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The Effects of Interscalene Block Performed Alone or with Ultrasonography-Guided Peripheric Nerve Stimulator on Block Success, Hemodynamic Parameters and Perfusion Index

Yalnız Başına veya Ultrasonografi Eşliğinde Periferik Sinir Stimülatörü ile Gerçekleştirilen İnterskalen Bloğun Blok Başarısı, Hemodinamik Parametreler ve Perfüzyon İndeksine Etkileri

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ABSTRACT Objective: We aimed the comparison between traditional methods and perfusion index (PI) on evaluating the block success and sufficiency of interscalene block that we applied to shoulder surgery cases by using ultrasonography (USG) and peripheric nerve stimulator or only peripheric nerve stimulator only. **Material and Methods:** After ethics committee and patient approvals; ASA I-III, 50 adult patients (18-70 ages) who underwent shoulder, arm surgery were allocated to this prospective research. Interscalene block was applied to all patients by using USG and peripheric nerve stimulation or peripheric nerve stimulation with bupivacaine 0.5% 1 mg/kg+prilocaine 2% 4 mg/kg+NaCl 0.9% to complete the anesthetic solution to 30 mlt. We recorded heart rate, mean arterial pressure, peripheric oxygen saturation, PI, motor block times and pin-prick test values of the patients. **Results:** When the PI values of the patients on different times were compared, the difference between the groups was insignificant. Loss of cold sensation time was 10.3±3.9 min in Group 1 and 11.3±4.3 min in Group 2. Pin-prick test time to be positive was 16.3±3.8 min in Group 1 and 17.6±5.1 min in Group 2. Motor block onset time was 14.2±3.7 min in Group 1 and 16.1±4.3 min in Group 2. **Conclusion:** Using USG enables us to benefit from local anesthetic more effectively and to encounter fewer complications. Another conclusion can be about PI parameters which significantly increase with block success in time within the groups. So, PI can be used due to being easily applicable and non-invasive technique for predicting the block success.

Keywords: Interscalene block; perfusion index; ultrasonography; regional block

ÖZET Amaç: Bu çalışmada; ultrasonografi (USG) rehberliğinde periferik sinir stimülatörüyle veya yalnızca periferik sinir stimülatörüyle uyguladığımız interskalen bloğun, hemodinamik parametrelerle birlikte, blok başarısını ve yeterliliğini değerlendirmede perfüzyon indeksi (Pİ)'ne etkilerinin karşılaştırılması amaçlandı. **Gereç ve Yöntemler:** Etik kurul ve hastaların onayı alındıktan sonra omuz, kol ve dirsek cerrahisi geçirecek ASA I-III grubuna giren 18-70 yaş arası 50 hasta prospektif olarak çalışmaya alındı. Tüm hastalara; 1 mg/kg %0,5 bupivakain +4 mg/kg %2 prilokain + toplamda 30 mlt'ye tamamlanacak şekilde %0,9'luk NaCl eklenerek lokal anestezik solüsyon ile USG ve periferik sinir stimülatörü veya periferik sinir stimülatörü eşliğinde interskalen blok uygulandı. Hastaların kalp atım hızı, ortalama arteryal kan basınçları, periferik oksijen saturasyonları, Pİ, motor blok başlama zamanı, tam motor blok oluşma zamanı, soğuk duyusu kaybı zamanı ve pin prick testi pozitif olma zamanı değerlendirilerek veriler kaydedildi. **Bulgular:** Çalışmaya alınan bireylerin değişik zamanlarda ölçülen PI değerleri karşılaştırıldığında, gruplar arasındaki farklılık önemsiz bulundu (p>0,05). Soğuk duyusu kaybı zamanı; Grup 1'de 10,3±3,9 dk ve Grup 2'de 11,3±4,3 dk olarak bulundu. Pin-prick testi pozitif olma zamanı; Grup 1'de 16,3±3,8 dk ve Grup 2'de 17,6±5,1 dk olarak bulundu. Motor blok başlangıç zamanı; Grup 1'de 14,2±3,7 dk ve Grup 2'de 16,1±4,3 dk olarak bulundu. **Sonuç:** USG kullanımı; lokal anestezik ilaçlardan daha etkin yararlanmamızı ve daha az komplikasyonla karşılaşmamızı sağlar. Gruplar içindeki zamana göre blok başarısı ile önemli ölçüde artan Pİ, blok başarısını tahmin etmek için kolay uygulanabilir ve invazif olmayan bir teknik olarak kullanılabilir.

