Injection Pressure as a Marker of Intraneural Injection in Procedures of Peripheral Nerves Blockade

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Abstract

The blockade of peripheral nerves carries a certain risk of unwanted complications, which can follow after unintentional intraneural injection of a local anesthetic. Up till today, the research of measuring injection pressure has been based on animal models, even though the histological structure of periphery nerve is different for animal and human population, so the application pressure which presages intraneural injection in human population is still unknown. As material in performing this study there have been used 12 Wistar rats and 12 delivered stillborns. After bilateral access to the median nerve, we applied 3 ml of 2% lidocaine with epinephrine, with the help of automatic syringe charger. The needle was at first placed perineural on one side, and then intraneural on the other side of both examination groups. During every application the pressure values were monitored using the manometer, and then they were analyzed by special software program BioBench. All perineural injections resulted with the pressure ≤ 27,92 kPa, while the majority of intraneural injections were combined with the injection pressure ≥ 69,8 kPa. The difference between intraneural and perineural injection pressures for the two different examination groups (rats and delivered stillborns) was not statistically significant (P>0,05). As prevention from intraneural injections today are in use two methods: the method of causing paresthesia or the method of using the peripheral nerve stimulator. However the nerve injury can still occur, independent from the technique used. If our results are used in clinical practice on human population, than the high injection pressure could be the marker of intraneural lodging of a needle.

KEY WORDS: regional anesthesia, blockade of peripheral nerves, intraneural injection, median nerve

Introduction

In the last few years there has been a great leap forward in the development of regional anesthesia. Since 2000 the concept of ambulatory surgery and the concept of acute pain is developing, the equipment for regional anesthesia is improving, the new pharmacological resources and new techniques of regional anesthesia are being found (1). At the same time, safer methods of access and outcome for patients are developing, and the advantages of regional anesthesia (more physiological and economical) are taken in consideration, while the general anesthesia is being pushed into the second plan. However, the blockade of peripheral nerves, as any other medical procedure, carries a certain risk of unwanted complications (2,3,4,5,6). Perioperative neural injury after the blockade of peripheral nerves can be a result of several factors. These factors can be generally divided into two categories:

1. Ones which are unconnected with the techniques of regional anesthesia and
2. Ones which are directly connected with the techniques of regional anesthesia.

Factors that are unconnected to the techniques of regional anesthesia are: improper patient positioning or surgical retractor, surgical trauma, ischemia caused by bandaging, improperly applied casts or already existing neurological diseases which now become clinically visible. In contrast to that, the factors which directly facilitate perioperative neural injuries include:

1. mechanical trauma caused by needle or catheter
2. ischemic injury due to vasoconstrictors or neural edema and
3. chemical injury which can be a result of neurotoxic effect of local anesthetic.

It is known, from the researches so far, that the unwanted complications during nerve blockade can happen after unintentional intraneural injection of local anesthetic in the surrounding neural structures (7,8,9). How to prevent mentioned complications are the themes that are most frequently discussed on the congresses of anesthesiologists. As prevention from intraneural injections and consequential complications today are in use two methods of locating nerves. Those are: the method of causing paresthesia or the method of using the peripheral nerve stimulator. However the injury can still occur, independent from used techniques. Relatively new method in

detection of nerve structures is ultrasound, which beside certain advantages has significant defects. All this presented the need for development new, better and safer method in prevention of unwanted complications. Injection application in different tissues results in different values of injection pressures, which depends on structure, compactness and elasticity of tissue. Up till today, the research of measuring injection pressure has been based on animal models, even though the histological structure of peripheral nerve is different for animal and human population, so the application pressure which presages intanueral injection in human population is still unknown. In experimental animals, like a rat or a rabbit, the peripheral nerves consist of 2-3 fasciculi with the diameter of 0,01 to 1,15 mm, with approximately 27,000 axons (6% are myelinated motor axons, 23% and 48% are myelinated and unmyelinated sensitive axons, and 23% are unmyelinated sympathetic axons), (10). Human peripheral nerves consist of 12 to 18 fasciculi with coefficient of variation around 50%, and the diameter of 0,04 to 3 mm (11). In other words, humans mainly have polyfascicular nerves, unlike the experimental animals in whom dominates the oligofascicular type of nerves.

