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Comparative analgesic efficacy of ultrasound-guided nerve blocks induced by three anesthetics with different duration of action in the treatment of resistant neuropathic pain in the lower extremities

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Abstract
The neuropathic pain (NP) treatment is a big medical and socioeconomical problem. The new sorts of NP treatment have been developed and are applied in case of medical treatment failure.

**Aim:** Investigation of the efficacy of the ultrasound-assisted treatment of the resistant and chronic peripheral neuropathic pain with local anesthetic nerve blocks. Due to the inefficacy of conventional treatment, three local anesthetics (short-acting, medium-term and long-acting) were administered in a series of the same minimal dose on a daily basis. Complications, side effects, the execution time of procedure and the onset time of local anesthetic were investigated as well.

**Method:** In this prospective, randomized and double-blinded study, 108 patients (of which 53 were diagnosed with diabetes and 55 with radiculopathy) with the resistant and chronic peripheral neuropathic pain in the lower extremities were treated with a series of ultrasound assisted peripheral nerve blocks. The conventional treatment was exhausted. The presence of this neuropathic pain was confirmed by, at least, one of the three scales - the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS scale), the Dolour Neuropathic 4 questions (DN4 scale) and the pain DETECT(PD-Q) scale. Other therapies were not applied. The nerve blocks were administered on a daily basis until the relief of pain (VAS<30), and after that, two additional nerve blocks were given. The three local anesthetics with the different duration of therapeutic effect were given at the same minimal dose: the short-acting (1% procaine-chloride solution), medium-term (1% lidocaine-chloride solution) and long-acting (0,25% levobupivacaine-chloride solution) local anesthetics were used. The therapeutic efficacy was measured with the percent reduction in pain intensity on the VAS scale before and after the therapy and one month after the treatment: >50% - excellent results; 31-49% - good results; <30% the therapy does not work. The side effects, complications, the execution duration of procedure, the onset time of numbness, the number of corrections of the needle direction were recorded as well.

**Results:** For all three groups: nerve blocks took 5,04±1,48 minutes to do(without difference between groups), the onset of numbness occurred, on average, within 3,75±2,62 minutes(without differences between groups), and the need for corrections of needle direction was minimal ( 1,03±0,17 corrections). All the patients experienced the loss of pain sensation VAS<30: when a long-acting anesthetic was used, the number of required
nerve blocks was the significant (p<0.001) smallest (4.33±0.63 blocks), than in other two

group, and the percentage pain reduction was the significant (p<0.001) highest (73.13%).
The pain relief lasted one month after the therapy without the application of any other
therapy. Neither complications nor side effects were observed.

**Conclusion:** This is a safe, efficient and easy-to-perform procedure which does not lead to
any complications and side effects. The pain relief is achieved most effectively and rapidly
with long-acting local anesthetics, and maintained even for one month without the
introduction of any additional therapy.

**Key words:** chronic neuropatic pain, neural blocks, ultrasound, lower extremity.

**INTRODUCTION**

The neuropathic pain (NP) is a pain arising as a consequence of the damage affecting the somatosensory part of the central(CNS) or peripheral nervous system. There are two types of NP - central and peripheral (1,2). By its nature, it is chronic (it lasts longer than three months, or could even last for years (2)), and it is commonly seen in the clinical practice: 5% up to 20% of the general population suffer from NP (2-4). The Canadian Association for the Study and Treatment of the Neuropathic Pain thinks that the annual amount of around 11 200 Canadian dollars is spent for the treatment of only one patient with the NP (5).

The year of 2014 - 2015 has been declared as the Global Year Against the Neuropathic Pain to stress the importance of prevention, identification, treatment and socioeconomic severity of this problem (6).