Anahtar Kelimeler: İnterskalen blok; perfüzyon indeksi; ultrasonografi; rejyonel blok

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Peripheral nerve block has a wide range of applications for anesthesia, differential diagnosis, medical treatment, postoperative analgesia and pain treatment by applying appropriate doses of local anesthetics to appropriate peripheral nerves or ganglions.[1] It is widely preferred in anesthesiology and algology due to its easy applicability, its efficacy and its low cost compared to general anesthesia.[2]

The sufficiency of an effective and successful block is determined by evaluating sensory block, motor block and sympathetic block levels.[3] Traditional methods of assessing loss of sensory response to a given stimulus require very good communication with the patient, and evaluation of the results may vary due to individual differences. As a result, different methods have been described, including the perfusion index (PI), which enables quantitative evaluation of the autonomic innervation.[4] After achieving successful block with these methods, local vasodilatation and increased blood flow, which occur as a result of sympathetic nerve block in the blocked area, were assessed. However, none of these methods responds fast enough in terms of clinical use in intensive operating room conditions and in urgent cases where time is important.[4]

The PI represents the ratio of pulsatile blood flow in the peripheral tissue to nonpulsatile or static blood flow and represents the measurement of peripheral perfusion obtained continuously and noninvasively from a pulse oximeter.[4] In a study, it was emphasized that PI measurement could be used in evaluating peripheral circulation, and PI could predict hypovolemia without a reduction of more than 20% in stroke volume.[5]

One of the preferred brachial plexus approaches in upper extremity surgeries is interscalene brachial plexus blockade (ISBPB). The most important indications of this block are anesthesia and analgesia in shoulder, humerus, clavicle, elbow, arm and forearm surgeries. It is applied at the C5-C6 root level. The medial antebrachial cutaneous nerve and medial brachial cutaneous nerve, which are sensory branches of the ulnar nerve, cannot be blocked because the classical interscalene block cannot block the roots of C8 and T1. Unintentional blockage of the cervical plexus in interscalene block may result in recurrent laryngeal nerve blockage and weakness in the forearm and in the hand.[6] Acute postoperative pain; is common in adults after surgery (for example shoulder surgery), and about 45% of patients experience sudden pain in the postoperative period.[7] Interscalane block provides reduction of postoperative opioid consumption and decrease of opioid side effects in certain operations of upper extremity, by reducing postoperative pain due to its analgesic activity.[8]

Interest in the use of ultrasonography (USG) in regional blocks is increasing rapidly in recent years. The reason for this is that the success rate is higher and the complication rate is lower in ultrasound-guided blocks. USG of the brachial plexus is easy to visualize between the anterior and middle scalene muscles. Another advantage of using USG is the ability to monitor the distribution of the injected local anesthetic.

The objective of our study is to evaluate the block success rates of the patients who underwent interscalene block using only peripheric nerve stimulator and the patients who underwent interscalene block using ultrasound-guided peripheric nerve stimulator, and to compare hemodynamic parameters, motor block onset time, time of motor block completion, time of pin-prick test being positive, time of cold sensory loss, additional anesthetic requirements, first analgesic use times, to predict block success rates with PI and complications that may develop after the block application of both methods with each other.

MATERIAL AND METHODS

Ethics cmmittee approval and consent of the patients were taken for the study with decision date of 13.10.2015 and numbered 2015-10/05. This study is designed on principles of Helsinki Declaration properly. Fifty patients between the ages of 18-70 in ASA I-II-III groups, who were to be operated in the shoulder, arm and elbow regions were prospectively included in the study. All patients were informed verbally and in writing about all the details of the study and an informed consent document was issued for the participants. Patients who did not consent to the study, who were not in the 18-70 age group, who had a history of allergy to one of the medications used

in the study, who were higher than ASA III, who had nerve blockage contraindications such as infection and open wound in the area to be punctured and who had coagulopathy and received antithrombotic treatment were not included to the study. Patients with limited pulmonary reserve and chronic obstructive pulmonary disease were also excluded from the study to obtain more healthy results and to avoid risks.

