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ORIGINAL ARTICLE

Evaluation of the effectiveness duration of peripheral blocks applied with high concentration local anesthetic and steroid in trigeminal neuralgia

Trigeminal nevraljide yüksek konsantrasyonlu lokal anestezik ve steroid ile uygulanan periferik blokların etkinlik süresinin değerlendirilmesi

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Summary

Objectives: The aim of this study was to investigate the effectiveness duration of the peripheral blocks applied with high concentration local anesthetic and steroid in trigeminal neuralgia.

Methods: The data of 48 patients (nine patients received medical treatment and 39 patients underwent interventional procedure for peripheral block and Gasser ganglion radiofrequency thermocoagulation [RFT]) were analyzed retrospectively. The medications used by patients, pre-operative and post-operative visual analog scale scores who underwent interventional procedures, and duration for effectiveness of the procedure were evaluated with 36 months follow-up.

Results: Forty-eight patients (32 females and 16 males) who were treated with primary and secondary etiologies were evaluated. Three patients V1, 12 patients V2, 25 patients V3, and eight patients V2+V3 trigeminal nerve branches described appropriate clinical symptoms. Only peripheral block was applied to 31 patients and Gasser ganglion RFT was applied to eight patients after peripheral block. In 24 patients who underwent peripheral block, pain severity reduction was ≥50%, mean effectiveness duration of peripheral block was 7.5 months. The eight patients undergoing Gasser ganglion RFT had ≥50% pain intensity reduction, mean effectiveness duration of Gasser ganglion RFT was 22.7 months (p=0.002). While one patient had hypoesthesia in the palate after RFT, no serious side effects were recorded.

Conclusion: The duration of pain control for peripheral branch blocks in trigeminal neuralgia is not as long as RFT, but it is a relatively less invasive and less complicated interventional technique with good efficacy duration due to neurotoxicity of the used high concentrated local anesthetic.

Keywords: Highly concentrated local anesthetic; peripheral block; radiofrequency thermocoagulation; trigeminal neuralgia.

Özet

Amaç: Bu çalışmanın amacı, trigeminal nevraljide yüksek konsantrasyonda lokal anestezik ve steroid ile uygulanan periferik blokların etkinlik süresinin araştırılmasıdır.

Gereç ve Yöntem: Kırk sekiz hastanın (dokuz hastaya medikal tedavi, 39 hastaya girişimsel işlem: periferik blok ve gasser ganglion radyofrekans termokoagülasyon [RFT]) verileri retrospektif olarak incelendi. Hastaların kullandığı ilaçlar, girişimsel işlem uygulanan hastaların işlem öncesi ve sonrası visuel analog skala (VAS) skorları, işlemin etkililik süresi 36 aylık takiplerle değerlendirildi.

Bulgular: Primer ve sekonder etyolojilerle tedavi edilen 48 hasta (32'si kadın, 16'sı erkek) değerlendirildi. Üç hasta V1, 12 hasta V2, 25 hasta V3, sekiz hasta V2+V3 trigeminal sinir dallarına uygun klinik semptomları tanımladı. Otuz bir hastaya sadece periferik blok, sekiz hastaya ise periferik blok sonrası gasser ganglion RFT uygulandı. Periferik blok uygulanan ağrı şiddetinde ≥%50 azalma gözlenen hastalarda periferik blokların ortalama etkinlik süresi 7,5 aydı. Gasser ganglion RFT uygulanan sekiz hastanın hepsinde ağrı şiddeti ≥%50 azalma gösterdi, gasser ganglion RFT'nin ortalama etkinlik süresi 22,7 aydı (p=0,002). RFT sonrası bir hastada damakta hipoestezi varken ciddi bir yan etki kaydedilmedi.

Sonuç: Trigeminal nevraljide periferik dal blokları için ağrı kontrolü süresi RFT kadar uzun değildir. Ancak periferik blok uygulaması kullanılan yüksek konsantrasyonlu lokal anesteziğin nörotoksisitesinden dolayı iyi etkinlik süresi ile nispeten daha az invaziv ve daha kolay uygulanan bir girişimsel tekniktir.

Anahtar sözcükler: Yüksek konsantrasyonlu lokal anestezik; periferik blok; radyofrekans termokoagülasyon; trigeminal nevralji.

