Ilvana Hasanbegović[1], Eldan Kapur[1], Esad Ćosović[2], Amela Kulenovic[1] and Zakira Mornjakovic[2]

Blockade of peripheral nerves and prevention of unwanted consequences

[1] Department of Anatomy, Faculty of Medicine, University of Sarajevo
[2] Department of Histology and Embryology, Faculty of Medicine, University of Sarajevo

Original scientific paper

Abstract
The Regional anesthesia is evolving rapidly and becoming increasingly popular. The reason is that conductive anesthesia is widely integrated in the treatment of pain, during the pre, intra and postoperative period. Nerve blocks are available for the management of sports related injuries and injection of local anesthetics in the vicinity of nerve is used for both diagnostic and therapeutic purpose in sports medicine. However, regional anesthesia carries certain risk from nerve injury, caused by intraneural injection. For their prevention today are in use few different methods, but the nerve injury can still occur.
The purpose of this work is to determine the values of pressures which appear during intraneural and perineural application of local anesthetic, and to compare those values in order to avoid cases of intraneural injections in clinical practice with consequential complications.
In this experimental study there have been used 12 Wistar rats. After general anesthesia, the sciatic nerves (n=24) were exposed bilaterally. Under the direct visual control, the needle was placed intraneural or perineural and 3 ml of lidocaine 2% was injected using an automated infusion pump (3 ml/min). Injection pressure data were acquired using a manometer coupled to a computer. After application and awakening from general anesthesia, the animals were subjected to neurological examination during the next 7 days.
Even though all perineural injections resulted with the pressure ≤ 27,92 kPa, the majority of intraneural injections were combined with the injection pressure ≥ 69,8 kPa. The difference between average values of intra and perineural injections (with 95% safe interval) was significant (t=3,14; df=6; P=0,02). Also, residual neurologic impairment was present only in those hind limb after intraneural injections which was associated with injection pressures > 69,8 kPa.
Injection application in different tissues results in different values of injection pressures, which depends on structure, compactness and elasticity of tissue. As long as the injection pressure is low, injection into poorly compliant tissue can be avoided and the neurological damage can be prevented.

Key words: **sport injuries, nerve blocks, injection pressure**

Sažetak
Reginalna anestezija se razvija veoma brzo i postaje sve popularnija. Razlog tome je što je regionalna anestezija široko integrirana u terapiji bola, u toku pre, intra i postoperativnog perioda. Blokade perifernih nerava se koriste kod sportskih ozljeda, a injiciranje lokalnih anestetika u blizini nerava ima primjenu i za dijagnostičke i terapijske svrhe u sportskoj medicini. Međutim, regionalna anestezija nosi određeni rizik od nervne ozljede, prouzrokovane intraneuralnom injekcijom. Za njihovu prevenciju danas su u upotrebi nekoliko različitih metoda, ali ozljede nerava se još uvijek dešavaju.
Cilj ovog rada je ustanoviti vrijednosti pritisaka koji se javljaju tokom intraneuralnih i perineuralnih aplikacija lokalnog anestetika, i usporediti te vrijednosti kako bi se izbjegli slučajevi intraneuralnih injekcija u kliničkoj praksi sa posljedičnim komplikacijama.
U ovoj eksperimentalnoj studiji koristi smo 12 Wistar pacova. Nakon opće anestezije, ishijadični nervi (n = 24) su bili izloženi bilateralno. Pod direktnom vizualnom kontrolom, igla je plasirana intraneuralno ili perineuralno, a 3 ml 2% lidokaina je ubrizgano koristeći automatsku infuzionu pumpu (3 ml/min). Podaci o pritisku su dobiveni pomoću manometra spojenim za kompjuter. Nakon aplikacije i buđenja iz opće anestezije životinje su podvrgnute neurološkom pregledu tokom narednih 7 dana.
Iako su sve perineuralne injekcija rezultirale pritiskom ≤ 27,92 kPa, većina intraneuralnih injekcija su bile udružene sa injekcionim pritiskom ≥ 69,8 kPa. Razlika između prosječnih vrijednosti intra i perineuralnih injekcija (sa 95% sigurnosnim intervalom) je bila signifikantna (t= 3,14; df = 6, P = 0,02). Također, rezidualni neurološki deficit bio je prisutan samo na onim stražnjim ekstremitetima nakon intraneuralnih injekcija udruženih sa injekcionim pritiskom > 69,8 kPa.
Injekciona aplikacija u različita tkiva rezultira različitim vrijednostima injekcionog pritiska, što ovisi o strukturi, kompaktnosti i elastičnosti tkiva. Sve dok je injekcioni pritisak nizak, injekcija u slabo popustljivo tkivo može biti izbjegnuta, a neurološka ozljeda prevenirana.