Neuropathic pain may occur in its single, or more often, in a mixed form (7,8). The neuropathic pain component is diagnosed in up to 35% of all pain syndromes (3,4): radiculopathy, the Failed Back Surgery Syndrome – FBSS, the pain in malignant diseases (particularly in bronchus), systemic and rheumatic diseases, the pain following the treatment with certain medications (for instance, chemotherapy), a part of the central pain (following an injury, surgery, ischemia, or the CNS infection), metabolic disorders (for instance, thyroid diseases) etc. It is essential to be familiar with specific questionnaires and ways to identify the neuropathic component of a mixed pain (10-14).
According to the International Association for the Study of Pain (IASP) classification, one of typical forms of the NP is the peripheral neuropathy (13). More than 100 types of peripheral neuropathy have been identified (13), of which the diabetic neuropathy is very common - 60-80% of patients with both type of diabetes may develop this form of NP (3,13).

The diabetic neuropathy is very similar to the neuropathy nerve pain occurring after Failed Back Surgery Syndrome (FBSS); when combined, they represent the most common form of the chronic peripheral neuropathic pain (15).

Therefore, the painful diabetic neuropathy and radiculopathy with the neuropathic component is chosen as the model of chronic, localized peripheral NP for the study, better understanding and identification of NP as a component of a mixed pain. The NP is confirmed on the basis of the following:

1. The confirmation that the nerve system has been damaged with some agent;
2. The overt manifestation of the damage, and
3. The identification of typical somatosensory symptoms (16,17). The presence of symptoms or signs only (for instance, allodynia or hyperpathia) does not justify the use of the term and diagnosis of neuropathic pain (15,16-18).

In the practice, the presence of neuropathic pain component is most easily identified using several questionnaires such as The Leeds assessment of neuropathic symptoms and signs-LANSS scale (12), Douleur Neuropathique en 4 Questions (DN4) scale (9), Pain DETECT (PD-Q) scale (14), which can detect the component of the NP. The questionnaires are most often used together in order to increase the accuracy of NP detection in the course of pain analyses.

The treatment efficacy is most often measured by Visual Analogue Scale (VAS): the excellent result - by > 50% pain reduction; a good result – by 31-49% pain reduction, the unsatisfactory result - by < 30 % pain reduction (19).

All the pharmacological treatments have been found to be ineffective in 20 to 40% of patients (non-responders) due to the common development of unacceptable side effects (15,20,21). There is a great number of protocols for the neuropathic pain treatment that are recommended by the leading associations of the countries, pain societies and federations. The primary treatment of the NP is non-surgical – it is treated with a combination of several medications in 3-4 steps (5,22,23). The first-line treatment involves the application
of antidepressants and anticonvulsants, the local application of drugs often in combination with opioids that are most often considered the second or third-line treatment (5,24,25). There is neither unique way for the NP treatment nor unique combination of medications for the same type of pain.

When the medical therapy is exhausted, the minimally invasive – interventional therapy is applied. It is any procedure requiring a small incision or a procedure during which the instruments are inserted into the body cavity reducing, thus, the tissue damage to a minimum (26,27). The Special Interesting Group on Neuropathic Pain (NeuPSIG) has been established within the framework of the IASP. According to the NeuPSIG definition, the interventional procedure is "an invasive procedure involving the delivery of drugs into the target location" (15,24). The high vitamin D doses, local anesthetics (LA), magnesium, gentamicin with or without corticosteroids are most common currently used in NP treatment (28-32). The success of the neuropathic pain management is limited the most frequently by the development of unwanted effects (29). Therefore, the local application of medications such as gels, plasters or injections has a significant place in the NP treatment (17,24,25,31,32). During the application of a gel or plaster to the skin, a medication penetrates only 5mm below the skin's surface, and lidocaine and capsaicin can only be used on that way (24). The USA and Germany have the longest experience in the application of LA in the form of a gel or an plasters – eight years, and their application in the NP treatment has officially been approved in some 50 countries (24). On the other side, there is a much greater number of LA that can be used at any dose and dilution for peripheral nerve blocks in the area where the NP is localized.

In addition to the needle prick, as lack of methods were mentioned the damage to a nerve or a blood vessel, nonselective effects of LA - the development of transient motor weakness, and, when very high doses are applied, cardiovascular and side effects of the CNS (24,31).

