Pain Medicine

Pain Medicine 2012; 13: 443–451
Wiley Periodicals, Inc.

NEUROPATHIC PAIN SECTION

Original Research Articles

Management of Neuropathic Pain with Methylprednisolone at the Site of Nerve Injury

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All funding sources of the submitted work were supported by Baskent University.

Conflict of interest: None.

Abstract

Objective. Peripheral nerve blocks with methylprednisolone may provide effective pain therapy by decreasing ectopic neuronal discharge and the release of local inflammatory mediators at the site of nerve injury. In this study, we aimed to compare the efficacy of lidocaine alone with a combination of depo-methylprednisolone plus lidocaine in the management of neuropathic pain due to peripheral nerve damage.

Design. Randomized, double-blind comparator trial

Setting. Group control (N = 44) received 0.5% lidocaine and group methylprednisolone (N = 44) received 80 mg depo-methylprednisolone + 0.5% lidocaine proximal to the site of nerve injury with a total amount of 10–20 mL solution according to the type of peripheral nerve block with nerve stimulator.

Outcome Measures. Demographic data, preblock numerical rating scales (NRSs), the Leeds assessment of neuropathic symptoms and signs ($LANSS_0$) score, accompanying symptoms, and analgesic requirements were recorded. Postblock NRS scores were noted following peripheral nerve block and after 3 months. $LANSS_1$, accompanying symptoms, and analgesic requirements were also reevaluated 3 months after the injection.

Results. Demographic data, preblock NRS (8 ± 1.5 and 8.1 ± 1.2, respectively), postblock NRS (2.1 ± 1.2 and 2.4 ± 1.4, respectively), $LANSS_0$ (18.4 ± 2.2 and 18.2 ± 2.1, respectively), and accompanying symptoms were comparable between groups. Scores for the methylprednisolone group were significantly improved at 3-month postblock for NRS (2 ± 1.4 vs 5.2 ± 1.7) and $LANSS_1$ scores (4.14 ± 2.7 vs 14.1 ± 2.8), accompanying symptoms, and analgesic requirements ($P < 0.0001$).

Conclusions. Our results suggest that peripheral nerve block with 80 mg depo-methylprednisolone plus 0.5% lidocaine provides effective management in the treatment of neuropathic pain due to peripheral nerve damage.

Key Words. Depo-methylprednisolone; Peripheral Nerve Blocks; Neuropathic Pain

Introduction

A common cause of neuropathic pain is nerve injury either from an accident or surgery [1]. It is estimated that 5% of patients with nerve injury suffer from neuropathic pain. Both inflammatory and immune mechanisms are thought to play an important role in this process; sensitization and activation of injured nerves generate the secretion of inflammatory mediators and proinflammatory cytokines, initiating an inflammatory cascade [2]. The ectopic pacemaker-like activity from the injured site sensitizes nociceptors and contributes to the development of central sensitization and neuropathic pain [2–4]. Eventually, as this process advances through the entire neuron and gradually to the spinal cord and brain, neuropathic pain begins to appear at the site of nerve injury [5].

This progressive mechanism also complicates the management of neuropathic pain and may contribute to treatment failure with adjuvant analgesics [6,7]. Thus, it is helpful to consider agents such as corticosteroids that directly address inflammatory mechanisms. Although systemic corticosteroid administrations have been studied in both animal models and humans, pain relief with systemic steroids has only been achieved in a small fraction of

patients, with undesirable side effects in some [8–10]. Local administration of corticosteroids have also been studied but the reported results were generally contradictory, the study designs were frequently open label, the etiologies of neuropathic pain were limited, and the type of pain was not classified as neuropathic or nociceptive [11–13].

Thus, the efficacy of local corticosteroid administration for the treatment of neuropathic pain due to nerve damage remains incompletely studied, calling for prospective, double-blind controlled studies on suitable neuropathic pain models. In this randomized, double-blinded controlled study of patients with purely neuropathic pain symptoms due to selective peripheral nerve damage, we examine the effect of corticosteroids by comparing peripheral nerve blocks with lidocaine with similarly administered blocks with depo-methylprednisolone plus lidocaine.

Methods

The local ethics committee approved the study protocol (Project No: 5/21-3.12.2009) before patient enrollment, and the study protocol was carried out in accordance with the principles of Helsinki Declarations. All patients with neuropathic pain symptoms such as numbness, burning, sensitivity to touch, and sudden electric shock like pain that occurred after any type of nerve injury were referred to the pain clinic. The sample (N = 372) was recruited over a 1-year period from 389 patients referred to the pain clinic with neuropathic pain following injury whose pain was resistant to common analgesics and opioid; two declined participation due to the impossibility of attending all follow-ups. The Leeds assessment of neuropathic symptoms and signs (LANSS) pain scale was administered at the initial visit to help confirm the diagnosis [14]. Inclusion criteria were: 1) pain developed after any type of selective peripheral nerve injury due to pressure, stretching, direct trauma, exposure to ischemic mediators, surgical etiologies, etc.; 2) confirmation of neuropathic pain according to the validated Turkish version of LANSS pain scale: LANSS pain score $\geq$12 was considered as neuropathic pain (Appendix 1) [14,15]; 3) refractory pain despite medical neuropathic pain therapies; 4) average daily pain intensity: $\geq$5 on an 11-point numerical rating scale (NRS); and 5) age $\geq$18 years. The exclusion criteria were: 1) pain related to cancer or chronic infection; 2) the possibility that the pain is continuing from a preexisting problem; 3) patients with mixed etiologies (nociceptive and neuropathic); and 4) serious psychiatric disorders such as affective disorders, schizophrenia, or other psychotic disorders.