Ključne riječi: **sportske ozljede, nervne blokade, injekcioni pritisak**

Introduction

Regional anesthesia is evolving rapidly and increasing in popularity as evidences by the large number of publication on the topic (1,2,3). This is because conductive anesthesia is widely integrated in the treatment of pain, during the pre, intra and postoperative period. With its application, we can suppress pain from various injuries, sprains, dislocations, bone fractures, pain caused by nerve root compression or pain due to inflammatory processes.

Peripheral nerve block is commonly performed to provide surgical anesthesia and postoperative analgesia. Nerve blocks are available for the management of sports related injuries and injection of local anesthetics is used for both diagnostic and therapeutic purpose in sports medicine (4,5).

Nerve damage after regional anesthesia is appropriately regarded as a major complication. There are many possible causes for such injuries. One causative factor that has been the subject of intense discussion involves the direct intraneural injection of local anesthetics. The deleterious effect of such injuries was demonstrated by Salander nearly 30 years ago (6). Since that time, we have been advised to avoid direct contact between the needle and nerve.

Scientists have been searching for a method which would prevent intraneural injection. Today are in use few different methods: paresthesia, peripheral nerve stimulator and ultrasound. However the injury can still occur, independent from the used techniques.

Injection application in different tissues results in different values of injection pressures, which depends on structure, compactness and elasticity of tissue.

The purpose of this work is to determine the values of pressures which appear during intraneural and perineural application of local anesthetic, and to compare those values in order to avoid cases of intraneural injections in clinical practice with consequential complications.

Materials and Methods

In experimental study there have been used 12 Wistar rats (300-350 g, 3 months old). Animals were housed in central animal care facility and given rat chow and water ad libitum. The study was performed at the Faculty of Medicine in collaboration with Columbia University from New York. All study procedures were approved by the Ethical Committee of the Faculty of Medicine University of Sarajevo.

On the day of experiment, the rats were anesthetized with pentobarbital sodium (30 to 50 mg per kilogram of body weight) administered intraperitoneally. The sciatic nerves (n=24) were exposed bilaterally through a gluteal muscle-splitting incision using aseptic technique. Under the direct visual control, the needle (Becton Dickinson Microlance 000800), with the diameter 27 G (gauge), 12,7 mm long cut, under the angle of 45°, in the direction distal - proximal was placed intraneural (subperineural) into sciatic nerve on one side, and then perineural (subepineural) to the other side of both examination groups. Using the automatic syringe charger (PHD2000; Harvard Apparatus, Holliston, MA), which regulates the volume and the speed of applied solution, in previously mentioned structures we applied 3 ml of 2% lidocaine (Bosnalijek, Sarajevo), with speed of 3ml/min.
In this study the following methods have been used:

1. Measuring and analyzing of intraneural and perineural injection pressure
2. Evaluation of neurological status of the animals

- The data of achieved pressures during intraneural and perineural applications we registered using the manometer (PG5000; PSI-Tronics Technologies Inc, Tulare, CA) (Figure 1.) connected to the computer by analogue digital converter (DAQ card 6023; National Instruments, Austin, TX), The data of pressures we analyzed using the special software package BioBench 1,2; National Instruments, Austin, TX, intended for registration and analysis of data which are obtained in various medical researches, as well for educational needs. In this study we used BioBench program in order to register and analyze the values of pressures during intraneural and perineural application, registering also the time interval needed for the application.