The recommendation of the NeuPSIG Group is to conduct investigations that could contribute to the precise refining of nerve block protocols. This study was done in the accordance with this recommendation: the aim of the study was to investigate the efficacy of the ultrasound-guided treatment of the resistant chronic localized peripheral NP in the lower extremities (LE) with three different local anesthetics (LA)- schort-acting, medium-terme and long-acting.
METHODS

A prospective, randomized, double-blinded, clinical study was conducted. The study included 108 patients divided into three groups. Three types of randomly chosen LA with the different duration of therapeutic effect were used for nerve blocks: short-acting - 1% procaine-chloride solution; medium-acting - 1% lidocaine-chloride solution, and long-acting - 0.25% levobupivacaine-chloride. The solutions of LA were prepared in the Military Medical Academy Pharmacy Sector, and were marked as the X1, Y1, Z1 layers - the double-blinded study.

The inclusion criteria in the study:
- both genders, >18 age, the pain lasts longer than three months and shorter than six years;
- the presence of a resistant, chronic and localized peripheral NP in the LE arising as a consequence of diabetes mellitus or as a neuropathic component of radiculopathy;
- the NP is confirmed by the scores on the LANSS pain scale - ≥ 12 scores or the pain DETECT scale - ≥ 19 scores or the DN4 scale - ≥ 4 scores; each patient fill up each scale;
- the painful, lower-extremity diabetic neuropathy confirmed by a neurologist according to the valid recommendations of the 2010 EFNS guidelines (15). The glycemic values were measured four times a day; in cases with this type of pain and radiculopathy in the LE, radiculopathy was confirmed by clinical, neurological and EMNG examinations;
- the previous pharmacological treatment was ineffective (VAS>30), or side effects were unacceptable. All patients were mentally healthy and intellectually capable of understanding their participation in the study, and gave their informed consent for it.

The patients that were excluded from the study were those with ischaemic cerebral and/or myocardial diseases; metabolic mitochondrial diseases; liver diseases; acidosis; arrhythmias; hemorrhagic diathesis; psychiatric illnesses; epilepsy; organic CNS diseases confirmed by MRI; the allergic reaction to LA; the unregulated arterial hypertension. Other types of peripheral neuropathy detected through adequate analyses, additional testings and examinations were also excluded.

The single-shot nerve block therapy for the NP therapy was applied. Only one type of randomly chosen LA was given to one patient during the entire course of therapy. The nerve blocks were administered on a daily basis until the pain was released (VAS < 30mm), two additional nerve blocks were given to determine therapeutic effects, but no more than ten nerve blocks were used. Subgluteal sciatic nerve blocks (33) (always with
5ml of LA) and the lower inguinal lumbar plexus blocks (33) (the "3-in-1 block" always with 3ml of LA) were used to pain therapy in the entire extremity, i.e. only the nerve block administered in the painful region, in the radiculopathy pain distribution with the same dose of LA.

The treatment efficacy was evaluated by the VAS scores before and after the pain relief and one month after the completion of treatment. The evaluation was done in the following way: firstly, the VAS scores were measured before the therapy, at the end of therapy, and one month after the treatment. Then, the percentage of pain reduction was determined. The therapy results: excellent-by >50% of initially pain reduced; good-by 31-49% of initially pain reduced; the therapy does not work – by <30% of initially pain reduced.

In addition to VAS scores measured before and after the therapy as well as one month later, the onset of numbness (it occurs simultaneously with the pain relief), were recorded by each patient (after daily examination of each patient, during treatment and with ultrasound examination before the new block).

The 8-18 MHz high frequency linear probe of the ultrasound machine, the screening program for peripheral nerves, and the B- and Color Doppler mode (on the Toschiba Aplio 500 Ultrasound Maschine) were used (33). The blocks was performed a specialist, trained for the ultrasound examination of the peripheral nerves, with the nurses assistance; the execution duration of procedure, all side effects and complications, the number of corrections of the needle direction were recorded as well.

