

Duration of Analgesia in Axillary Block: Comparison of Lidocaine with Granisetron/Lidocaine Combination

Abstract

Background: Different medicines are utilized in giving nerve block. The different drugs are usually discussed concerning efficacy and persistence of pain relief. The present study aimed to compare the use of lidocaine alone with granisetron/lidocaine combination in terms of the efficacy and persistence of the analgesic effect, in the axillary block used in patients requiring elbow or below elbow surgery.

Methods: A double-blind randomized clinical trial was performed on 90 patients who were candidates for elbow surgery. In this regard, an ultrasonography-guided axillary block was performed by a linear transducer using a short-axis in-plane technique. The first group was given lidocaine, whereas the second group received granisetron/lidocaine combination. First, five mg/kg of lidocaine %0.5 was diluted to 40 ccs with 0.9% saline. In the first group, 40ml of lidocaine solution was injected after dipping the syringe in epinephrine. In the second group, 2 mg of granisetron was injected simultaneous with lidocaine solution.

Results: In total, 90 patients entered the study and were divided into two equal groups of 45. The mean age of the patients was 34.48 ± 9.0 years (18-58 years). 61 (67.8%) participants were male and 29 (32.2%) female. The onset time of sensory and motor block in the second group (granisetron/lidocaine combination) was significantly lower, compared to the lidocaine -alone group. Moreover, the continuity of sensory and motor block was significantly higher in the second group. Furthermore, the first analgesic requirement time was significantly lower in the granisetron/lidocaine combination group, compared to the lidocaine- alone group ($P < 0.001$).

Conclusion: The concomitant use of granisetron with lidocaine improved all pain indicators and also led to faster and more continuous sensory and motor blocks.

Keywords: Regional anesthesia, Lidocaine, Granisetron, Analgesia, Nerve Block

Received: 8 months before printing; Accepted: 1 Months before printing

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Introduction

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. If not controlled, this unpleasant feeling makes the patient uncomfortable and leads to uncontrollable behavioral responses in that individual. In addition, chronic pain disturbs their quality of life. Rapid and effective pain relief in patients is recognized as a humane act and the fundamental right of a patient^(1, 2). Some of the major complications of acute limb traumas include soft tissue damages, bone fractures, and joint dislocations that could cause pain and discomfort in patients and pain management is considered essential to improve care quality in patients^(2, 3). The use of medicines to relieve chronic or acute pain is a common action to reduce and manage pain, and their application is more common in patients with complaints of pain in the needed dosages^(3, 4). However, excessive use of these medicines may lead to severe complications^(5, 6).

One of the technics to relieve the patient's pain is hematoma block and nerve block, which can be performed in different parts of the hand, such as the armpits, elbows, or fingers. In the elbow area, median, ulnar, and radial nerves can be blocked, and anesthesia can be created in the distal forearm and hand area. Nerve block in the elbow will suffice for relieving pain in most severe injuries⁽⁶⁻⁸⁾. Blocking the three mentioned nerves leads to successful anesthesia of forearm and hand. However, proximal damage to the forearm requires superficial nerve block in the lateral, medial, and posterior regions. The radial nerve and the sensory branch of the musculocutaneous nerve lie together between the biceps and the brachioradialis on the anterolateral elbow⁽⁹⁻¹²⁾.

Lidocaine is used as the primary medicine in intravenous regional anesthesia (IVRA) in most clinical cases. Various studies have evaluated adding a second medicine to improve the effect of lidocaine on pain relief and time of onset of analgesia and increase the duration of anesthesia. Specific 5-HT₃ serotonin receptor antagonists, such as ondansetron, granisetron, and dolasetron, have a positive and uncomplicated effect on the treatment of nausea and vomiting. In some studies, the use of granisetron in combination with lidocaine in IVRA has led to effective results compared to lidocaine alone^(13, 14). With this background in mind, the present study aimed to evaluate the effectiveness, as a primary consequence, and persistent analgesic effect, as a secondary consequence, in the axillary

block with lidocaine in comparison with granisetron/lidocaine combination in patients requiring elbow or below elbow surgery.

Methods

A double-blind randomized clinical trial was performed on patients with bone trauma, who were candidates for surgery with axillary block. Inclusion criteria were age range of 15-60 years, being a candidate for elbow surgery, conscious level above 14 according to Glasgow criteria, no history of lidocaine and granisetron allergy, no history of use of medicines interacting with lidocaine and granisetron, no lesion or infection at the injection site, and no history of coagulation-related diseases. Exclusion criteria were unwillingness to participate in the study and sensitivity during medicine injection that lead to discontinuation of injection.