After executed injection application and awakening of animals from general anesthesia the methodic neurological examination has been implemented, in certain time intervals (immediately after awakening, each two hours during the 12 hours of first day, and one time during next 7 days). Neurological examination has been conducted by Thalhammer's neurological examination (7), and included assessment for the proprioception, motor function and nociception by the following criteria:

- Proprioception was evaluated by testing postural reactions (tactile placing response - the rat was kept in a normal resting posture, toes of one foot were flexed with their dorsal placed onto the supporting surface, and the ability to reposition the toes was evaluated). The functional deficit was graded as: 0 - normal; 1 - slightly impaired; 2 - severely impaired; 3 - absent.

- Motor function was evaluated by measuring the extensor postural thrust: the rat was held upright with the hind limb extended so that the body's weight was supported by the distal metatarsus and toes, and the extensor postural thrust could be measured as the force applied to the digital balance, the force that resists contact of the platform balance by the heel. The reduction in the force, representing reduced extensor muscle tone, was considered as a deficit of motor function and expressed as a percentage of the control force.

- Nocoception was evaluated by observing the withdrawal of the limb in response to a noxious stimulation as:
  4 - normal withdrawal reaction, brisk withdrawal of the paw, vocalization, bites the forceps;
  3 - slower withdrawal reaction, weaker withdrawal of the pinched extremity, vocalization, no attempts to bite the forceps;
  2 - slow withdrawal reaction, no vocalization, no attempts to bite the forceps;
  1 - barely perceptible withdrawal, no vocalization, no attempts to bite the forceps;
  0 - no withdrawal, no vocalization, no attempts to bite the forceps;
  The lasting of block is defined as time which passes until the response returns to score 3 (75 % of normal).

Statistics: Statistical analysis has been executed by using SPSS program, version 11.5. Maximum pressure value during intraneural and perineural injection has been compared using paired t-test. The occurrence of neurological injuries is compared between intraneural and perineural injections using McNemar's test for paired proportions. P value < 0.05 is considered significant.

Figure 1. Manometer

Results

The results of acquired application pressures

All injections were characterized by increase of pressure in the beginning of application, resulting in maximum pressure, which was then followed by significantly lower pressure during the remaining part of application.

Even though all perineural injections resulted with the pressure ≤ 27,92 kPa, the majority of intraneural injections were combined with the injection pressure ≥ 69,8 kPa.

In rats, during intraneural applications, the maximum pressure was 124,13 kPa, while the minimum pressure was 69,8 kPa, achieved in peak effect. Maximum pressure reached in all perineural applications was 26,52 kPa and minimum was 13,26 kPa, also achieved in peak effect (Charts 1, 2).

The average value of maximum pressure achieved in peak effect for intraneural injection was 94,23±30,01 kPa (the average value ± standard deviation), in comparison to 23,03±5,58 kPa for perineural injection (P ≤ 0,05). The difference between average values of intra and perineural injections (with 95% safe interval) was significant (t=3,14; df=6; P=0,02).