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Introduction

Trigeminal neuralgia is a condition characterized by unilateral, short lightning-like pains, suddenly starting and ending and limited by the distribution area of the first, second, and third branch of the trigeminal nerve.[1,2] The pain can occur with stimuli such as face washing, shaving, smoking, talking, and/or brushing teeth (trigger factors), and it can often be spontaneous. Trigeminal neuralgia can be idiopathic or rarely symptomatic (e.g., herpes zoster infection, structural lesion such as tumors, and multiple sclerosis). The first option in treatment is medical. In cases that do not respond to medical treatment or have medical treatment side effects, interventional procedures are an option. Interventional and surgical methods are percutaneous radiofrequency thermocoagulation (RFT), percutaneous balloon compression and percutaneous glycerol rhizolysis, and microvascular decompression.

RFT is a low-risk, minimally invasive technique with a very high success rate. RFT continues to be the most commonly used percutaneous treatment for trigeminal neuralgia.[3] This technique, which is used frequently, effectively, and safely, can be repeated in recurrence, although the efficacy is temporary.

Peripheral nerve blocks are used for diagnostic, prognostic, and therapeutic purposes. High concentrations of neurotoxic local anesthetics used in chronic pain with the long-term block effect are therapeutic. Histologically proven neurotoxicity of high concentrate lidocaine has been demonstrated alongside bupivacaine, tetracaine, mepivacaine, and prilocaine, whose neurotoxic effects are well known. In addition, this neurotoxicity effect appears to be suitable for long-term treatment, with the effect of painful fibers by showing selectivity without causing motor and sensory deficit.[4]

In this study, we aimed to evaluate the interventional procedure involving peripheral block and RFT according to affecting branch in the patients with trigeminal neuralgia who were admitted to our outpatient clinic with 36 months follow-up results.

Material and Methods

Patients and study design

After the institutional approval (2020/193 Ethic Committee of Adnan Menderes University), the study was carried out in Adnan Menderes University Faculty of Medicine, Department of Algology. Forty-eight patients' data diagnosed with trigeminal neuralgia with the criteria of International Headache Society between June 2016 and June 2017 were evaluated retrospectively. Nine patients with pain control under medical treatment were excluded from the study. Thirty-nine patients who underwent interventional treatment and completed the 36 months follow-up were included in the study. Demographic characteristics of the patients, medications used for opioid, medical treatment response, interventional procedure applied, and visual analog scale scores that were recorded initially and after the procedure, the process effectiveness duration were evaluated by examining the outpatient records.

Procedure

According to the peripheral branches held, the records of the patients who were applied supraorbital and supratrochlear block for V1, maxillary block for V2, mandibular block for V3, and maxillary and mandibular block for V2+V3 involvement were evaluated. RFT in foramen ovale midpoint for V2 distribution, foramen ovale lateral for V3, and two lesions for V2+V3 involvement were evaluated. The pain scores and side effects recorded follow-up outpatient visit.

Technique

Maxillary nerve block

Mandibular notch is defined, detected by opening and closing the patient's mouth. The 22-gauge needle was then placed perpendicular to the skin behind the notch near the middle of the zygoma. The needle was advanced until it meets the lateral pterygoid plate (4–5 cm). The needle was then pulled and directed forward and upward at an angle of about 45 degrees toward the upper root of the nose. The pterygopalatine is advanced to the fossa until a needle is obtained from a paresthesia. After negative aspiration, a mixture of 8 mg (2 mL) dexamethasone and 5 mL 0.5% bupivacaine was injected.

Mandibular nerve block

It was entered through the mandible notch with a 22-gauge spinal needle, and the infratemporal fossa was advanced and the lateral pterygoid plate was reached. In this case, the lateral pterygoid plate was touched, maintaining the same depth as the needle, lower lip, lower jaw, or ipsilateral tongue or ear until

paresthesia was obtained. After negative aspiration, a mixture of 8 mg (2 mL) dexamethasone and 5 mL 0.5% bupivacaine was injected.

Supraorbital nerve block

A 25–30-gauge needle was inserted in the medial and cephalad direction about 0.5 cm of the lower border of the supraorbital notch, the needle was gently advanced, being careful not to penetrate the supraorbital foramen. After negative aspiration, a mixture of 4 mg dexamethasone and 2 mL 0.5% bupivacaine was applied.