Subjects were selected by non-probability convenience sampling, and those who met the inclusion criteria were enrolled in the study. Sampling continued until reaching the required number of samples, and the patients were allocated to two groups using a balanced block randomization method. In addition, blinding was performed by simply not informing patients and the therapist of type of injected medicine (double-blinding). Written informed consent was obtained from all participants following receiving approvals from the ethics committee and registering the research on the Iranian Registry of Clinical Trials (IRCT).

Regional anesthesia technique. The ultrasonography-guided axillary block was

performed by a linear transducer using the short-axis in-plane technique. The patient was placed in the supine position with the outstretched arms and turned outwards. The ultrasound image should show the axillary artery and axillary vein in the terminal branches of the brachial plexus, conjoint tendon, biceps, triceps, and coracobrachialis muscle. The connection of the terminal branches with the axillary artery is as follows: median nerve (superficial), ulnar (on the side of the medial artery) and radial (on the side of the posterior artery), and musculocutaneous nerve (on the side of the lateral artery passing through the coracobrachialis muscle). Using the in-plane technique, a 5-7 cm block needle was directed toward the branches of the brachial plexus as it travels from the proximal to the distal. The first group received a total dose of 40 ccs lidocaine with 5 mg/kg of 0.5% lidocaine diluted with 0.9% saline by an epinephrine-coated syringe. The second group received 2 mg of granisetron/lidocaine combination. All injections were performed by a person blinded to the type of injected medicine.

Onset time and persistent effect. The onset time of sensory block was calculated from the time of anesthetic injection until the negative pinprick test in the elbow area and below it, and the onset time of motor block was estimated from the time of anesthesia injection until the patient was unable to obtain full flexion, extension, and reduction of fingers. Moreover, the duration of the sensory block was considered from the time of anesthetic injection until the

positive pinprick test in the elbow and lower area and the duration of the motor block from the time of anesthesia injection until the return of flexion, extension, of fingers. The duration of painlessness was from the time of onset of sensory block until the need for analgesia for pain relief by the patient.

Pain measurement criteria. The pain was measured in patients before and after the injection using the numeric rating scale (NRS) (0-10), where 0 is no pain and 10 is extreme pain. Patients determined the severity of their pain based on the presented images concerning NRS. Ultimately, the pain score was recorded numerically in the questionnaires.

Additional analgesic injection. This medicine was injected in patients with a pain score of ≥ 6 (a total dose of pethidine 0.5 mg/dl was injected).

Desired consequences. The onset time of sensory and motor block, duration of sensory and motor block, pain scores, and the first analgesic requirement time were recorded and compared 6 and 12 hours after the procedure. Moreover, blood pressure, heartbeat, and breathing of the patients were assessed and compared before the study, every 10 minutes during the procedure, and 2 and 6 hours after it.

Data analysis was performed in SPSS version 21 using descriptive and analytical statistics after completing the checklists and collecting data. Regarding descriptive statistics, quantitative data were reported as mean \pm standard deviation (SD), whereas the qualitative data were reported as percentage. The research

hypotheses were assessed using analytical statistics. After examining the normality of data using the Kolmogorov-Smirnov test, independent samples t-test in quantitative variables or chi-square test in qualitative variables were used to investigate the differences between the variables in both groups. A p-value less than 0.05 was considered statistically significant.