Chart 1. Intraneural application in rats

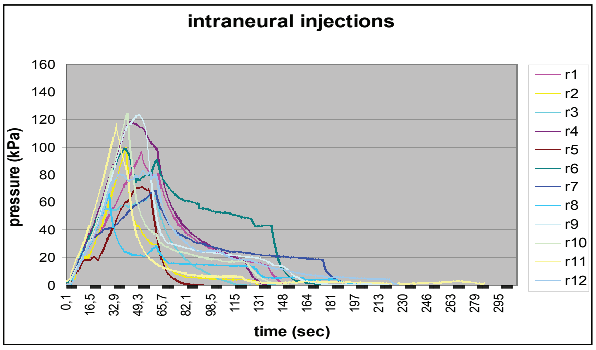
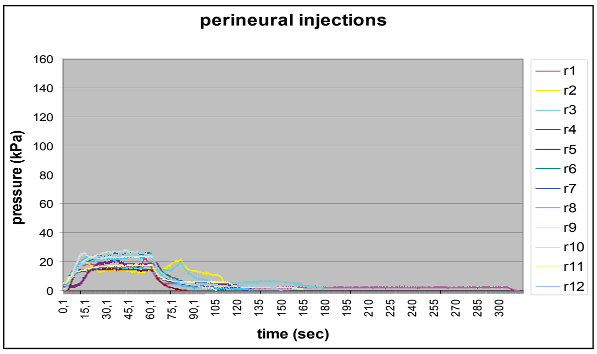


Chart 2. Perineural application in rats



Results of neurological examination of experimental animals

After executed neurological exam, it has been established that all intraneural injections joined with high application pressure resulted with failings which lasted more than 24 hours, and neurological deficits were evident yet at the end of experiment, after 7 days, which clearly shows that intraneural injection caused the nerve damage.On the contrary, all injections combined with low injection pressure, whether they intraneural or perineural didn't result with neurological sequels at the end of experiment. Furthermore, in most cases neurological deficit has withdrawn within first 24 hours of experiment, (Charts 3,4,5).

Chart 3. Proprioception of hind limb after injection application of 2 % of lidocaine

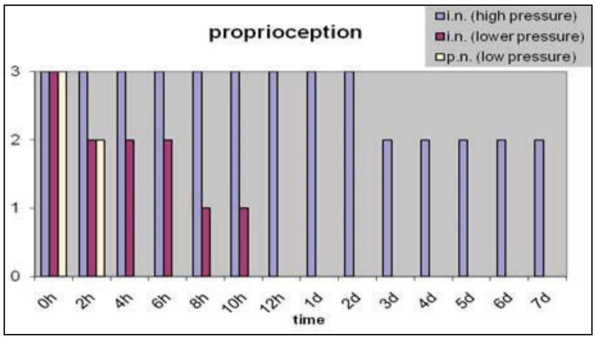


Chart 4. Motor function of hind limb after injection application of 2% of lidocaine

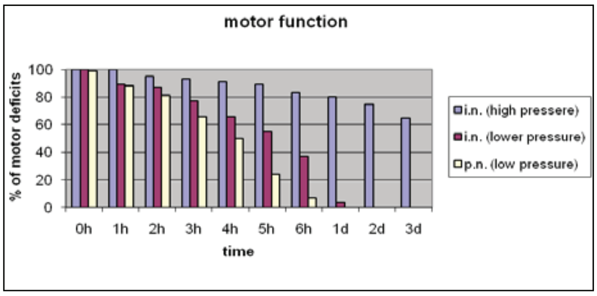
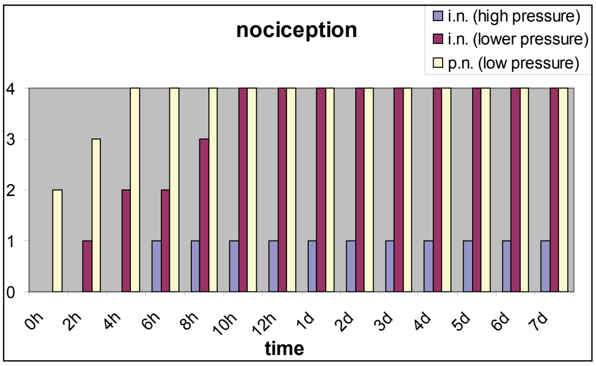


Chart 5. Nocioception of hind limb after injection application of 2% of lidocaine



Discussion

In the last few decades there has been a great development of regional anesthesia; all the postulates are defined and all the techniques of usage are perfected. The world trend of favoring various techniques of regional anesthesia is a result of the advantages that the regional anesthesia comes with, especially in comparison with the general anesthesia, like avoiding hemodynamic instability and lung complications and enabling faster mobilization and earlier release of the patients to their homes (8). In this healthcare environment, continual assessment of the safety and efficacy of clinical practice is critical. Neurologic complications of regional anesthesia can result in disability and are feared by patients and clinicians. Our study shows that detection of pressure during peripheral nerve blocks is unique as a nerve localizing technique in terms of being able to avoid needle-nerve contact and potentially prevent direct trauma to nerves.

