

Effect of Adding Different doses of Atracurium to Lidocaine on the Quality and Safety of Local Intravenous Anaesthesia for Upper Extremities Surgery

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Abstract

Background: Intravenous regional anesthesia (IVRA) was first described by August Bier in 1908 for anesthesia of the hand and forearm. The primary advantages of IVRA are its simplicity, reliability, and cost-effectiveness with high success rates. Various adjuncts added to LA have been investigated in an attempt to improve the quality of IVRA, including muscle relaxants. Non-depolarizing neuromuscular blocking agents can be of benefit in hastening the onset of motor block and creating a more profound muscle relaxation state. These benefits have been found to facilitate fracture reduction and also improve overall analgesia in young, muscular patients without clinically evident side effects.

Aim of Study: The aim of this study was to evaluate the effects and safety of different doses of atracurium when added to lidocaine for IVRA, on quality and duration of anaesthesia by determining the duration of onset and regression times of sensory and motor blocks, intraoperative and postoperative analgesia.

Patients and Methods: The current randomized, clinical trial was conducted on 60 patients considered candidates for upper extremities surgery in Alqassim National Hospital, Saudia Arabia. The patients were randomly assigned into four groups. Group 1 (control group) only received 3mg/kg lidocaine, Group 2 received 3mg/kg lidocaine plus 3mg atracurium, Group 3 received lidocaine 3mg/kg plus 5mg/kg atracurium, and group 4 received lidocaine 3mg/kg plus 10mg/kg atracurium. The sensory and motor blocks, tourniquet pain, the amount of administered intraoperative analgesics, patient and surgeon satisfaction, and side effects were analyzed in the groups using statistical tests.

Results: The time for onset of sensory and motor blocks in group 2, group 3, and group 4 was significantly shorter than group 1 ($p < 0.05$). The total intraoperative pethidine was significant in the three studied groups when compared to the control group ($p < 0.05$) it was less in group 2, group 3, and group 4 than in group 1. In terms of the recovery time of the

sensory block, there were no significant differences between the control group and the other three studied groups. The tourniquet pain in groups 2, 3, and 4 was significantly lower than in group 1 ($p < 0.05$). Motor recovery time was significantly more rapid in the control group in comparison to the other three groups ($p < 0.05$). As regards the quality of anesthesia evaluated by the anesthesiologist and the surgeons it was significantly more satisfaction in group 3 and group 4 compared with group 2 and the control group ($p < 0.05$). No significant difference was observed in the postoperative pain and the side effects of the lidocaine or the atracurium among the groups ($p > 0.05$).

Conclusion: The addition of different doses of atracurium to lidocaine for IVRA resulted in fast onset of sensory and motor block, a decrease in the severity of tourniquet pain, more satisfaction for the patients and surgeons without side effects from increasing atracurium doses.

Key Words: Intravenous anaesthesia – Regional – Atracurium – Lidocaine.

Introduction

INTRAVENOUS regional anesthesia (IVRA) was first described by August Bier in 1908 for anesthesia of the hand and forearm. IVRA is suitable for operations of the distal extremities, in situations where it is safe and easy to apply an occlusive tourniquet. It is mainly used for surgical procedures of the upper extremity, but it can also be used for procedures involving the lower extremity [1]. The primary advantages of IVRA are its simplicity, reliability, and cost-effectiveness with success rates varying between 94% and 98% [2,3]. Lidocaine is the most frequently used local anesthetics (LA) for IVRA. Despite its benefits, it has a relatively brief duration of action which may limit the post-operative analgesia that can be provided [4].

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Various adjuncts added to LA have been investigated in an attempt to improve the quality of IVRA, including opioids, muscle relaxants, non-steroidal anti-inflammatory drugs (NSAIDs), clonidine, potassium, and alkalizing agents. Evidence indicates that non-depolarizing neuromuscular blocking agents can be of benefit in hastening the onset of motor block and creating a more profound muscle relaxation state. These benefits have been found to facilitate fracture reduction and also improve overall analgesia in young, muscular patients [5].

In addition to making the surgery easier, blockade of the muscle spindles may theoretically alleviate muscle spasm and reduce pain during and after surgery. Muscle relaxants act at the level of the muscle spindle and reduce the central input from these structures [6].