Results

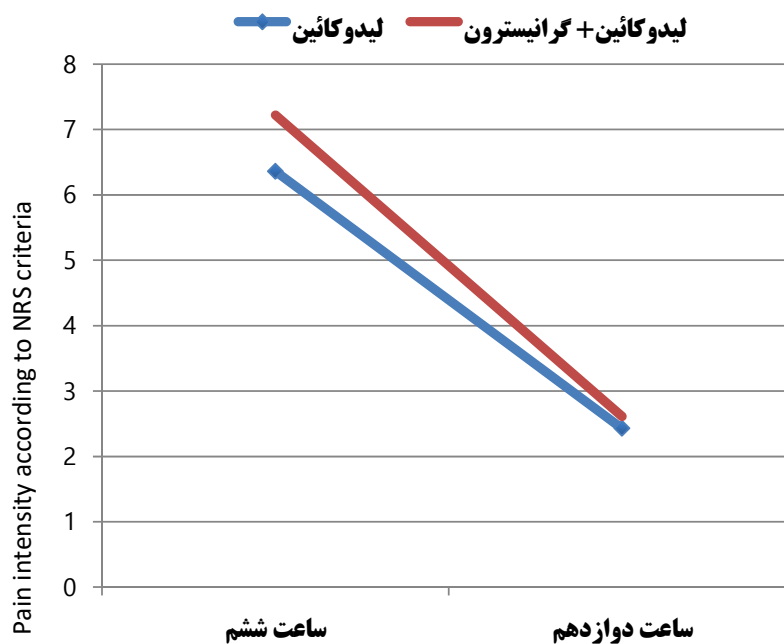
In total, 90 patients were entered into the study into two equal groups, 45 patients each. The mean age of the participants was 34.48 ± 9.00 years, ranging from 18 to 58 years. Of all the participated patients, 61 (67.8%) were male and 29 (32.2%) female. Surgery was performed for patients to treat elbow dislocation associated with distal radius fracture. The mean surgery duration was 1.5 ± 0.35 hours with no statistically significant difference between the groups in this regard ($P=0.135$). In addition, the groups were assessed in terms of vital signs (e.g., systolic/diastolic blood pressure, heartbeat, and respiratory rate) before the procedure, and no significant difference was observed between the groups in this respect (Table 1). Moreover, the vital signs of the patients in both groups were examined in subsequent evaluations, and there was no statistically significant difference in the mean obtained between the two groups. Furthermore, no complication was

observed in the participants, and pain intensity decreased in both groups 6 and 12 hours after axillary block, but there was no statistically significant difference between the groups (Diagram 1). The time of onset of sensory and motor block in the second group (granisetron/lidocaine combination) was significantly shorter than the first group (lidocaine alone). In other words, sensory and motor block occurred faster in the group receiving granisetron. In addition, the persistence of sensory and motor block in the second group was significantly higher than in the first group. In other words, sensory and motor block continued for a longer time in the group receiving granisetron. During the surgery, five participants in each group required additional analgesic administration (11%). In this regard, pethidine was received in both groups to create intense analgesia during surgery, and no significant difference was observed between the groups regarding the therapeutic dose and number of injections ($P=0.121$). The first analgesic requirement time in the first group was significantly lower than the second group. In other words, those who received lidocaine required an additional analgesic sooner than those who received the granisetron/lidocaine combination (Table 2).

Table 1. Demographic and clinical characteristics of the participants at the beginning of the study

Age and demographic and clinical characteristics of patients		Lidocaine group Mean \pm SD	Granisetron/lidocaine combination group Mean \pm SD	Statistical test
Age (year)		34.27 \pm 11.56	33.68 \pm 11.04	P=0.800
Heart beat (per minute)		76.64 \pm 7.38	80.29 \pm 6.47	P=0.110
Respiratory rate (per minute)		17.24 \pm 1.76	17.60 \pm 1.04	P=0.217
Systolic blood pressure (cmH ₂ O)		12.43 \pm 1.19	12.13 \pm 0.54	P=0.120
Diastolic blood pressure (cmH ₂ O)		7.66 \pm 0.87	7.82 \pm 0.50	P=0.268
Gender	Male	32 (71.1%)	29 (64.4%)	P=0.499
	Female	13 (28.9%)	16 (35.6%)	

P<0.05 was significant

**Diagram 1. Comparison of mean pain intensity at different times after axillary block in each group****Table 2. Comparison of mean of onset time and continuity of sensory and motor block and the first analgesic requirement time in each group**

Variable	Lidocaine group Mean \pm SD	Granisetron/lidocaine combination group Mean \pm SD	Statistical result
Onset time of sensory block (minute)	18.00 \pm 2.03	14.73 \pm 1.33	P=0.001
Onset time of motor block (minute)	25.67 \pm 3.43	21.95 \pm 4.19	P=0.001
Continuity of sensory block (minute)	136.44 \pm 8.35	185.70 \pm 5.95	P=0.001
Continuity of motor block (minute)	149.64 \pm 8.00	213.79 \pm 6.56	P=0.001
The first analgesic requirement time (minute)	162.98 \pm 33.58	200.34 \pm 10.54	P=0.001