**Ethics**

The Ethical Committee of the Military Medical Academy, Belgrade, Serbia, approved all the study procedures (Ethical Committee meeting dated November 30, 2015.).
Statistical analysis

All the data were collected and processed using the SPSS program for Windows. They are presented in the standard way as the mean values with the standard deviation. The value of <0.05 was considered statistically significant, and the value of <0.001 as high significant and used for multiple comparison tests.

The number of patients included into the study is based on the expected difference in satisfactory pain relief results among three anesthetics. The minimally satisfying degree of analgesia is 30%, statistic test power is 80% (0.08). Taking this into consideration (with statistic errors type 1) we calculated that the number of patients should be 36 per group making the total patients number 108. The commercial statistical program GPower 3.1. was applied for calculations.

Normality of dates was assessed by Kolmogorov-Smirnov test. After that, the Friedman test, Wilcoxon Signed Ranks test, the Chi square test, Mann Whitney or Kruskal-Wallis test was used.

RESULTS

Three groups of patients treated with local anaesthetics, each consisted of randomly chosen 36 patients are: group 1 - patients treated with 1% procaine-chloride solution(X1), group 2 - patients treated with 1% lidocaine-chloride solution(Y1) and group 3 - patients treated with 0.25% levobupivacaine – chloride solution(Z1). The groups included roughly the same number of men and women (p=0.65), with similar mean age (p= 0.83) and the neuropathic pain lasting, on average for about 3 years (p=0.74). There was no significant differences (p=0.75) between number of patients in subgroups with diabetic neuropathy (DN) and radiculopathy with neuropathic component (R) in all groups.
Table 1. The efficacy of treatment with different anesthetics: the number of the blocks (N) for groups and subgroups treatment and level of the pain measured by VAS scale (before treatment-VASp, immediately after treatment-VASpp and one month after treatment-VASm).

<table>
<thead>
<tr>
<th>Group/diagnosis</th>
<th>Blocks</th>
<th>VASp</th>
<th>VASp</th>
<th>VASm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup1 DN</td>
<td>10±0</td>
<td>83,31±8,65</td>
<td>34,31±8,44</td>
<td>28,94±8,61</td>
</tr>
<tr>
<td>Subgroup1 R</td>
<td>9,75±0,72</td>
<td>77,45±14,35</td>
<td>27,40±8,92</td>
<td>25,6±6,28</td>
</tr>
<tr>
<td>Group 1</td>
<td>9,86±0,54</td>
<td>80,06±12,35</td>
<td>30,47±9,26</td>
<td>27,08±7,48</td>
</tr>
<tr>
<td>Subgroup2 DN</td>
<td>7,33±2,54</td>
<td>77,83±14,18</td>
<td>30,22±9,31</td>
<td>28,89±6,05</td>
</tr>
<tr>
<td>Subgroup2 R</td>
<td>7,28±2,05</td>
<td>75,22±12,48</td>
<td>26,17±4,87</td>
<td>26,61±6,47</td>
</tr>
<tr>
<td>Group 2</td>
<td>7,31±2,28</td>
<td>76,53±13,23</td>
<td>28,19±7,60</td>
<td>27,75±6,28</td>
</tr>
<tr>
<td>Subgroup3 DN</td>
<td>4,37±0,68</td>
<td>80,11±15,87</td>
<td>19,16±6,71</td>
<td>17,53±7,27</td>
</tr>
<tr>
<td>Subgroup3 R</td>
<td>4,29±0,58</td>
<td>80,24±19,78</td>
<td>23,18±7,65</td>
<td>20,94±7,97</td>
</tr>
<tr>
<td>Group 3</td>
<td>4,33±0,63</td>
<td>80,17±17,56</td>
<td>21,06±7,35</td>
<td>19,14±7,7</td>
</tr>
<tr>
<td>Total DN</td>
<td>7,08±2,76</td>
<td>80,30±13,4</td>
<td>27,49±10,33</td>
<td>24,83±9,06</td>
</tr>
<tr>
<td>Total R</td>
<td>7,25±2,58</td>
<td>77,58±15,54</td>
<td>25,69±7,48</td>
<td>24,49±7,2</td>
</tr>
</tbody>
</table>