Patients and Methods

The study protocol was approved by the ethical committee of Alqassim National Hospital from January 2021 to March 2022. Informed consent was obtained from sixty adult (18 to 65 years), ASA physical status I & II patients scheduled for elective hand surgery (carpal tunnel, trigger finger, tendon release and tendon repair). Patients with Raynaud disease, sickle cell anemia, a history of allergy to any drug used or crushed hand injury were excluded. Also, Patients who had bleeding tendency, on anticoagulant or antiplatelet therapy, had history of muscle weakness were excluded.

Routine monitoring was established, including electrocardiography, non-invasive blood pressure and oxygen saturation. Then two cannulae were placed: One in a vein on the dorsum of the operative hand for local anesthetic and muscle relaxant injection and the other in the opposite hand for crystalloid infusion. A double tourniquet was positioned on the upper operative arm. The operative arm was elevated for 2min and was then exsanguinated with an Esmarch bandage; a pneumatic tourniquet was then placed around the upper arm, and the proximal cuff was inflated to 100mmHg more than the systolic blood pressure to a maximum of 250mmHg, and the bandage was removed. Circulatory isolation of the arm was verified by absence of a radial pulse, and a loss of the pulse oximetry tracing in the ipsilateral index finger.

Patients were randomly allocated into Four equal groups (15 patients each): Group 1: IVRA was achieved using 3mg/kg body weight lidocaine 2 % diluted with saline to a total volume of 40ml,

Group 2: IVRA was achieved using 3mg of atracurium besylate plus 3mg/kg body weight lidocaine 2% diluted with saline to a total volume of 40ml, Group 3: IVRA was achieved using 5mg of atracurium besylate plus 3mg/kg lidocaine 2% diluted with saline to a total volume of 40ml and Group 4: Received a mixture of 10mg/kg of atracurium besylate, plus 3mg/kg lidocaine 2% diluted with saline to a total volume of 40ml.

Sensory block was assessed by pinprick with a 22-gauge short-beveled needle, every 30 second. Patient response was evaluated in the dermatomal sensory distribution of the medial and lateral antebrachial cutaneous, ulnar, median, and radial nerves. Motor function was assessed by asking the patient to flex and extend his/her wrist and fingers; complete motor block was noted when no voluntary movement was possible.

Onset of sensory block was defined as the time elapsed from injection of the study drug to sensory block achieved in all dermatomes, and onset of motor block was defined as the time elapsed from injection of the study drug to complete motor block.

After sensory and motor block onset, the tourniquet (distal cuff) was inflated to 250mm Hg, the proximal tourniquet was released, and surgery was started. Heart rate, systolic and diastolic blood pressure and oxygen saturation were monitored before tourniquet application and then throughout the surgery. All the procedures were performed by anesthesia specialist who was blind to the random allocations.

The onset and regression times for sensory and motor blocks and the severity of intraoperative pain (tourniquet pain) were recorded.

The severity of intraoperative pain was assessed using 10cm VAS (Visual Analogue Scale) every 5 minutes after tourniquet application where 0 = the absence of pain and 10 = worst possible pain. Patients with intraoperative VAS score more than 3 were given pethidine 50mg slowly intravenous. The number of patients and total dose of pethidine were recorded. The tourniquet was not deflated before 45min. At the end of the surgery, the tourniquet was deflated gradually. Sensory recovery time (the time elapsed from tourniquet deflation to recovery of sensation in all dermatomes, determined by pinprick test) and motor block recovery time (the time elapsed from tourniquet deflation until movement of fingers) were recorded.

Postoperative pain was assessed by VAS at 5 minutes after tourniquet deflation and at 1, 2, 4,

6, 8 hours postoperatively. Intravenous pethidine 50mg was administered if the VAS was more than 3 in the first 8 hours postoperatively. The first analgesic requirement time was also noted (the time elapsed from tourniquet release until the first request for analgesic). At the end of the procedure, the IVRA cannula is removed and the cuff deflated - close observation of the patient is crucial at this point, as this may result in the systemic release of local anaesthetic and muscle relaxant. Incidence of side effects such as tinnitus, dizziness, convulsions, respiratory compromise, muscle weakness were recorded in the four studied group.

After the operation the anesthesiologist blinded with the type of adjuvant recorded the quality of anesthesia as follow: Excellent = 4 where the patients were completely satisfied with the anesthesia without complaint, very good = 3 where the patients slightly complained but continued without analgesics, good = 2 where the patients slightly complained and continued with supplemental analgesics, bad = 1, patients couldn't continue and received general anesthesia.

Qualification of the surgical condition such as disturbing movement of the arm and too much bleeding was assessed by the surgeon who did not know group allocation according to the following numeric scale: 0 = unsuccessful, 1 = poor, 2 = acceptable and 3 = perfect [7].