Supratrochlear nerve block

The place where the supratrochlear nerve touches the bone is above the angle formed by the eyebrow and nasal spine. For the supratrochlear nerve block, a mixture of 4 mg dexamethasone and 2 mL 0.25% bupivacaine was applied immediately after the supraorbital nerve block.

Gasser ganglion radiofrequencylesion

The patient was taken to the operating room in the supine position. The patient was administered intravenous fentanyl (1 µcg/kg) and midazolam (0.05 mg/kg) as mild sedation, provided that the patient was awake enough to respond to the test with electrical stimulation. In fluoroscopy, oblique projection was angled to approximately 15 degrees lateral to approximately 30 degrees to caudal, and foramen ovale was seen in the upper inner quadrant. The entry point was 2–3 cm side of the commissura labialis directed toward the pupil when viewed from the front of the face. A 10 cm long 5 mm active tip RF cannula was inserted into the foramen ovale as a tunnel vision (Fig. 1a), fluoroscopy was taken laterally, and the cannula entered into the bone tunnel of the foramen ovale (Fig. 1b). The direction of the needle was verified in submental, lateral, and posterior-anterior view under fluoroscopy so that the tip of the cannula does not exceed 2 mm from the clivus plane. Sensory and motor stimulants were given before radiofrequency. Paresthesia was taken in the appropriate dermatome area at 0.1–0.5 V at 50 Hz at appropriate localization for sensorial stimulation. Masseter contraction was observed by stimulating 0.1–1.5 V at 2 Hz for the mandibular branch for motor stimulation. After completion of stimulation, radiofrequency was applied after negative aspiration, after the patient provided deep sedation with either midazolam, fentanyl, or propofol (0.5 mg/kg). RF lesion was performed at 80°C for 90 s. The patient was observed for 24 h after the procedure for side effects.

Statistical analysis

Research data were evaluated using SPSS 21.0 statistics program. The consistency of continuous variables to normal distribution was investigated using visual (histogram and probability graphs) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk tests). For the descriptive statistics of the study, the mean and standard deviation in the data matching the normal distribution were shown using the median, minimum, and maximum in the data that

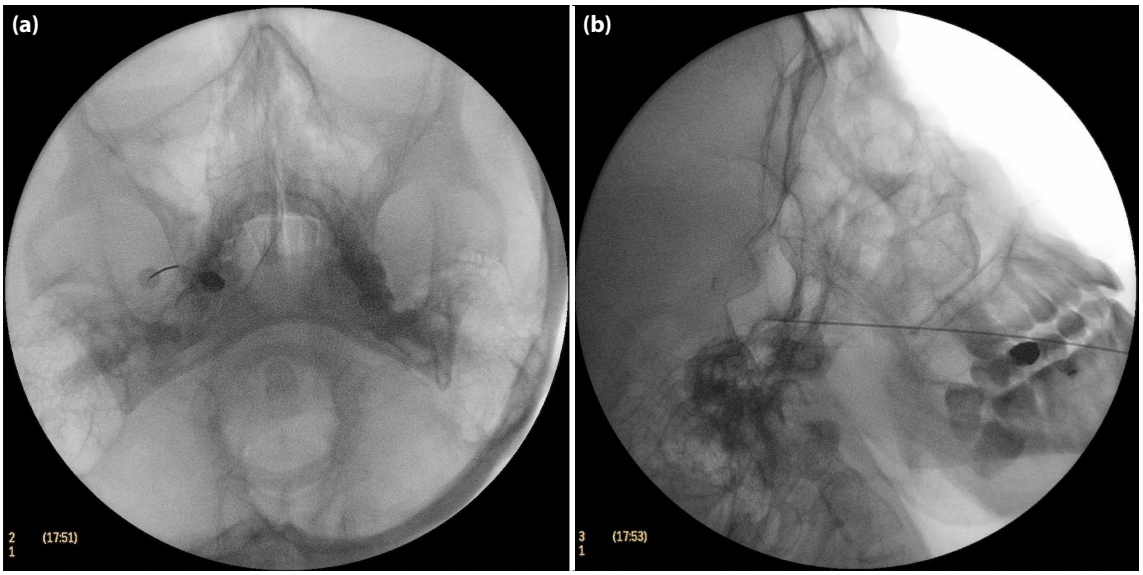

Figure 1. (a) Fluoroscopic image of the cannula in the foramen ovale in posterior-anterior position. **(b)** Fluoroscopic image of the cannula in the foramen ovale in the lateral position.

do not fit the normal distribution. Chi-square test was used to show whether there is a difference between categorical variables. Student's t-test or ANOVA was used for comparing the parametric properties of continuous variables in independent groups, and Mann–Whitney U-test or Kruskal–Wallis test was used in comparison of those that did not have the parametric properties of continuous variables in independent groups. For statistical significance, the condition of determining $p<0.05$ is sought.