There is a very significant difference between groups in the number of nerve blocks (N) for pain relief (VAS<30): Krusal-Wallis test, p<0,001; comparison of the N between pairs, by Mann-Whitney test, in all cases p<0,001. There is no difference between N for DN and R subgroups treatment, in any group (Wilcoxon test; for all results p>0,05). The very significant difference in N for the pain relief exists between all DN subgroups and all R subgroups, when is different anesthetics applied (Kruskal-Wallis test and Wilcoxon test in all cases p<0,001).

The efficacy of anesthetics measured by level of the pain with VAS scale, before (VASp) and after treatment (VASpp), and one month after treatment was completed (VASm): there is a very significant difference, for all anesthetics p<0,001. The positive trend in the pain relief is continued in group 2 and 3 as well; Friedman test, in all cases p<0,001.

There was no difference (measured by VAS score) between results of treatment subgroup DN and R in the same group (Wilcoxon test p>0,005, except group 3 immediately after treatment (p=0,039); after one month, this difference was disappear (p>0,05)).
The very significant differences, in value of VAS scores, exists between the same subgroup (DN and R) in all groups, when is different anesthetics applied (Friedman and Wilcoxon test, in all cases p<0.001). The lowest values of VAS score have been achieved in group 3. The trend of excellent results continued one month after therapy accomplished: in the subgroup with DN, after treatment with 1% procain-chloride solution and in the subgroup R after treatment with 0.25% levobupivacaine-chloride solution (p<0.05).
Table 2. The average execution duration of procedure (in minutes), and the onset time of nerve block (NB) (in minutes)

<table>
<thead>
<tr>
<th>Anesthetics</th>
<th>The duration of NB</th>
<th>The onset time of NB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>4,9±1,52</td>
<td>3,78±2,72</td>
</tr>
<tr>
<td>Group 2</td>
<td>5,1±1,53</td>
<td>3,82±2,58</td>
</tr>
<tr>
<td>Group 3</td>
<td>5,02±1,68</td>
<td>3,65±2,51</td>
</tr>
<tr>
<td>Total</td>
<td>5,04±1,58</td>
<td>3,75±2,62</td>
</tr>
</tbody>
</table>

The nerve block procedure lasted for some five minutes on average, the onset time of numbness after the completion of procedure is less than four minutes (p>0,05).

Table 3. The percentage of the pain reduction measured by VAS score: before/after treatment and before/one month after treatment completed.

<table>
<thead>
<tr>
<th>Group</th>
<th>After treatment</th>
<th>A month after treatment completed</th>
<th>Assessment of results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>62,06%</td>
<td>66,23%</td>
<td>excellent</td>
</tr>
<tr>
<td>Group 2</td>
<td>63,02%</td>
<td>63,68%</td>
<td>excellent</td>
</tr>
<tr>
<td>Group 3</td>
<td>73,73%</td>
<td>76,13%</td>
<td>excellent</td>
</tr>
<tr>
<td>Total</td>
<td>67,47%</td>
<td>71,69%</td>
<td>excellent</td>
</tr>
</tbody>
</table>

The highest percentage in the pain reduction is achieved by the application of long-acting anesthetic (73,73%) in group 3. The positive trend in the pain relief in relation to VAS scores measured before the treatment is continued in all local anesthetic groups, but the trend is highest in the group of long-acting local anesthetic(76,13%).

There were no serious complications (injuries of the nerves or vessels) or unwanted effects recorded even though 7±2,7 nerve blocks on average were administered to each patient (over 750 nerve blocks / 108 patients). The only mild side effect that occurred occasionally was the development of subcutaneous hematomas not larger than 1 cm in diameter at the site of the needle insertion into the skin and subcutaneous tissue.