Statistical analysis:

Data were expressed as frequency and percentage for categorical variables, and mean \pm standard deviation (SD) for the continuous variables. To compare continuous variables, the analysis of variance (ANOVA), and to compare categorical variables, chi-square tests were used. To analyze data about the level of pain at different intervals, repeated measures ANOVA was used. Data analysis was performed with SPSS version 22 at a p -value <0.05 as the level of significance.

Results

Sixty patients were assessed for eligibility to participate in the study, all of them were randomized, allocated into 4 groups, and all of them continued the study to be analyzed. There was no significant difference between the four groups as regards demographic data, ASA classification, surgery duration, and tourniquet time (Table 1). As regards the characteristics of the block, it was found that the onset of sensory block was significantly rapid in group 4 (1.43 ± 1.33 min) followed

by group 3 (1.73 ± 0.38 min), group 2 (1.75 ± 0.48 min), and finally the control group (3.51 ± 0.24 min). This difference was significant to the control group. The onset of motor block was significantly faster in group 4 (2.69 ± 0.29 min), group 3 (2.80 ± 0.43 min), and group 2 (4.11 ± 0.77 min) in comparison to the control group (7.60 ± 0.77 min). Sensory recovery time after tourniquet deflation was earlier in the control group (7.53 ± 0.67 min) when compared to the other groups, as group 4 was (9.26 ± 1.45 min), group 3 (7.87 ± 1.91 min), and group 2 (7.93 ± 1.67 min) without significant difference between the adjunct groups. Motor recovery time was significantly more rapid in the control group (4.80 ± 1.22 min) in comparison to the other three groups where it was (11.80 ± 3.22 min) in group 2, (23.963 ± 3.79 min) in group 3, and (25.66 ± 3.36 min) in group 4 with significant difference between group 3 and group 4 in comparison to group 2 (Table 2). As regards the tourniquet pain which was assessed by the VAS it was significantly higher in the control group than the adjuvant groups at all study times (5min interval). There was no significant difference between the three adjuvant groups (Fig. 1). Intraoperative Pethidine doses required to overcome tourniquet pain were significantly higher in the control group (55.66 ± 4.41 mg) when compared to the adjuvant groups as it was (34.66 ± 8.41 mg) in group 2, (28.23 ± 7.35 mg) in group 3, and (27.33 ± 5.61 mg) in group 4. There was no significant difference between the three adjuvant groups (Table 3).

As regards postoperative pain which was assessed by VAS it was significantly higher in the control group more than the adjuvant groups at all the study times (first 8 hours postoperative) (Fig. 2), and the time to first analgesic request was more prolonged in group 3 (11.08 ± 1.81 min), followed by group 4 (10.13 ± 1.31 min), group 2 (9.13 ± 1.49 min), and control group (8.53 ± 1.49 min). There was no significant difference between the three adjuvant groups and the control group (Table 3). As regards the quality of anesthesia evaluated by the anesthesiologist and the surgeons there were significant differences in group 3 and group 4 when compared to group 2 and the control group (Table 4).

As regards the side effects, there was one patient in group 4 and one patient in group 3 suffered from transient post deflation diplopia after deflation of the tourniquet and he was reassured, two patients in group 1, two patients in group 2 and one patient in group 3 complained from tinnitus.

Table (1): Demographic data.

	Group 1 (n=15)	Group 2 (n=15)	Group 3 (n=15)	Group 4 (n=15)	p- value
Age (years)	38.53±14.80	36.53±14.80	41.33±9.11	36.86±10.19	0.132
<i>Gender:</i>					
Male / Female	11/4	10/5	10/5	9/6	0.883
Weight	76.6±5.1	71.7±4.8	69.8±6.9	68.8±4.9	0.876
Duration of surgery	49±5.68	44±5.78	51.46±6.03	48.49±9.73	0.491
ASA I/II	10/5	12/3	10/5	13/2	0.782
Duration of tourniquet (min)	55.7±1.9	48.9±2.6	57.7±3.1	56.8±1.9	0.892

**p*<0.05.

Table (2): Motor and sensory block (onset and recovery).