Materials and Methods

As material in performing this study there have been used: 12 grown up Wistar rats and 12 delivered stillborns. The study was approved by the Ethical Committee of the Medical School University of Sarajevo. We made a bilateral access to n. medianus. 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 n. medianus on one side (Figure 1. and 2.), 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% lidocain with epinephrine (Bosnalijek, Sarajevo), with speed of 3ml/min. .The data of achieved pressures during intraneural and perineural applications we registered using the manometer (PG5000; PSI-Tronics Technologies Inc, Tulare, CA) 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 vari-
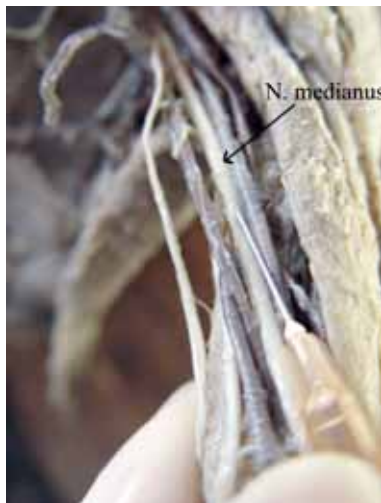
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FIGURE 1. Midhumeral access to n. medianus of delivered stillborns and application of local anesthetic
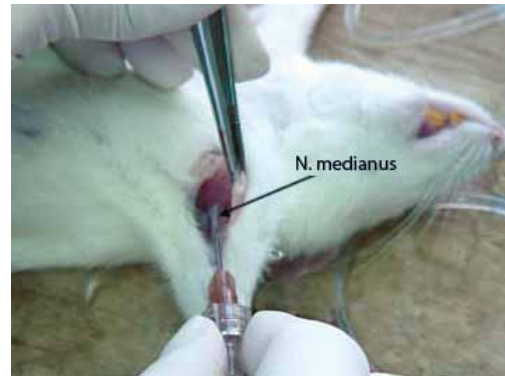

FIGURE 2. Midhumeral accesss to n. medianus of rats and application of local anesthetic

ous medical researches, as well for educational needs. BioBench can be used for following:

- *Manipulations of data* – BioBench automatically saves measuring tracks of users, date and time when every record is made. BioBench has intuitive schematic manipulation of data which enables us to organize data into testing groups. It can also combine a group of data with any testing group.

- *Storing data* – BioBench simplifies getting the data and their adjustment using built-in base of data, which also has all information for majority of physiological monitors and amplifiers.

- *Automatic creation of record* – BioBench automatically generates incoming information which then saves to record in order to show the change of stimulated levels of voltage by the user or whether the data is entered or not. It can also input its own data into the record.

- *Analysis of files* – BioBench analysis can be used to open and analyze already entered data.

- *Exporting of files* – BioBench can inscribe in ASCII document file the data which can be used for further analysis in other software applications.

- *Recording graphics* – BioBench graphics have the form of traditional physio- graphics and lined tables which are routinely used.

- *Configuration settings* – BioBench can record, save and reset different settings. This saves time when there are more users that have different configuration settings.

- *Examples of files with data for the purpose of learning* - BioBench has many examples of files with the data that can be looked at without using and additional hardware or equipment for physiological monitoring.

In this study we used BioBench program in order to register and analyze the values of pressures (expressed in psi - pound per square inch; 1 psi = 6,98 kPa) , during intraneural and perineural application, registering also the time interval needed for the application.