Results

The demographic characteristics of the patients are shown in Table 1. While 45 patients were diagnosed with idiopathic trigeminal neuralgia; secondary etiology (trauma in one patient, maxillary fracture in one patient, and cerebellopontine corner tumor in one patient) was detected in three patients. Six patients were connected to dental problems due to pain, jaw surgery and tooth extraction were performed and three patients additionally had temporomandibular joint dislocation.

While nine patients were provided with pain control with medical treatment, 39 patients underwent interventional procedures. Supraorbital and supratrochlear blocks were applied to three patients suitable for V1 distribution, maxillary block for 10 patients suitable for V2 distribution, mandibular block for 20 patients with symptoms in V3 distribution, and maxillary and mandibular block for six patients for V2+V3 distribution. Only 31 patients underwent peripheral block and eight patients underwent Gasser ganglion RFT after peripheral block.

The mean efficacy duration of the peripheral block was 7.5 months in 24 patients with a decrease pain intensity ≥50%, and the duration of peripheral block effectiveness was 5.1 months in 15 patients with a decrease in pain intensity <50% (p=0.057) (Table 2). In all eight patients who underwent Gasser ganglion RFT, the pain intensity decrease was ≥50%, and the mean efficacy duration of the Gasser ganglion RFT was 22.7 months (p=0.002) (Table 3).

The duration of effectiveness according to nerve distributions for the peripheral block for V1(3), V2(10), V3(20), and V2+V3(6) was 4.3, 5.8, 7.2, and 6.8 months, respectively (p:0.38), and the duration of activity for RFT for V2(2), V3(3), and V2+V3(3) was 19, 32, and 16 months, respectively (p=0.093) (Table 4).

Table 1. Demographic characteristics of the patients

	n	%
Age (mean: 61.5±15)	48	
Min: 24		
Max: 91		
Gender		
Female	32	66.7
Male	16	33.3
Side		
Right	26	54.2
Left	21	43.8
Right and left	1	2.1
Localization		
V1	3	6.3
V2	12	25
V3	25	52.1
V2+V3	8	16.7
Etiology		
Idiopathic	45	93.7
Secondary	3	6.3
Opioid used		
Yes	36	75
No	12	25

In comparison of nerve distributions in patients with peripheral block, there was no significant difference in pain intensity (p=0.988) (Table 5).

While one patient had hypoesthesia in the palate after Gasser ganglion RFT, serious side effects such as difficulty chewing, anesthesia dolorosa, and keratitis were not recorded.

Discussion

In this study, we demonstrated the long duration of efficacy of peripheral blocks performed with high concentration local anesthetic and steroid, which is one of the minimally invasive procedures in trigeminal neuralgia. Twenty-four patients with whom we applied peripheral block had ≥50% pain regression and the mean efficacy period was 7.5 months. Although the use of peripheral blocks used for diagnostic and prognostic purposes in treatment seems to be inap-

Table 2. Effectiveness duration of interventional procedure in patients applied peripheral block and RFT

	n	$\bar{X}$	Median	Min	Max	SD	p
Peripheral block							
Pain relief							
<50%							
Duration of treatment effectiveness (months)	15	5.1	5	0.3	10	2.9	0.057
≥50%							
Duration of treatment effectiveness (months)	24	7.5	6.5	1	18	4.16	
RFT							
Pain relief							
<50%							
Duration of treatment effectiveness (months)	0						–
≥50%							
Duration of treatment effectiveness (months)	8	22.7	21	12	36	9.19	

RFT: Radiofrequency thermocoagulation.