Randomization was based on a computer-generated code that was prepared at a remote site and sealed in opaque, sequentially numbered envelopes. Randomization was based on blocks of 50 patients using randomly sealed envelopes.

According to the technique, patients were randomly divided into two groups. Group l consisted of the patients receiving ultrasound-guided peripheral nerve stimulation (n=25) and Group 2 consisted of the patients receiving only peripheral nerve stimulation (n=25). A total of 60 patients were selected. Five patients did not meet the criteria, 3 patients did not want to participate and 2 patients were excluded because they needed general anesthesia. A total of 50 patients were randomized. The number of patients undergoing each type of surgery (shoulder, arm and elbow surgery) was equal in Group 1 and Group 2. The age, weight, height and gender of all patients were recorded priorly.

Patients were monitored on a routine basis to include electrocardiography, noninvasive arterial blood pressure and pulse oximetry (SpO_2). Peripheral vascular access was established in the patient's suitable arm and volume replacement with 6-8 ml/kg of crystalloid solution was given. All patients were given 0.02-0.03 mg/kg midazolam and 1 μg/kg fentanyl I.V. for sedoanalgesia 30 minutes prior to the procedure. All patients were given 2-4 liters/minute of oxygen by nasal route during the block procedure and operation. In addition to the basic hemodynamic measurements, a pulse oximetry sensor (M-LNCS adult adhesive sensors Masimo SET® Radical™ pulse oximeters; Masimo Corp., Irvine, CA USA) was fitted on the second finger of the upper extremity, which was to be operated, to perform the PI measurement. The sensor was connected to a Rad-87™ Pulse CO-Oximeter.

Baseline values were measured 10 minutes prior to the procedure. Firstly, patients' mean blood pressure, heart rate and peripheral oxygen saturation values were measured and recorded. The PI value measured on the pulse CO-Oximeter was recorded. All blocks were performed by the same anesthetist. Another anesthetist recorded the obtained data.

For injection, we prepared our local anesthesia solution by adding 0.9% NaCl to 1 mg/kg of 0.5% bupivacaine (Bustesin® 0.5%) and 4 mg/kg of 2% prilocain (Priloc® 2%) to obtain a total of 30 ml of solution, and 2 ml prilocain (Priloc® 2%) was applied to the planned injection site cutaneous-subcutaneously.

In Group 1, where the peripheral nerve stimulator was used with ultrasound guidance, the patients were lying in supine position and their faces were positioned so that they could face the opposite side of the direction to be treated by about 45 degrees. The arm on the side, which was to be blocked was positioned and fixed to the patient's abdomen. The area to be injected was cleaned with povidone iodine. An eZono™ 3000 portable ultrasound model (Germany) ultrasonic device and a 6-10 MHz linear probe were used for the block. Ultrasound gel was applied to the linear probe and the probe was covered with a sterile nylon sheath. Sterile gel was applied to the region to be treated and long axis image was obtained with the ultrasound (eZono™ 3000 portable ultrasound Germany). The C6 level nerve roots to be blocked were detected and the neurostimulator was used to reduce the current through the use of an echogenic needle (Stimuplex, B. Braun, Melsungen AG) with a 22 G 80 mm electro-neurostimulation port and a motor response of 0.2-0.5 mA was observed and the injection point was verified. Plexus root peripheries were injected, and the distribution of local anesthesia that expanded the tissues and separated nerve roots from other tissues was observed.

In Group 2, where the peripheral nerve stimulator was used alone, patients were placed in the same position and an aseptic area was achieved. The stimulation needle to be used for the block was concurrently connected to the nerve stimulator. At the C6 level, immediately after the sternocleidomastoid mus-

cle, the needle entry point was determined by the Winnie technique. After the skin was punctured with an echogenic needle (Stimuplex, B. Braun, Melsungen AG) with a 22 G 80 mm electro-neurostimulation port, the nerve stimulator (Stimuplex HNS 11, Braun Medical, Melsungen, Germany) was started at 1 mA current and 2 Hz (0.1 millisecond bandwidth) frequency. The needle was moved in caudal, dorsal and medial directions, passing between the anterior and medial scalene muscles. After receiving motor response in the deltoid or biceps muscles via the nerve stimulator, the value of the current was decreased until the motor response value registered at 0.3-0.5 mA range, and the point that responded within this range was injected.