Results

Statistical analysis was executed using SPSS program, version 11,5. Maximum value of pressure (psi) during intraneural and perineural injection is compared using paired t-test. P value < 0,05 is considered significant. Generally speaking, all injections were characterized by small increase of pressure in the beginning of application (first 10-15 seconds), 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 pres-
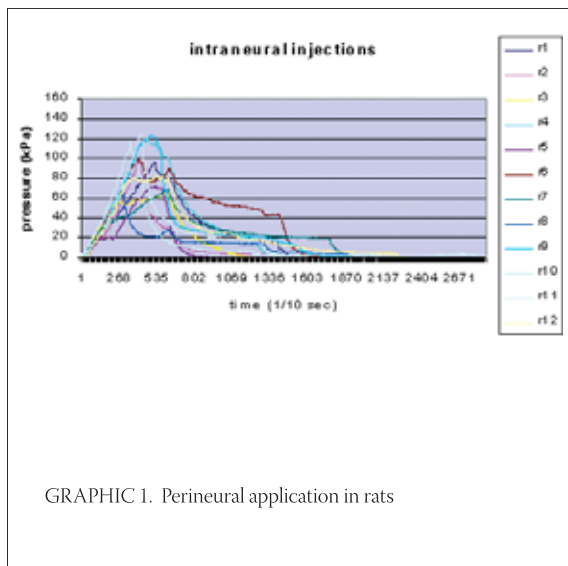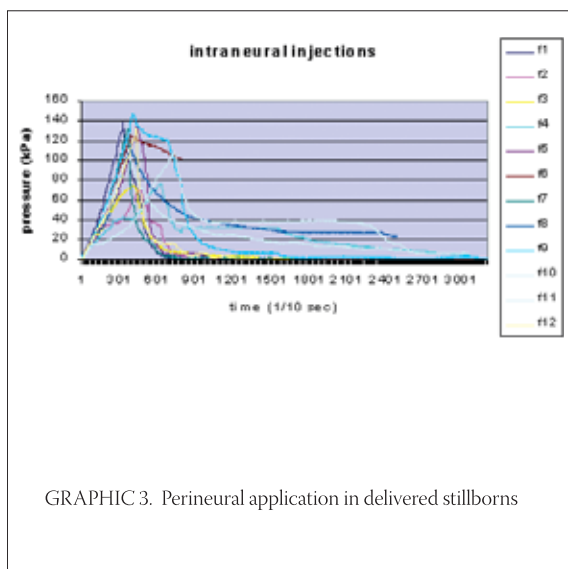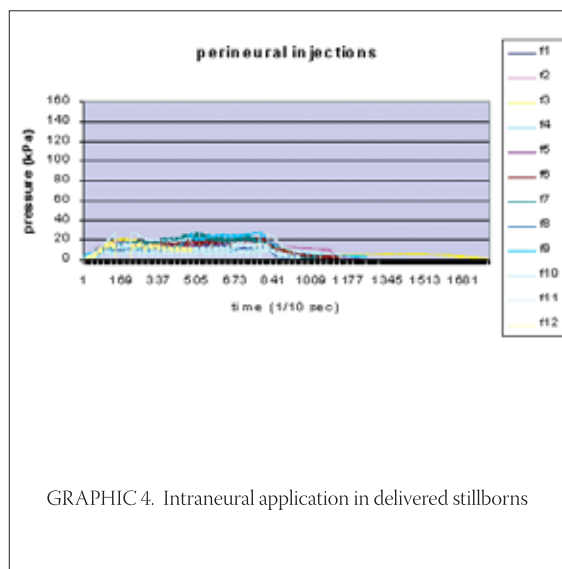
GRAPHIC 1. Perineural application in rats
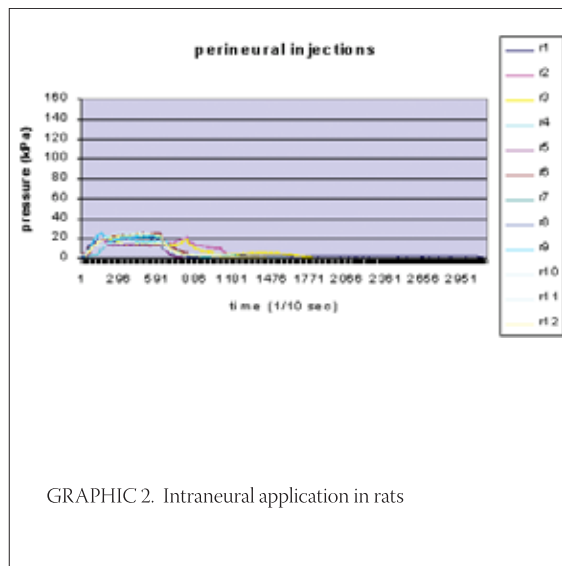
GRAPHIC 2. Intraneural application in rats

sure reached in all perineural applications was 26,52 kPa and minimum was 13,26 kPa, also achieved in peak effect (Graphic 1. and 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). In delivered stillborns, during intraneural applications, the maximum pressure was 145,88 kPa, while the minimum pressure was 73,29 kPa, achieved in peak effect. Maximum pressure in all perineural applications was 27,92 kPa and minimum was 7,67 kPa, also achieved in peak effect. (Graphic 3. and 4.). The average value of maximum pressure of intraneural injection achieved in peak effect for delivered stillborns was 105,34±38,39 kPa (the average value ± standard

deviation), in comparison to 20,24±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=0,03). The values of maximum pressure during intraneural and perneural applications show separation between minimum pressure at peak for intraneural and maximum pressure at peak for perineural injections (Graphic 5.). The difference of intraneural and perineural injection pressures for the two different examination groups (rats and delivered stillborns) was not statistically significant (P>0,05), (Graphic 5.). The pressure gradient slope from the beginning of the procedure to the attainment of the peak pressure was different between intraneural and perineural groups (0.032 + 0.009 versus 0.015 + 0.008), (p < 0.0001). The lowest pressure attained in the period following the peak pressure was significantly higher in the intraneural group than in perineural group (4.4 +