Table 3. Comparison of efficacy duration and ≥50% in pain relief in patients applied peripheral block and RFT

	n	$\bar{X}$	Median	Min	Max	SD	p
Peripheral block							
Pain relief							
≥50%							
Duration of treatment effectiveness (months)	24	7.5	6.5	1	18	4.16	0.002
RFT							
Pain relief							
≥50%							
Duration of treatment effectiveness (months)	8	22.7	21	12	36	9.19	

RFT: Radiofrequency thermocoagulation.

Table 4. Comparison of treatment efficacy duration of patients with peripheral block and RFT according to pain localization

	Duration of treatment effectiveness (months)						p
	n	$\bar{X}$	Median	Min	Max	SD	
Peripheral block							
V1	3	4.3	4	3	6	1.53	0.380
V2	10	5.8	5	1	18	4.94	
V3	20	7.2	7	0.33	14	3.86	
V2+V3	6	6.8	7	4	10	2.56	
RFT							
V1	0	–	–	–	–	–	0.093
V2	2	19	19	14	24	7.07	
V3	3	32	36	24	36	6.93	
V2+V3	3	16	18	12	18	3.46	

RFT: Radiofrequency thermocoagulation.

Table 5. Comparison of pain relief according to pain localization in patients undergoing peripheral block

	Pain relief				p
	<50%		≥50%		
	n	%	n	%	
Peripheral block					
Pain localization					
V1	1	6.7	2	8.3	0.988
V2	4	26.7	6	25	
V3	8	53.3	12	50	
V2+V3	2	13.3	4	16.7	

propriate due to the short duration of efficacy, the efficacy period was quite long in our study. It is known that as the concentration of local anesthetic increases, it shows permanent effectiveness in block time with its selective neurotoxic effect. Studies have shown only high concentrations of neurological symptoms in intrathecal applications, as well as histological evidence of concentration-related local anesthetic neurotoxicity. In addition, it has been shown that local anesthetic neurotoxicity shows selectivity and histological evidence is not seen in the anterior roots but in the posterior roots.[5–7] After the block, muscle weakness is short term and sensory impairment and long pain palliation show the selective effect of local anesthetics on the region of the trigeminal nerve that produces pathological ectopic discharges. The selective neurotoxic effects of local anesthetics to fibers are not evident for lidocaine, while the ropivacaine which is n-propyl derivative of bupivacaine blocks the sensory fibers more than motor fibers.[8] Similar to ropivacaine, bupivacaine can be used for selective pain relief with selective neurotoxic effect.

In the same direction to our study, there are studies showing that peripheral blocks applied in trigeminal neuralgia have long-term therapeutic effects. In a study performed with 10% lidocaine in trigeminal neuralgia, a decrease in pain intensity and attack frequency was shown for 3–172 weeks, and the prolonged block effect was explained by the neurotoxic effect of lidocaine due to its high concentration.[9] Another study, which has been shown to reduce the frequency of pain episodes of peripheral branch blocks of the trigeminal nerve added to pharmacotherapy for 30–90 days, suggested that the longer-term effect of local analgesics results from clearing inflammatory exudates that irritate the nerve.[10] In a randomized study, trigger point block with ropivacaine added to medical therapy extended the pain control period up to 6–12 months.[11] In our study, we wanted to emphasize that an effective and long-term block can be used in treatment using bupivacaine due to its neurotoxic effect, and it may be an option in medical resistant patients who are not suitable for surgical/percutaneous invasive intervention.

There are very few comparative data on local toxicity on human nerve cells. One study investigated neural cell toxicity after a short exposure to various local anesthetics using *in vitro* human neuroblastoma. In this study in which the toxicity differences of amide group local anesthetics compared to lidocaine were evaluated, bupivacaine was found to be the most toxic local anesthetic, although variation in the cell model, cell subtype and contact time, and culture conditions were dependent.[12] Different molecular and cellular mechanisms are the cause of local anesthetic toxicity. These toxic effects can be directly on neuron or neural microenvironment. *In vitro* and *in vivo* studies have demonstrated the neurotoxic effect for lidocaine by oxidative stress with the activation of mitochondrial damage and apoptotic pathways,[13,14] and for bupivacaine by inducing apoptosis pathways by producing reactive oxygen species in neuronal cells and Schwann cells.[15] In animal models, even in clinical concentrations, neurotoxic effect has been demonstrated by inducing apoptosis by activation of the p38 mitogen-activated protein kinase (MAPK) system. In the study comparing primary sensory neuron cultures with the equivalent doses of lidocaine, bupivacaine, and ropivacaine in blocking sodium currents, the neurotoxic potential of lidocaine does not appear to differ significantly from bupivacaine and ropivacaine *in vitro*, and its neurotoxic effects are manifested through activation of specific MAPK.[16]