	Group 1 (n=15)	Group 2 (n=15)	Group 3 (n=15)	Group 4 (n=15)	p- value
Onset of sensory blockade (min)	3.51±0.24	1.75±0.48*	1.73±0.38*	1.43±0.33*	0.001
Onset of motor blockade (min)	7.60±0.77	4.11±0.77*	2.80±0.03*	2.69±0.09*	0.001
Recovery from sensory blockade (min)	7.53±0.67	7.93±1.67	7.87±1.91	9.26±1.45	0.537
Recovery from motor blockade (min)	4.80±1.22	11.80±3.22*	23.963±3.79*#	25.66±3.36*#	0.001

**p*<0.05. # Intergroup differences.

Table (3): Intraoperative and postoperative analgesic needs.

	Group 1 (n=15)	Group 2 (n=15)	Group 3 (n=15)	Group 4 (n=15)	p- value
Intraoperative pethidine (mg)	55.66±4.41	34.66±8.41*	28.23±7.35*	27.33±5.61*	0.001
Time to first pethidine request (min)	8.53±1.49	9.13±1.49	11.08±1.81	10.13±1.31	0.631

**p*<0.05.

Table (4): Quality of anesthesia evaluated by patients and surgeon.

	Group 1 (n=15)	Group 2 (n=15)	Group 3 (n=15)	Group 4 (n=15)	p- value
Quality of anesthesia (patients)	3 (2-4)	3 (2-4)	1 (1-3)*	1 (1-3)*	0.00
Quality of anesthesia (surgeon)	3 (2-4)	3 (2-4)	1 (1-3)*	1 (1-3)*	0.00

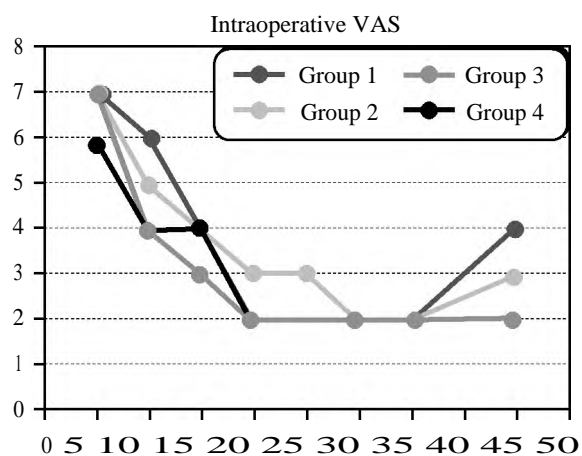
Values are presented as median (range). **p*<0.05.

Fig. (1): Intraoperative pain score (VAS).

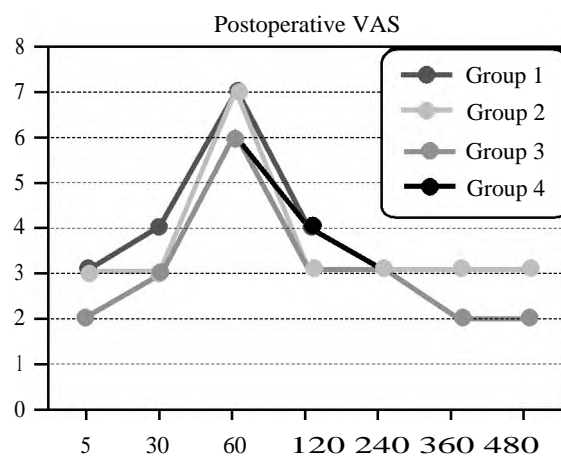


Fig. (2): Postoperative pain score (VAS).

Discussion

Intravenous regional anesthesia (IVRA) is a common, safe, and simple technique, is applicable for short, simple surgeries on the upper and lower limbs. IVRA is still being used in the emergency room, outpatients and high-risk patients who required safe anesthesia. IVRA offers a favorable risk benefit ratio, cost-effectiveness, sufficient muscle relaxation and analgesia. New upcoming methods for monitoring, specialized personnel and improved emergency equipment made IVRA safer than other anesthetic plans [8].

Anaesthesia during IVRA is produced by multiple mechanisms, a block of peripheral small nerves and nerve endings, a block of nerve trunks at a proximal site and ischemia which blocks nerve conduction and motor end plate function [1].

A major limiting factor for the use of IVRA is the tourniquet pain and lack of adequate postoperative analgesia. The etiology of tourniquet pain remains unclear. It may arise from ischemia of peripheral neurons or nociceptors distal to the tourniquet, or nerve fiber activation directly under it, again because of ischemia [5].

Several clinical studies have demonstrated that the use of additives to the local anesthetic agents in IVRA may overcome these two problems thus producing better tourniquet tolerance and satisfactory postoperative analgesia [6].