GRAPHIC 3. Perineural application in delivered stillborns

GRAPHIC 4. Intraneural application in delivered stillborns

GRAPHIC 5. The values of maximum pressures achieved at peak effect during intraneural and perineural applications in rats and stillborns
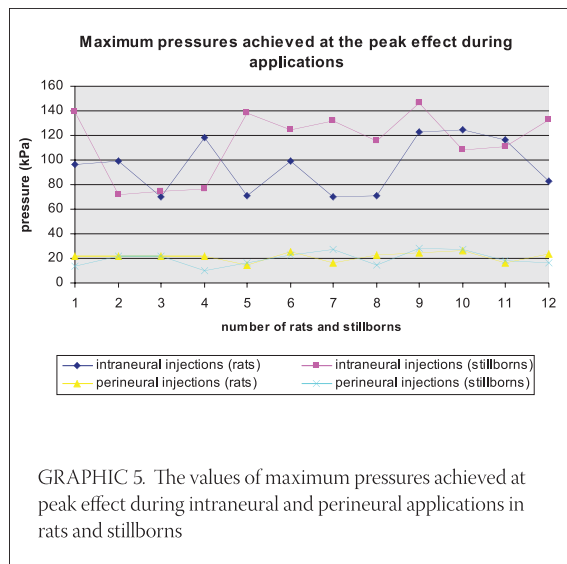
1.6 versus 1.4 + 0.4), (p < 0.0001). Discriminant analysis was used to determine which aspect of recorded injection pressure provided separation between perineural and intraneural injections. It has been shown that the peak pressure and slope-to-peak both provided 100% sensitivity and 100% specificity. Examination of means and 95% safe interval around the average value of perineural and intraneural groups of pressures showed that the earliest time at which the lowest pressure of intraneural group exceeds the highest pressure of perineural group was 38 seconds in rats, or 32 seconds in stillborns.

Discussion

In present clinical practice there is no consensus in technique or method which reduces risk from intraneural injection. This produced the need for development of objective monitoring and reliable prevention of intraneural injections and consecutive neurological injuries. There are many discussions about how to prevent intraneural injection and nerve injury combined with peripheral nerve block, and all these discussions are focused on the methods of nerve localization (paresthesia versus nerve stimulator). However, there is still no evidence that one method is safer than the other because neurological sequels follow both methods (12,13,14,15,16,17,18,19,20). The oldest method in detection of nerve structures during peripheral nerve blockade is method of paresthesia. Whether causing paresthesia presents direct trauma with a needle, which increases the risk of nerve injury, still remains unknown, although today exists the tendency towards abandoning this method in many centers. This comes from the fact that paresthesia can be compromised in cases of sedated or anesthetized patients, which can potentially expose them to failure

of recognizing intraneural injection. Given that causing paresthesia can be lessened in partially anesthetized nerve, for example in incompletely attained anesthesia, than the supplementary block can theoretically increase the risk of nerve injury. This method is unacceptable for pediatric patients, because a child is not able to precisely report paresthesia or to distinguish it from other discomforts during the block execution. Children under 4 years of age distinguish pain with principle all or nothing «either it hurts or it doesn't». 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 (21,22,23). Because of this the nerve stimulators undergo the tests of preciseness. Unfortunately, the majority of manufacturers make the tests using the current of 1,0 mA. It would be much more efficient if they would do these tests with clinically relevant current range from 0,1 to 0,5 mA. In present clinical practice there is no consensus about standard strength of current for peripheral nerve stimulator used by the executors. While one group of anesthesiologists uses higher current in the beginning, which is then lowered as the needle advances into the tissue, the other group uses the opposite procedure. Also, using the current for peripheral nerve stimulator that is too low comes with increased risk of intraneural injection. 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 (20kHz). 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 central-ly located hyperechoic shadow (24,25,26,27,28). So far the experience of using ultrasound in procedures of re-gional 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 unneces-sary randomized movements by executor in trying to achieve wanted level of anesthesia;
- observation of spreading of local anesthetic during the injection securing its deposit around the nerve;