The average number of corrections of the needle direction was 1,03±0,17 corrections.
DISCUSSION

The treatment of neuropathic pain is often inefficient – limited, most often, caused by the development of side effects(3,5,15). Therefore, new methods involving the local application of medications in the areas of nerve structures that innervates the location where the pain is localized are to be found(25).

The local application of medications in the neuropathic pain treatment may be non-invasive- topical, in a form of a gel or skin patch, and invasive – various nerve structure blocks and the instillation of medications into the body cavity where nerve structures are located(3,5,15).

The development of non-invasive methods started in 1998, when a gel and skin patch with the 5% lidocaine-chlorid solution intended for the management of acute pain was first produced in the USA. Nowadays, there are gels and skin patches containing the combination of 2,5% procaine-chlorid and 2.5% lidocaine-chlorid(24). They are the only FDA recommendation for the neuropathic pain therapy in the post-herpetic neuralgia. Besides the USA, the Italian and German Chronic Pain Schools have the longest experience in their application – eight years. However, skin pathes and gels are registerd in 50 other countries besides the USA. In the EU countries, they have been in use since 2008(34-36). In addition to the fact that patients are not always enabled to officially access them, patches and gels contain only lidocaine and procaine-type local anesthetic, which penetrate only five millimeters below the skin's surface, and that is why they are almost ineffective in obese patients or in the areas of deeper target – nerve structures(34).

The therapy of chronic neuropathic pain has become more important over the recent years because it allows for the application of a larger number of diverse medications: higher doses of the vitamins D and D3; various local anesthetics, magnesium, gentamicin with or without corticosteroids, various concentrations, doses with a much greater accuracy and a considerably smaller number of complications(33,37).

The ultrasound guidance for the performance of nerve blocks has allowed for the reduction of applied doses and complications in particular. The description of the nerve structure and the execution of nerve block procedure take place in a real-time, what, thus, reduces the number of damages to nerve structures and major blood vessels by some 30%(32,33,38). Although La Grange et sar used the ultrasound for the first time in 1978(39), only two
studies on that issue have been published until 2002, when, in the next year, that number amounted up to 43(38). The ultrasound-guided low-extremity nerve block was introduced much later in Germany, the country with one of the strongest associations for the ultrasound clinical application. This method has been used in the low-extremity treatment for the last six to seven years(32,33,35). It is, therefore, not surprising that, in its current recommendation on the interventional treatment of neuropathic pain, the NeuPSIG Group stresses the need for further and more thorough study of peripheral nerve and plexus block protocols, as well as for defining their place, doses of medications to be used for such purposes and the execution protocols(21).

There are not many studies devoted to this issue, published series are very little and insufficient for deriving serious conclusions because this is a very actual issue, which is still developing.

Despite the fact that local anesthetics have, for a long time, been used for the management of acute pain during surgical procedures, nerve blocks with local anesthetics have recently been introduced in the treatment of chronic and neuropathic pain in particular. In the treatment of acute pain during a surgery, local anesthetics are also used for developing motor paralyses in the extremities, what explains the use of doses 60-200 times higher than those applied in our study and which proved to be sufficient to treat outpatients with neuropathic pain(32,33).

The occurrence of motor paralyses in outpatients with neuropathic pain is not desirable, because, it is very disturbing for the patient who is even warned that it could develop and is transient. The motor weakness requires the hospitalization of outpatients and their close monitoring, and in case of chest muscle blocks, their vital functions should be monitored for at least two hours. Due to all that, the motor weakness is not desirable and represent a side effect or even a complication.

Higher concentrations of LA accelerate onset on effect in the isolated nerve. The duration of effect depends on the dosage and concentration of local anesthetic, resorption from tissue into the blood, and its building to the membrane receptors (protein-building activity). To avoid motor weaknesses of lower extremity, we applied lower dose and concentration LA during pain treatment study. The subgluteal and inguinal region were anatomically poorly vascularized, with low resorption into the blood consequently. The potency in vitro (isolated nerve) for procaine(X1), lidocaine(Y1) and levobupivacaine(Z1) is 1;4;16 in order.
The protein binding for X1, Y1 and Z1 is 5.8%; 64-70% and 97% respectively. The duration of single-dose injection effects is 0.5-1h; 2-4h and 4-7h for X1, Y1 and Z1 respectively. The duration of anesthesia, after single-dose injection, is significantly longer with Z1 than with any other LA(32).