The incidence of permanent nerve damages during periphery nerve blocks varies between 0,02% and 0,04%, depending on the type of damage and the amount of time spent observing (9). The incidence of persistent neurological damage decreases with time. The proofs of neurological abnormality can be found in 19 % of patients in first 24 hours, then they are decreasing to 3-8% through 4-6 weeks, and in 1 year they are reduced to 1% (10).

Based on the available data it can be noticed that so far none of the methods of prevention of unwanted complications of regional anesthesia can insure the avoidance of intraneural injection of local anesthetic. There are many discussions about how to prevent intraneural injection and nerve damage coupled with periphery nerve block, and all debates are focused on methods of nerve localization (paresthesia, nerve stimulator and ultrasound).

The oldest method in detection of nerve structures during peripheral nerve blockade is method of paresthesia. Many anesthesiologists intentionally cause paresthesia during the execution of periphery nerve blockade in order to reliably localize nerve structures. But causing paresthesia can represent a direct trauma with needle and theoretically increased risk of neurological injury. Selander and associates reported a high incidence of nerve damages in patients that had parasthesia that was intentionally caused during the axillary block (11). Aurory and associates noticed that all cases of radiculopathy, after blockade of periphery nerve, were coupled either with paresthesia during the placement of the needle or with painful response to injection and they had the same topographic distribution like connected paresthesia (12). Does causing parasthesia present direct needle trauma, which increases the risk of nerve injury, still remains questionable. However today there is a tendency toward the abandonment of this method in many centers.

In present clinical practice for the detection of nerve structures most often are used periphery nerve stimulators. However, it should be pointed out that the nerve stimulators used in blockade of peripheral nerves quite vary in their characteristics, like stimulating frequencies, maximal production of voltage, duration of stimulus and their preciseness (13,14).

Today's progress of ultrasound technology enables visualization of nerve before the insertion of a needle, which represents one new, not invasive method in localization of nerve structures in procedures of regional anesthesia. Observing the advancement of a needle in real time under ultrasound navigation improves the preciseness and safety of the procedure of peripheral nerve block. Ultrasound apparatus sends sound waves with the frequency greater than 20,000 cycles per second (20 kHz). Ultrasound controls the beam under the laws of reflection and refraction. However, the quantity of ultrasound reflection depends on acoustic mismatch. Propagation through dense objects, like bone for example which is filled with almost all reflected rays of ultrasound, produces hyperechoic (bright) image, as a strong signal returned to the emitter. In the contrary, fatty tissue and tendons have low reflection, therefore they produce hypoechoic (dark) images. The contours of structures are best delineated when the ultrasound beam is used under the angle of 90 degrees. Generally speaking, in transversal presentation the nerves can be seen as round or oval structures which are nodular and hypoechoic, usually with centrally located hyperechoic shadow (15,16,17).

So far the experience of using ultrasound in procedures of regional anesthesia showed to be useful for the following: visualization of nerves which helps in defining the best place for the insertion of a needle, placement and advancement of a needle securing the real time navigation of the needle towards the targeted nerve, which avoids or at least minimizes unnecessary randomized movements by executor in trying to achieve wanted level of anesthesia and observation of spreading of local anesthetic during the injection securing its deposit around the nerve.

