)	406.93 (166.88) (356.76, 467.12)	421.43 (157.31) (364.71, 478.16)	0.722
Duration of complete sensory return (min)	376.87 (131.89) (329.32, 424.43)	399.68 (120.64) (356.18, 443.19)	0.473
Duration of complete motor return (min)	365.68 (112.36) (325.17, 406.21)	382.18 (113.14) (341.39, 422.99)	0.561
Block procedure time (min)	5.46 (2.00) (4.75, 6.19)	4.87 (1.83) (4.22, 5.53)	0.264

Data expressed as mean (standard deviation) (95% confidence interval). LA=local anaesthesia, *n*=number of patients

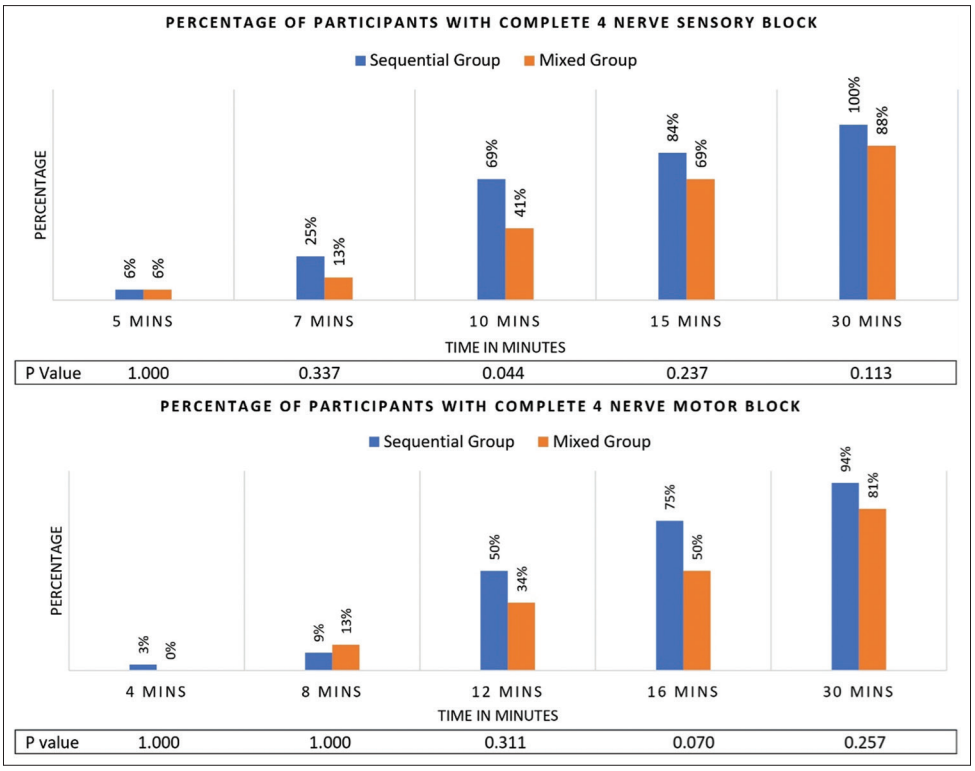

Figure 3: Block characteristics of complete sensory and motor block. MINS = minutes

Roberman *et al*.[7] reported that the time to complete sensory block was similar in the sequential versus the mixed injection groups. However, in contrast to the current study, the time to complete the motor block was faster in the mixed group. One main difference in this study was a 90-second gap between injections in the sequential group, although that does not explain why motor block would be faster in the mixed group. Another recent similar study by Gunjiyal *et al*.,[14] with 2% lidocaine and 0.5% bupivacaine, had a 120-second gap in the sequential group and found no differences in sensory and motor block characteristics between the sequential and the freshly mixed group.

In the current study, at the end of the block assessment period of 30 minutes, Group M had a higher percentage of patients who failed to achieve a total of four nerve sensory or motor blocks compared to Group S, which is perhaps a reflection of the density of block, which may be compromised due to dilution of the drug in Group M. However, these did not lead to block failure or any issues during the surgery in those patients.

In the present study, the percentage of patients with first sensory and motor block onset (any one nerve) was higher in Group S at various time points from LA injection (but clinically and statistically insignificant). In the study by Roberman *et al*.[7] and Gunjiyal *et al*.,[14] the time to onset of the first sensory block was similar in both sequential and mixed groups, identical to the current study's finding.

The total duration of sensory and motor block, as well as the duration of analgesia, was also similar in Group S versus Group M in the current study, which is in line with the findings of Roberman *et al*. and Gadsden *et al*.[7,8] This possibly reiterates that the duration of action is related to the total dose of the LA given, either as a mixed or a sequential injection, even if there are differences in the initial block characteristics.[1,2]

In the current study, there was no significant difference in the time taken to perform the block using sequential versus mixed injection of the LAs. Although the sequential technique involved more needle path changes than Group M, there were no specific complaints from the patients in Group S and no complications related to the block in either of the groups. Unlike the two studies above, in the present study, there was no planned delay between the two LA in the sequential group.[7,14]

The study has a few limitations. The study can only be extrapolated to the technique of giving mixtures of LA, not mixture versus single agent. A third only ropivacaine group can be added as a control in future

studies. Due to the small margins of the time requiring a high measurement frequency of multiple variables, the exact measurement of time to event was not feasible for the onset parameters. Thus, we performed a population analysis at various time points from block injection (percentage of patients or success rate of a certain block characteristic).

CONCLUSION

Compared to the mixed injection technique, the sequential injection of lignocaine and ropivacaine has a higher rate of sensory and motor block onset initially. Still, the difference is minimal 30 minutes after block injection. Both groups have similar total durations of sensory and motor block and duration of analgesia.

Study data availability

De-identified data may be requested with reasonable justification from the authors (email to the corresponding author) and shall be shared after approval as per the authors' Institution policy.

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Conflicts of interest

There are no conflicts of interest.

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