Amongst these additives that were used, atracurium. The probable mechanism of atracurium might be the blockage of the function of motor end plate before the appearance of upper extremity ischemia in IVRA; thus the sensory and motor block onset time are shortened and the quality of anaesthesia enhanced [2]. On the other hand, atracurium besylate primarily undergoes pH and temperature-dependent chemical (or Hoffman) degradation. Hoffman degradation is inhibited in the ischemic limb because of metabolic acidosis [8].

We observed from this study that adding atracurium to lidocaine for IVRA fastened the onset and delayed the offset of the motor block, reduced the tourniquet induced pain but did not affect the postoperative analgesic requirements. However, increasing the doses of atracurium added to lidocaine fastened the onset and delayed the offset motor blocks improved patient and surgeon satisfaction. In this study, we reported minor side effects in all the studied groups in the form of mild tinnitus and postdeflation diplopia which disappeared spontaneously.

In line with the findings of the present study, Elhakim M, Sadek RA, [10] studied the clinical advantages of using muscle relaxant with lidocaine for IVRA in Forty adult patients undergoing hand surgery. Two groups received either 40ml 0.5% lidocaine or 40ml 0.5% lidocaine with 2mg of atracurium. The atracurium group of patients had a significantly greater degree of muscle relaxation, easier reduction of fractures, and better operative conditions ($p < 0.01$). Less pain was also reported during surgery ($p < 0.025$), 5 and 15min after release of the tourniquet ($p < 0.01$). there was no difference in the speed of onset of block between the two groups.

Esmaoglu et al., [2] determined the onset and regression time of motor and sensory block, and the quality of anaesthesia and postoperative analgesia by the addition of cisatracurium to local anesthetic solution in small doses in IVRA. The onset time of sensory and motor block in the cisatracurium group was significantly shorter than in the control group. The quality of anaesthesia was better in the cisatracurium group than in the control group, and the difference was statistically significant which is consistent with the present study.

On the other hand, Kurt et al. [11] investigated 33 patients. Plain lidocaine solution was administered to group 1. Alfentanil (0.5mg) and atracurium (3mg) were added to the lidocaine solution in groups 2 and 3, respectively. The onset of the motor block, intra- and postoperative pain scores, and the duration of postoperative analgesia were similar in all groups. They concluded that no clinical benefits of adding alfentanil or atracurium to lidocaine solution for intravenous regional anaesthesia of the arm which is not agreed with the present study.

Haider, H.S., & Mahdi, F.A. [12] concluded that drug combination of ketamine and atracurium to small doses of lidocaine lead to rapid onset of sensory block, motor block, and low VAS score for pain and decrease the adverse effect of Bier's block when compared to lidocaine group which is agreed with our results.

In this study, all of patients in the four groups tolerated the IVRA without complications, and the surgeons were well satisfied with the anesthetic method. McGlone et al., [9] found that the addition of 2mg of Atracurium to the Bier's Block improved the ease of reduction (p less than 0.025) and the quality of analgesia (p less than 0.05). The authors concluded that the addition of Atracurium to a Bier's Block is useful in selected patients with a wrist fracture.

Flamer and Peng [13] stated in their review that the combination of fentanyl and muscle relaxants (pancuronium, atracurium, mivacurium, cisatracurium) can yield the same value of IVRA with a 50% decrease in the local anesthetic dose, but with potentially slower onset of sensory block.

In conclusion, the addition of different doses of atracurium to lidocaine for IVRA resulted in fast onset of sensory and motor block, with a prolonged offset of motor block, a decrease in the severity of tourniquet pain, improving surgical manipulation and patient satisfaction without causing significant systemic side effects.

One of the strengths of the current study was a random allocation of participants and a lack of difference regarding demographic characteristics among the study groups; hence, the confounding impacts of such features were eliminated due to the homogeneity of the study groups. And the use of different doses of agents administered in the current study to compare their effectiveness and side effects.

Declarations:

- *Competing interests:* The authors declare that they have no competing interests. No support from any organization for the submitted work and no financial relations with any organizations.
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- *Authors contributions:* Mohamed Abdallah Abdelnaser performed the study, analyzed data, and co-wrote the paper. Magdy Hassan Abdeldayem shared in the study design. Mohamed Ahmed Elsayy shared in data collection and Ahmed Fetouh co-wrote the paper. All authors read and approved the final version of the manuscript.