Contrary to high successfulness in achieving wanted level of anesthesia and even higher safety during the procedure of regional anesthesia, the use of ultrasound method has also some important disadvantages (high price of ultrasound apparatus, making it less accessible, and its big size, making it less portable). This is exactly what distinguishes our methods, detection of nerve structures using application pressure. Also, presently available ultrasound technology does not differentiate between peripheral nerves and tendon fibers, which with sometimes poor picture resolution presents additional disadvantage of this method.

Anesthesiologists often rely on subjective estimate of abnormal resistance to injection during the performance of periphery nerve block, knowing that intraneural injection results with bigger resistance to injection. Hadzic and associates showed that the perception of the resistance can rather vary among the anesthesiologists and that this method is inconsistent and can be affected by different designs of needles (18). The earlier studies carried out on rabbits showed that generally higher pressure (higher than 76,78 kPa) is needed in order to inject local anesthetic into intraneural space, in comparison to paraneural application (19). Also the injection of local anesthetic into sciatic nerve of a dog resulted in high application pressure (20,21). In our study the majority of intraneural injections into sciatic nerve of rats were combined with injection pressure greater then 69,8 kPa, while not even one perineural injection resulted in pressure greater then 27,92 kPa.

As in previous studies, in our study as well all perineural injections of local anesthetic (appropriate doses and concentrations) have not resulted with significant damage of nerve fibers.

In contrast to perineural injections, the intraneural injections of local anesthetic may result with nerve damage. In summary, high injection pressure during intraneural injection may be indicative of intrafascicular injection and predicts development of neurologic injury.

Conclusion

Based on our research it is obvious that the measuring of pressure during the nerve blockade is very important in order to decrease the risk of neurological complications. It is also clear that a small, mobile, and financially quite available apparatus for pressure measurement can help in differentiation between paraneural and intraneural injection. Avoiding high injection pressure prevents from lodging the needle into intraneural space followed by consequential complications.

The usage of this apparatus can find its application in other blockades of periphery nerves, and in other branches of medicine as well, for example in everyday practice of giving intramuscular injections of different medicines (antibiotics-penicillin, corticosteroids and similar) into gluteal or deltoid region, because the application into different tissues results with different values of injection pressures, which greatly depends on structure, compactness and extensibility of the tissue.

The method of monitoring application pressure in detection of neural structures is still in its developmental stage, and the clinical experience of its usage is limited. However this study shows that there exist a great potential in improvement of block performance resulting in better successfulness and lesser risk of lesions of nerves and blood vessels. In the near future the monitoring of injection pressure might exist in order to avoid intraneural injection and to more objectively document the procedure of periphery nerve block. Applying these results to clinical practice, during periphery nerve blocks, the risk of unwanted complications can be reduced. It should be pointed out that none of the techniques can be a substitute to a good knowledge of anatomic relations.

References

Kettner SC, Willschke H, Marhofer P. (2011). Does regional anaesthesia really improve outcome? Br J Anaesth; 107 Suppl 1:i90-5.

Reske AW, Reske AP, Meier V, Wiegel M. (2009). Peripheral nerve blocks of the lower extremities. Clinical and practical aspects. Anaesthesist; 58(10):1055-70.

Capdevila X, Ponrouch M, Choquet O. (2008). Continuous peripheral nerve blocks in clinical practice. Curr Opin Anaesthesiol; 21(5):619-23.

Edkin BS, McCarty EC, Spindler KP, Flanagan JF. (1999). Analgesia with femoral nerve block for anterior cruciate ligament reconstruction. Clin Orthop Relat Res; (369):289-95.

Pagnotto MR, Pagnano MW. (2012). Multimodal pain management with peripheral nerve blocks for total knee arthroplasty. Instr Course Lect; 61:389-95.

Selander D, Edshage S, Wolff T. (1979). Paresthesiae or no paresthesiae? Nerve lesions after axillary blocks. Acta Anaesthesiol Scand; 23(1):27-33.

Thalhammer JG, Vladimirova M, Bershadshy B, Strichartz GR. (1995). Neurologic evaluation of the rat during sciatic nerve block with lidocaine. Anesthesiology; 82:1013-25.