At the extremity of the operation; sensory evaluation was made with pin-prick test and cold sensation loss test. All results were recorded on the basis of Modified Bromage Scale (0=no motor block, 1=no shoulder abduction, 2=no shoulder abduction and elbow flexion, 3 = full motor block).

SpO_2, MAP, HR values were recorded at 10 min, 20 min, 30 min, postoperative 30th minute after the block operation was completed (removal of the needle from the skin was considered as 0. minute). Also, the PI values measured at the same time intervals on the pulse oximeter (Masimo SET® Radical™ pulse oximeters) were recorded. The neuromotor examination of the patients was repeated frequently to determine the time for the pin-prick test to be positive, to measure cold sensation loss time with the cold sensation loss test and motor strength was assessed with the Modified Bromage Scale; the motor block starting time and the complete motor block generation time were recorded. In the sensory examination performed 30 minutes after the injection, the absence of pain in all dermatomes was considered a successful block and the patient was delivered to the surgeon for the operation. The adequacy of anesthesia for surgery was considered to be the case in which the "pin-prick" sensation disappeared in all dermatomes between C4 and T1 and the "Modified Bromage Score" was ≥ 2. At the start of surgery, patients with pain were recorded and 1 mg/kg ketamine I.V was administered with a 5-minute break to the surgery. Preparation for general anesthesia was made for the patients with pain at the end of 5 minutes and those patients were excluded from the study. Patients who did not undergo general anesthesia but needed additional analgesia and the amount of medication administered were recorded. After injection, the presence of rough voice, Horner's syndrome, respiratory distress, and local anesthetic toxicity were continuously assessed and recorded. After the surgery, a chest X-ray was taken and diaphragm elevation was assessed by comparing it with the preoperative chest X-ray. After the block procedure and during the first postoperative 24 hours, complications related to the block and the first analgesic requirement time of the patients were questioned. All patients describing pain with Visual Analogue Scale (VAS) values of 60 mm and over were treated intramuscularly with 1 mg/kg of diclofenac sodium as analgesic unless contraindicated. During the postoperative period, the first analgesic drug application time was recorded.

STATISTICAL METHOD

When the data obtained from our study were loaded on Statistical Package for Social Sciences (SPSS) ver. 22.0 and evaluated; the significance test of the difference between the two means in the independent groups (Kolmogorov-Smirnov) was performed when the parametric test assumptions were fulfilled, and the Mann Whitney U test, Chi-square test and Fisher exact Chi-square test were performed when the parametric test assumptions were not fulfilled and the level of error was taken as 0.05.

RESULTS

The age, body weight and height of the cases in the study were not significantly different between the groups ($p>0.05$).

When the mean arterial pressure values measured in different time periods in both groups were compared, the difference between the groups was not significant ($p>0.05$). Mean arterial pressures were found to decrease over 30 min in both groups. When the heart rate values measured at different times in both groups were compared, the difference between the groups was not significant ($p>0.05$). The heart rate values were found to decrease over 30 minutes in both groups. When the SpO_2 values measured in dif-

ferent time points in both groups were compared, the difference between the groups was not significant (p>0.05). SpO_2 values in both groups were found to decrease over 30 min.

When the PI values measured at different times in the cases in both groups were compared, the difference between the groups was not significant (p>0.05). When the measurements in each group were compared as two; difference between baseline and 10 min, 20 min, 30 min and postop 30 min (p= 0.001), difference between 10 min and 20 min, 30 min and postop 30 min (p= 0.001), difference between 20 min and 30 min and postop 30 min (p =0.001) and difference between 30 min and postop 30 min were significant (p =0.001) (p<0.05). In both groups, it was determined that PI value increased for 30 minutes compared to baseline. In Group 1 and Group 2, an increase of 185% and 172%, respectively, were detected at 10th minute compared to baseline. This increase rate continued to decrease for 30 minutes (Table 1).

When the time of motor block onset, time of complete motor block generation, time of loss of cold sensation and time of positive pin-prick test were examined in both groups, the difference between groups was found to be insignificant (p>0.05).

When the two groups were compared in terms of Horner's syndrome, the difference was significant (p<0.05). When the two groups were compared in terms of phrenic nerve paralysis and vascular puncture, the difference was not significant (p>0.05).