We showed that by adding dexamethasone as a steroid with the adjuvant effect of long-acting bupivacaine with neurotoxic effect, we obtained more effective and long-term therapeutic block. In a case report, ultrasound guided infraorbital block activity duration was extended to 21 months in trigeminal neuralgia by adding dexamethasone to lidocaine.[17] In a prospective study, dexamethasone added to

local anesthetics for pre-operative block has been shown to be a good acting adjuvant by reducing the need for post-operative oral/intravenous analgesia with prolonged analgesia effect.[18] A recent study of peripheral block using lidocaine and triamcinolone in trigeminal neuralgia highlighted the short-to-medium-term efficacy of peripheral blocks.[19] The use of steroids adjuvant effectively with local anesthetics in peripheral blocks causes vasoconstriction and prolongs the duration of action by reducing local anesthetic absorption, and increases the activity of inhibitory potassium channels on nociceptive C fibers and changes the membrane lipid phase balance.[20]

All eight patients who benefited from the peripheral block and applied RFT afterward had ≥50% pain reduction and the average efficacy duration was 22.75 months. As it is shown in their studies, it is a procedure with known RFT efficacy that is relatively safe compared to other percutaneous methods, and it can be applied in a short time and has little complication in experienced centers.

RFT performed with percutaneous foramen ovale approach under fluoroscopic guidance has a treatment success rate higher than 75%, success in isolated V3 involvement is higher.[21] The success rate in RFT is close to 100%, the chance of success in microvascular decompression is 85%, while there is a risk of 0.2–0.5% mortality. RFT also has more effective results than other methods such as percutaneous glycerol rhizolysis and Gamma Knife radiosurgery.[22,23]

For the RFT applied according to the nerve distribution, we determined the duration of activity as 19, 32, and 16 months for V2, V3, and V2+V3, respectively. Reported rate for Gasser RFT in a similar study; in V2 was 9 months, V3 was 36 months, and V2+V3 was 12 months, similar to our study. The success rate of interventions for the V3 branch is higher and the duration of effectiveness is longer, which is explained by the fact that it is easier to reach the V3 branch technically and anatomically. With similar logic, the duration and success rates of the intervention for V2 and multiple branches are lower, which is explained by the difficulty of anatomical access. To apply a lesion to the V2 branch with RFT, the cannula requires further medial and deeper advancement, and in this case, the V2 effective lesion may not be created by reaching the ophthalmic branch.[24]

The mean duration of peripheral blocks applied according to peripheral branch involvement is 4.33, 5.8, 7.22, and 6.83 months for V1, V2, V3, and V2+V3, respectively, and the efficiency and success rates of the procedures are in favor of V3 in peripheral blocks as well as in RFT. It can be explained by the technical reasons, it is easier to reach V3 fibers.

Limitations

The limitations of the study were retrospective analysis and the low number of patients. This study is based on the analysis of the results of interventional procedures performed in patients with trigeminal neuralgia, and it requires long-term follow-up to evaluate the duration of efficacy and therefore limits the number of patients included, especially for RFT, due to the presence of patients who cannot complete the follow-up period or without long-term follow-up results. Prospective studies with long-term follow-up results with large numbers of patients will shed light on our study.

Conclusion

In this study, we reviewed the methods that can be applied before surgery in the medical therapy resistant group in patients with trigeminal neuralgia. We found RFT efficacy and long duration of efficacy similar to what's indicated in the literature. We have shown that, as an alternative to RFT and other percutaneous methods, the blockade of peripheral branches with local anesthetics with neurotoxic effects can be an effective and reliable alternative method with an average duration of 7.5 months. We think that it would be beneficial to apply adjuvant effective steroid injection added to local anesthetics to the peripheral branches, for patients who are medical resistant, not suitable for surgery and especially before the percutaneous methods in elderly population.

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Ethical Approval: ***The study was approved by The Faculty of Medicine Non-Invasive Clinical Research Clinical Research Ethics Committee (Date: 06/10/2020, No: 2020/193).***

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