Ultrasound is successfully being used for defining ana-tomical structures of brachial plexus in interscalene, supraclavicular, infraclavicular and axillary access. Al-though the method is new, so far many experiences of successful procedures and use of ultrasound method in anesthesia of brachial plexus have been published. Gen-erally speaking, the picture of high resolution is achieved using high frequency (>7MHz), when brachial plexus takes superficial localization, 1-2 cm from the skin in in-terscalene, supraclavicular and axillary access. For deep-er localization, in infraclavicular access, it is necessary to use lower frequency (<7MHz), which is significantly reflected on the picture resolution. 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 appa-ratus, 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 technolo-gy does not differentiate between peripheral nerves and tendon fibers, which with sometimes poor picture reso-lution presents additional disadvantage of this method. Anesthesiologists often rely on subjective estimate of ab-normal resistance to injection during the performance of peripheral nerve block, knowing that intraneural injection results with bigger resistance to injection and consecutive mechanical damage of the nerve. However, Hadžić and associates showed that the perception of certain resistance can rather vary among the anesthe-siologists and that this method is inconsistent and can be affected by different designs of needles (29). The fail-ures of this procedure are shown in one experimental study in which 5% of testers executed the application of local anesthetic under the pressure of 209,4 kPa, un-

able to evaluate this pressure as abnormally high and not even one stopped the injection (30). Ability of different performers to assess and control the injection pressure is made more difficult by the difference in the strength of the hand, experience among the operators, as well as by the difference in resistance of injection trough differ-ent types of needles (different length and the caliber of the lumen). Resistance to injection is greater for needles with a smaller diameter, and such needles are used for peripheral blockades. Even more importantly, the achieved pressure during injection significantly varies among the needles of same length and diameter but of different manufacturers. This is probably due to the dif-ference in inner diameter of tested needles, even though the diameter and the length of the needles are similar. This has a big clinical implication for anesthesiologists who use needles from different manufacturers. In ear-lier preformed study that was carried out on rabbits it was shown that generally higher pressure (higher than 76,78 kPa) is needed in order to inject local anesthetic and other solutions into the fasciculus of sciatic nerve of a rabbit, in comparison to perineural application (31). Also the injection of local anesthetic into sciatic nerve of a dog or median nerve of a rat resulted in high applica-tion pressure (32,33). In our study the majority of intra-neural injections into median nerve of rats and delivered stillborns were combined with injection pressure greater then 69,8 kPa, while not even one perineural injection resulted in pressure greater then 27,92 kPa. Peak pres-sure and slope-to-peak effect provided good separation between intraneural and perineural groups of pressures. However, since the slope-to peak was 38 seconds in rats, or 32 seconds in delivered stillborns, the rate of pressure rise did not offer information of great advantage over simple monitoring of absolute injection pressure. Inabil-ity of attaining statistically significant values between in-traneural and perineural pressures for two different test-ed groups (rats and delivered stillborns) is not the result of different numbers of fasciculi, but of compliancy and compatibility of nerve tissue in which the application is conducted. This means that differences in pressures during intraneural and perineural applications can be expected in other species as well as in other age groups. This study shows that a certain pressure level must be overcome in order to allow fluid to flow out from the needle and go into relatively noncompliant nerve tissue. There are two phases of fluid administration: First is iso-static phase during which there is no flow at the tip of the needle. A certain opening pressure must be reached within the syringe-tubing-needle system in order to initi-ate the injection into a tissue compartment. During this

phase the pressure is equal throughout the entire closed system (including the tip of the open needle; Pascal's law). Second phase is dynamic phase. Once the opening pressure is overcome and the injection is initiated, the injection pressure becomes affected by the rate of injection and the flow characteristics of the fluid which passes through (Bernoulli's principle). Therefore intraneural injection results with significantly higher injection pressures prior to penetration of the internal bundle of fasciculi. The pressure continues to be high probably due to the restricted diffusion space within the bundle.

Conclusion

1. Intraneural application of local anesthetic into median nerve of human or animal origin in most cases results in high injection pressure (> 69,8 kPa).
2. Perineural application of local anesthetic into median nerve of rats or delivered stillborns results in low application pressure (< 27,92 kPa).
3. The condition for avoiding intraneural application in clinical practice and consecutive damaging of periphery nerve is differentiating nerve structures based on pressures registered by manometer, but also good knowledge of anatomical relations in the region of application.

The pressure information displayed by manometar reliably indicate the pressure at the tip of the needle, regardless to the size of the needle or the rate of injection applied. As long as the injection pressure is low, injection into poorly compliant tissue can be avoided and the neurological damage can be prevented. 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. If our results are used in clinical practice on human population, than the high injection pressure could be the marker of intraneural (intrafascicular) lodging of a needle, which carries a risk of neural injury. Also, very small manometer, which is easily portable, and financially quite available apparatus for measuring the pressure, can help in differentiation between perineural and intraneural injection.

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