In comparison of two groups in terms of operative time, the difference between the groups was not significant (p>0.05). When both groups were compared in terms of time of first analgesic requirement, the difference between the groups was significant (p<0.05) (Table 2).

When the time of complete sensory block was assessed by loss of cold sensation, the results were 10.38±3.96 min in Group 1 and 11.35±4.30 min in Group 2. The motor block start time was 14.24±3.76 min in Group 1 and 16.17±4.35 min in Group 2.

Group 1: 25/25 (100%) and Group 2: 25/27 (92.5%) were found when the groups were evaluated in terms of block success rate. In Group 2, general anesthesia was needed in two cases and these two cases were excluded from the study. When the two

TABLE 1: Comparison of perfusion index (PI) values measured at different time points in both groups.

	Group 1		Group 2		
	Mean	SD	Mean	SD	p value
Operative Time (min)	106	22	103	24	p= 0.62
Time of First Analgesic Requirement (min)	598	85	417	64	p= 0.001*

*p<0.05 statistically significant.

TABLE 2: Evaluation of the duration of surgery and the time of first analgesic requirement in both groups.

	Group 1		Group 2		
Perfusion Index	Mean	SD	Mean	SD	p value
Baseline	2.38[a]	0.96	2.35[a]	1.30	p= 0.924
10. minute	6.79[b]	1.30	6.40[b]	2.41	p= 0.485
20. minute	8.89[c]	1.36	9.12[c]	2.15	p= 0.645
30. minute	10.15[d]	1.53	10.18[d]	2.45	p= 0.962
Postoperative 30. minute	5.95	1.13	6.20	1.67	p= 0.550

[a]p<0.05; Comparison between PI 10th, 20th, 30th and postoperative 30th minutes
[b]p<0.05; Comparison between PI 20th, 30th and postoperative 30th minutes
[c]p<0.05; Comparison between PI 30th and postoperative 30th minutes
[d]p<0.05; Comparison between PI postoperative 30th minutes

groups were compared in terms of block success rate, the difference between the groups was not significant (p=0.348) (p>0.05).

When additional anesthetic requirements were assessed, additional anesthesia was needed in 3 patients in Group 1 and 6 in Group 2, and ketamine sedation was administered. Patients who were treated with ketamine sedation without general anesthesia were included in the study. When the two groups were compared in terms of need for additional anesthesia, the difference between the groups was not significant (p>0.05).

DISCUSSION

When assessing hemodynamic parameters, in a study comparing the efficacy of ultrasound and nerve stimulator techniques in interscalene brachial plexus block applications, Mizrak et al. performed blockage with 25 ml of 0.5% levobupivacaine in the presence of ultrasound and peripheral nerve stimulator, and in terms of mean arterial pressure and heart rate, have achieved similar results in both groups. However, when the groups were assessed individually, the heart rate and mean arterial pressure values in the USG group tended to decrease over the next 90 minutes after the procedure was performed. In the peripheral nerve stimulator group, heart rate and mean arterial pressure values tended to remain the same over 90 minutes.[9] In our study, heart rate and mean arterial pressure values were found to be continuously decreasing for 30 min in both groups. When examined, SpO_2 values decreased in both groups, unlike the other studies. In our study, we related the decrease in SpO_2 values to the higher incidence of phrenic nerve paralysis in the interscalene approach. There was no significant difference between the groups in terms of other hemodynamic parameters. This may be due to the unchanged dose of local anesthetic administered. While the distribution and localization of local anesthesia can be seen in the USG-guided block, the risk of intravascular injection is higher in the block applied with PNS alone. We thought that this difference between these techniques could be reflected in the hemodynamic parameters, but we did not see a significant difference in hemodynamic parameters.

In patients undergoing regional anesthesia, primarily sympathetic block is formed depending on the block, followed by sensory block and motor block.[10] Local vasodilatation occurs in the area where sympathetic block is formed and consequently, perfusion increases in that area. For this reason, PI can be used to show sympathetic block formation.[4] In a study by Ginosar et al. who evaluated sympathectomy with epidural anesthesia, it was found that PI revealed sympathetic block due to epidural anesthesia earlier, clearer, and more successful than the mean arterial pressure and skin temperature.[11] In a similar study, PI was found to be faster and more sensitive in revealing the sympathectomy after caudal anesthesia under basal ketamine anesthesia.[12]