Since the minimum dose of local anesthetics was applied, no complications or side effects were observed in the course of our investigation. The pain relief was achieved by daily repetitive nerve blocks (the cumulative analgetic effect of local anesthetics(32,33)), the application of local anesthetic directly to the surface of the nerve structure that conducts the pain, and the use of ultrasound based on the knowledge of the ultrasound anatomy of the nerve and the nerve block area.

Thus, a patient experiences the pain relief immediately, simultaneously with the clinical sensation of numbness because sensitive nerve fibers are always grouped together.

The comparison of the three local anesthetic groups with the various duration of therapeutic effect showed a greater efficacy of long-acting local anesthetics: the pain relief is achieved with a smaller number of nerve blocks, and the decline in the pain intensity is greater as compared with the use of medium-terme and short-acting local anesthetics p<0.001). This effect is probably a consequence of longer de-excitation of nociceptive and supraspinal systems, and by that, the achievement of balance between nociceptive systems and activities of antinociceptive pathways. However, further investigations in that direction are certainly needed(33).

We can discuss a greater efficacy of local anesthetics with certainty because three groups of patients treated with different local anesthetics had very similar mean VAS scores at the beginning of the study, and those scores were also similar when compared according to the gender, age of patients, the number of patients with diabetes and radiculopathy in each group.

It is well known that the mechanism of action of local anesthetics and antiepileptics is very similar – that the target site of action are voltage-dependent sodium channels. To fully achieve the effect of antiepileptic drugs, the continuous use of medications for four weeks is required (15), and that is why we, in our study, re-evaluated the treatment efficacy after that period. Therefore, it is not surprising that the effectiveness of therapy in our study was even greater after four weeks, without the introduction of any additional therapy.
Based on this experience, we can stress that disadvantages of this method, without any doubt, are invasiveness, the patient’s need for the daily visits, what is particularly difficult for patients living far away. The method requires specific training – knowledge about the ultrasound examination of peripheral nerves, the ultrasound anatomy and certain skills, because, if the in-plane technique is used, the one we applied in our study, the needle should always remain within the 1mm wide beam from the ultrasound probe.

Based on the clinical experience, we suggested the application of protocol involving daily administration of minimal local anesthetic dose ("3-in-1 block" with 3ml, i.e. 5ml of local anesthetic for subgluteal sciatic nerve blocks), to prevent the possibility of side effects, and the development of transient paralyses of muscle groups in particular, since it requires the observation and hospitalization of a patient after the nerve block.

By performing ultrasound-guided nerve blocks, we excluded the possibility of complications (the damage to a nerve or a blood vessel). Having compared local anesthetics with different duration of therapeutic effect, we showed that a long-acting local anesthetic is the most effective and allows for the achievement of pain relief in patients after the smallest number of nerve blocks. On the other side, this treatment protocol requires patient’s visits on a daily basis, represents an invasive and painful procedure that is gladly accepted by patients for they feel relief almost after the first block. Therefore, this method may be applied in the treatment of neuropathic pain only when all pharmaceutical options are exhausted.

CONCLUSION

The method that was applied in our study is efficient and easy-to-perform. No complications were observed due to the use of ultrasound-guided nerve blocks and the reduction of the local anesthetic dose to only 3 ml and 5 ml.

Based on the percentage pain reduction and the smallest number of nerve blocks required to achieve the pain relief (VAS<30), long-acting local anesthetics were found to be the most efficient. Further investigations are required to highlight the mechanisms of pain relief, the cumulative effect of local anesthetics and the achievement of full effect four weeks after the initiating of therapy.


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