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تأثير إضافة جرعات مختلفة من عقار الأتراكوريوم إلى عقار الليدوكائين على جودة وسلامة التخدير الوريدي الموضعي لجراحة الأطراف العلوية

تم وصف التخدير الموضعي بالوريدي في عام ١٩٠٨ لأول مرة بواسطة أوغسط بيار لتخدير اليد والساعد. ومن المميزات الأساسية لهذا النوع من التخدير البساطة وسرعة التنفيذ والفاعلية من حيث التكلفة المادية مع معدلات نجاح عالية. في العادة يتم التخدير بحقن عقار الليدوكائين في الوريد الموجود في اليد المراد إجراء الجراحة بها بعد استخدام رباط في أعلى الكوع (العاصبة) لمنع وصول العقار إلى الدورة الدموية وتركيز الدواء في الذراع المصاب. ولتحسين هذا النوع من التخدير يتم إضافة بعض العقاقير إلى الليدوكائين لزيادة فاعلية التخدير ولزيادة فترة تسكين الألم أثناء وبعد الجراحة. من هذه العقاقير عقار الأتراكوريوم وهو ينتمي إلى مجموعة مرخيات العضلات الذي يستخدم بكثرة في التخدير العام. يعمل عقار الأتراكوريوم على إرخاء عضلات الذراع ومن ثم يقلل أو يلغي حركة العضلات في هذا الذراع وبذلك يكون الإجراء الجراحي أكثر سهولة.

أجريت التجربة السريرية العشوائية الحالية على ٦٠ مريضاً يعتبرون مرشحين لجراحة الأطراف العلوية. تم تقسيم المرضى بشكل عشوائي إلى أربع مجموعات. تم حقن المجموعة الأولى (المجموعة الضابطة) فقط ٣ ملغم/كغم من الليدوكائين، تلقت المجموعة الثانية ٣ ملغم/كغم من الليدوكائين بالإضافة إلى ٣ ملغم/كغم أتراكوريوم، والمجموعة الرابعة تلقت ليوكائين ٣ ملغم/كغم مع ١٠ مجم/كجم أتراكوريوم. تم تحليل معدل الاحساس والحركة والألم أثناء وبعد الجراحة وكمية المسكنات المعطاة أثناء العملية وبعد العملية ومعدل رضا المريض والجراح والآثار الجانبية في المجموعات باستخدام الاختبارات الإحصائية.

وكانت النتائج كالآتي: كان وقت اختفاء الاحساس والحركة في المجموعة الثانية والمجموعة الثالثة والمجموعة الرابعة أقصر بشكل ملحوظ إحصائياً عندما تم مقارنته بالمجموعة الأولى. أما بالنسبة للاحتياج لأعطاء مسكن البيثيديين أثناء الجراحة لوحظ أن احتياج المرضى للمسكن في المجموعات الرابعة والثالثة والثانية كان أقل بشكل ملحوظ إحصائياً على الترتيب عندما قورن باحتياج المرضى في المجموعة الأولى. أما من حيث وقت استعادة الاحساس بعد انتهاء الجراحة، لم تكن هناك فروق ذات دلالة إحصائية بين المجموعة الضابطة والمجموعات الثلاث الأخرى. وكان الاحساس بألم العاصبة في المجموعات الثانية والثالثة والرابعة أقل بكثير من المجموعة الأولى. كان وقت استعادة الحركة أسرع في المجموعة الأولى والثانية عن المجموعة الثالثة والرابعة. وكان ذلك ذو دلالة إحصائية أما فيما يتعلق بجودة التخدير التي تم تقييمها من قبل طبيب التخدير والجراحين، كان الرضا أكثر وذو دلالة إحصائية بشكل ملحوظ في المجموعة الثالثة والمجموعة الرابعة مقارنة بالمجموعة الثانية والمجموعة الضابطة. لم يلاحظ وجود اختلاف في ألم ما بعد الجراحة والآثار الجانبية لليدوكائين أو الأتراكوريوم بين المجموعات الأربعة.

ومن خلال ذلك استنتجنا: في هذه الدراسة ان إضافة جرعات مختلفة من عقار الأتراكوريوم إلى عقار الليدوكائين للتخدير الموضعي الوريدي حسن من الإجراء الجراحي وقلل من شدة ألم العاصبة ومن ثم قلل من الاحتياج إلى مسكنات إضافية أثناء الجراحة مع زيادة الرضا لدى المرضى والجراحين دون آثار جانبية من زيادة جرعات عقار الأتراكوريوم.