P<0.05 was significant

Discussion

The present study was performed to reduce pain experienced by patients and persistent pain relief in patients requiring elbow surgery. Granisetron was used as an adjuvant, and its effects were assessed in both groups. While the first group received lidocaine alone, the second group received the granisetron/lidocaine combination. Changes in vital signs were measured during the study at regular intervals of 10 minutes for 1 hour, then every hour, and finally 6 hours later. The graph showed slight changes over time, which were not statistically significant. In both study groups, these changes were studied separately in each period, and there was no statistically significant difference between the two groups. Similar results have been obtained in other studies. Change in vital signs in some studies were evaluated and compared at intervals of 15 minutes for the first hour and intervals of 30 minutes for three hours, and no statistically significant difference was observed in this regard ^(15, 16). In the current research, none of the patients had abnormal vital signs during the study. However, in another research ⁽¹⁷⁾, one patient was excluded from the study due to palpitations and increased heart rate and respiration, which was reported to be caused by a reaction to medicine.

In the second part, patients' pain and anesthesia were analyzed. At the beginning of the study, none of the

patients reported any pain. Therefore, it was expected to detect no pain after the injection of solutions. After the block, the pain increased in both groups so that patients in both groups required analgesics. However, despite receiving the first dose of analgesia about three hours following the block, the pain in both groups was still higher than five points in the evaluation performed at the 6th hour. Nonetheless, the pain gradually decreased to three points in patients at the 12th hour of the block by receiving the next doses of analgesic. Sensory and motor block indices were also used to evaluate the effectiveness of the medicine in the groups. The first index involved determining the sensory block time that was below 15 minutes in the granisetron/lidocaine combination group and below 20 minutes in the lidocaine group. In addition, the motor block was initiated faster in the granisetron/lidocaine combination group than the lidocaine group (the 21st minute vs. the 25th minute). The significance of the sensory and motor block time showed the early impact of the granisetron/lidocaine combination compared to lidocaine. In a study by Honarmand et al. ⁽¹³⁾, the addition of 8 mg of ondansetron resulted in rapid sensory and motor block compared to patients receiving lidocaine. In addition, patients receiving lidocaine and ondansetron experienced rapid anesthesia in the study by Farouk et al. ⁽¹⁴⁾.

In the present research, the persistence of sensory and motor block was also assessed. The onset of sensory and

motor block is important in the patient's analgesia and leads to relaxation of the patient and the physician during the procedure. The difference between the mean duration of sensory and motor block in the granisetron/lidocaine combination and lidocaine group was about 50 and 65 minutes, respectively, which is significant. The difference in obtained anesthesia time can be very valuable in performing the procedure. Consistent results were obtained in similar studies. For instance, the group receiving lidocaine combined with 8 mg of ondansetron experienced higher persistence of sensory and motor block than the lidocaine group in the research by Honarmand et al.⁽¹³⁾ Likewise, the group receiving ondansetron had a shorter onset time and longer effect in the study by Farouk et al.⁽¹⁴⁾ The persistence of block was significantly higher in the ondansetron group than the magnesium group in the study by Kayalha et al.⁽¹⁷⁾ The increase of the first analgesic requirement time was significantly higher in the granisetron/lidocaine combination group than the lidocaine group (200 minutes vs. 162 minutes), which is in line with other related studies. In a study by Farouk et al.⁽¹⁴⁾, the first analgesic requirement time was longer (172 minutes vs. 85 minutes) and the number of patients requiring analgesics after surgery was lower in the ondansetron group. In research by El Bahnasawy et al.⁽¹⁵⁾, the number of patients requiring analgesics was lower and the intervals were longer in the group receiving ondansetron compared to the other groups. Kayalha

et al.⁽¹⁷⁾ reported a higher need for analgesics at shorter intervals in the group receiving lidocaine.

Given the present study results, it is recommended that the granisetron/lidocaine combination be used in sensory and motor block by physicians in various fields (i.e., emergency, orthopedics, surgery, and anesthesia) to perform upper limb procedures. It is also suggested that clinical assessments and studies be conducted for the block of lower limb blocks under the supervision of clinicians to assess the effect of the granisetron/lidocaine combination on other limbs.

Conclusion

According to the present study, the use of granisetron combined with lidocaine improved all pain indicators in patients. In addition, the granisetron/lidocaine combination led to more persistent sensory and motor blocks.

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