In patients undergoing peripheral block, block success was assessed using PI. Galvin et al. used a single injection technique for axillary block and sciatic block to evaluate the change of PI in patients treated with axillary block and sciatic block, using 40 ml mepivacaine for axillary block and 20 ml mepivacain for sciatic block and as a result, they concluded that PI was simple, early, objective and had a high specificity and sensitivity compared to conventional methods. In the same study, a 1.55-fold increase in PI compared to baseline values was considered as a successful block and it was seen that axillary block was reached at 10 min and sciatic block at 12 min.[13] In a study by Kus et al. evaluating the PI change in infraclavicular block, a 30 ml solution consisting of 20 ml levobupivacaine and 10 ml lidocaine was filled around the axillary artery at a 3-11 o'clock alignment and they reached the conclusion that PI was a successful indicator of infraclavicular block. They found that an increase of 120±119% (± standard deviation) relative to the baseline value of PI in the 10^{th} minute was significant.[4]

In the literature, we did not find any studies in which PI was assessed in patients undergoing interscalene block. In this study, we observed that the PI value increased for 30 minutes in both groups compared to the baseline. When the PI values measured at different times were compared among the groups, it was found that the difference was not significant. Compared to baseline at the 10. minute, Group 1 and Group 2 showed an increase of 185% and 172%, re-

spectively. This increase lasted for 30 minutes, but the rate of increase gradually decreased during this period. This result was shorter than the time values obtained in the other studies in the literature and we related this to the rapid onset of the effect of prilocaine and the use of the interscalene block technique.

In the literature, the duration of interscalene block formation is 5-15 min with lidocaine and 20-30 min with bupivacaine.[14] Mizrak et al. applied blocks using 25 ml of 0.5% levobupivacaine to study the effects of peripheral nerve stimulator and USG in patients treated with interscalene block and used pin-prick test to evaluate sensory block. The sensory block time was found to be 8.9±2.4 min in the USG group and 11.4±5.9 min in the peripheral nerve stimulator group.[8] Similarly to the studies in the literature, in our study, when the time of complete sensory block formation was assessed using the pin-prick test, and the results were 16.38±3.84 min in Group 1 and 17.66±5.14 min in Group 2. When the time of complete sensory block was assessed by loss of cold sensation, the results were 10.38±3.96 min in Group 1 and 11.35±4.30 min in Group 2.

Mizrak et al. found in the study they applied 25 ml of 0.5% levobupivacaine for interscalene brachial plexus block, that the motor block start time was 18.8 ± 3 min in the USG group and 26.1±9 min in the PNS group. They used the Modified Bromage Scale for evaluation.[9] We preferred the Modified Bromage Scale for motor block evaluation in our study, as well. The motor block start time was 14.24±3.76 min in Group 1 and 16.17±4.35 min in Group 2.

Eker et al. applied interscalene block using 40 mL of 0.25% bupivacaine or 0.25% levobupivacaine and found that the first analgesic requirement time was 9.22±7.42 hours in the levobupivacaine group and 9.34±5.28 hours in the bupivacaine group.[15] In our study, the solution was prepared by adding 0.9% NaCl to 1 mg/kg 0.5% bupivacain+4 mg/kg 2% prilocain to be 30 ml in total, and the block was applied with the single injection technique. The first analgesic requirement times were 598.3±85.4 min for Group 1 and 417.6±64.1 min for Group 2. The lack of long-term analgesic need in our study may be due to the preference of bupivacaine, a long-acting local anesthetic agent, and the high volume of drug being used.

In this study, block success was evaluated as 100% in Group 1 and 92.5% in Group 2. Because of additional intravenous anesthetic requiements of 6 patients in Group 2, in terms of block success rates, similarly to the literature, our study also concluded that the use of USG increased the success rate.

CONCLUSION

Interest in the use of USG in regional blocks is increasing rapidly. The reason for this is that the success rate is higher and the complication rate is lower in ultrasound-guided blocks. USG of the brachial plexus is easy to visualize between the anterior and middle scalene muscles. Another advantage of using USG is the ability to monitor the distribution of the injected local anesthetic. This advantage enables us to benefit from local anesthetic more effectively and to encounter fewer complications. Another conclusion can be about PI parameters which significantly increase with block success in time within the groups. So, PI can be used due to its being easily applicable and non-invasive technique for predicting the block success.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

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