Williams BA, Orebaugh SL, Kentor ML, Hadzic A. (2009). Economic aspects of regional anaesthesia. Br J Anaesth; 103(4):613; author reply 613-4.

Cheney F.W., Domino K.B., Caplan R.A., Posner K.L. (1999). Nerve injury associated with anesthesia. Anesthesiology; 90:1062-1069.

Chambers W.A. (1992). Peripheral nerve damage and regional anesthesia. Br.J.Anaesth; 69:429-430.

Selander D. (1977). Catheter technique in axillary plexus block. Presentation of a new method. Acta Anaesthesiol Scand; 21(4):324-9.

Auroy Y., Narchi P., Messiah A., Litt L., Rouvier B., Samii K. (1997). Serious complications related to regional anesthesia. Anesthesiology; 87:479-486.

Moore DC. (1997). „No paresthesias-no anesthesia," the nerve stimulator or neither? Reg Anesth; 22(4):388-90.

Lahori VU, Raina A, Gulati S, Kumar D, Gupta SD. (2011). A randomized comparative study of efficacy of axillary and infraclavicular approaches for brachial plexus block for upper limb surgery using peripheral nerve stimulator. Indian J Anaesth; 55(3):253-9.

Barrington MJ, Wong DM, Slater B, Ivanusic JJ, Ovens M. (2012). Ultrasound-Guided Regional Anesthesia: How Much Practice Do Novices Require Before Achieving Competency in Ultrasound Needle Visualization Using a Cadaver Model. Reg Anesth Pain Med ŠEpub ahead of printĆ.

Maalouf D, Liu SS, Movahedi R, Goytizolo E, Memstoudis SG, Yadeau JT, Gordon MA, Urban M, Ma Y, Wukovits B, Marcello D, Reid S, Cook A. (2012). Nerve stimulator versus ultrasound guidance for placement of popliteal catheters for foot and ankle surgery. J Clin Anesth; 24(1):44-50.

Shi J, Schwaiger J, Lueth TC. (2011). Nerve block using a navigation system and ultrasound imaging for regional anesthesia. Conf Proc IEEE Eng Med Biol Soc; 2011:1153-6.

Tsai TP, Vuckovic I, Dilberovic F, Obhodzas M, Kapur E, Divanovic KA, Hadzic A. (2008). Intensity of the stimulating current may not be a reliable indicator of intraneural needle placement. Reg Anesth Pain Med; 33(3):207-10.

Selander D, Brattsand R, Lundborg G, Nordborg C, Olsson Y. (1979). Local anesthetics: importance of mode of application, concentration and adrenaline for the appearance of nerve lesions. An experimental study of axonal degeneration and barrier damage after intrafascicular injection or topical application of bupivacaine (Marcain). Acta Anaesthesiol Scand; 23(2):127-36.

Hadžić A, Dilberović F, Shah S, Kulenović A, Kapur E, Začiragić A, Čosović E, Vučković I, Divanović KA, Mornjaković Z, Thys DM, Santos AC. (2004). Combination of intraneural injection and high injection pressure leads to fascicular injury and neurologic deficits in dogs. Reg Anesth Pain Med; 29(5):417-23.

Kapur E, Vuckovic I, Dilberovic F, Zaciragic A, Cosovic E, Divanovic KA, Mornjakovic Z, Babic M, Borgeat A, Thys DM, Hadzic A. (2007). Neurologic and histologic outcome after intraneural injections of lidocaine in canine sciatic nerves. Acta Anaesthesiol Scand; 51(1):101-7.

Submitted: April 08, 2012.
Accepted: May 22, 2012.

Correspondence to:
Ilvana Hasanbegovic, MD, PhD
Department of Anatomy
Faculty of Medicine, University of Sarajevo
Čekaluša 90.
Bosnia and Herzegovina
Phone number: +38761211249
E-mail: ilvanav@bih.net.ba