Patients with neuropathic pain received written information about the present study and any patient who wished to participate provided written informed consent. The trial was designed as a single center, prospective, randomized, double-blinded study. According to the first phase of the protocol, all patients initially received amitriptyline 10 mg, gabapentin 900 mg, and tramadol 200 mg daily. During a 4-week period, amitriptyline and gabapentin were titrated up to the tolerable levels for each patient. Patients whose average daily pain scores did not change with medical therapy at the end of the follow-up period were randomly assigned to two groups. A random allocation sequence was consecutively numbered for the patients resistant to medical therapy before the second phase of the protocol when opaque, sealed envelopes determining assignment to control or treatment group were generated with a computer.

Group control (N = 44) patients received 0.5% lidocaine and group methylprednisolone (N = 44) patients received 80 mg depo-methylprednisolone plus 0.5% lidocaine in a total of 10–20 mL of solution according to the type of nerve block. All data collection including recurrent pain questionnaire, sensory test calculations, and follow-ups was performed by an independent observer who knew the type of the block performed but not the drugs used and was not present during the procedures. The peripheral nerve blocks were performed by two anesthesiologists who were senior consultants for regional anesthesia. The first practitioner tried twice to perform the block, and then another practitioner came in and then tried again. These practitioners did not participate in any other part of the study and were blind to both the study protocol and which solution they were injecting by keeping solutions in 20-mL syringes covered with tape.

The injured peripheral nerves were located according to dermatomal spread of pain and sensory symptoms. The proximal site of pain generation was determined by performing peripheral nerve blocks. After aseptic preparation and local infiltration, a 10-cm 22-gauge insulated needle (Stimuplex®, B Braun, Melsungen, Germany) connected to a nerve stimulator was inserted perpendicular to all planes and advanced with nerve stimulation output at 1.5 mA, 2 Hz frequency, and 100-μs pulse width. The nerve was identified by persistence of the muscle response at 0.4 mA. At this point, 10–20 mL of 0.5% lidocaine was injected in group control according to the type of nerve block (10 mL amount of solution for common peroneal, suprascapular, popliteal, and lateral distal sciatic nerve block and 20 mL amount of solution for thoracic paravertebral, femoral, and sciatic nerve block). In group methylprednisolone, a total of 80 mg depo-methylprednisolone was added to 10–20 mL of 0.5% lidocaine according to the type of nerve block. The type of peripheral nerve block and injected total amount of solution were also noted. The patients were observed in the recovery room for half an hour following the intervention. The medications including neuropathic pain therapy were stopped and patients were offered tramadol 50 mg with a maximum dose of 4 times per day as required during a 3-month period.

At the initial visit, all patients were presented with a baseline data survey including age, sex, weight, height, affected side, intensity and history of pain, previous pharmacotherapy, and physiotherapy. NRS scores were recorded at initial visit, immediately, and 3 months after nerve blocks, and recorded as preblock NRS, postblock NRS, and 3-month postblock NRS, respectively. Neuropathic pain examination according to LANSS pain scale

was also noted at initial visits and repeated 3 months after nerve blocks and recorded as $LANSS_0$ and $LANSS_1$, respectively.

Accompanying symptoms of numbness and burning sensation and sensory tests for hyperalgesia and allodynia were analyzed separately. Allodynia was examined with a cotton wool lightly stroked across the painful area and hyperalgesia was determined by comparing the response to a 23-gauge needle mounted inside a 2-mL syringe barrel placed gently onto the skin in the painful area. The neuropathic pain symptoms evaluated according to the LANSS pain scale were: unpleasant sensation in the skin such as pricking, tingling; the skin color differing from normal in the painful area; sensitivity to touch when wearing tight clothes; sudden electric shocks like pain and jumping; and burning or freezing sensation in the painful area. The presence or absence of each symptom was scored and added to the LANSS pain scale calculation. This evaluation and calculation of pain scale score were repeated at 3 months. The daily tramadol consumption during the follow-up period was recorded.

Statistics

The primary outcome parameter of this study was the pain assessed by NRS scores. Estimated sample size for the primary variable was calculated based on the standard deviation (SD) of a pilot group of patients with posttraumatic neuropathic pain representing similar characteristics. The anticipated SD of NRS for this pilot group of patients was 2.4. A true difference of 1.5 units between NRS values of study and control group was considered clinically relevant. A power analysis with a type II error of 20% at a two-sided 5% significance level estimated 42 patients per group to be included.

Continuous numeric data were assessed for normal distribution with the Kolmogorov–Smirnov test. Data were presented as means with SD or numbers and percentages. Categorical data are presented with count and tests for significant differences between groups were analyzed with χ^2 test when appropriate. Differences between NRS and LANSS scores were analyzed with independent samples *t*-test for between-group comparison and with paired samples *t*-test for in-group comparisons. Data analyses were conducted using SPSS for windows, version 11.0 (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

Three hundred and seventy patients were assessed for eligibility in the study. Two hundred and fifty-two patients were successfully treated for neuropathic pain. Thirty patients discontinued the treatment as a result of drug-related side effects and refused to be included in the second phase of the trial, leaving 88 patients who were eligible for the second phase. Although the adequate number of patients according to the calculated power of the study was 84, a total of 88 patients were included in the study to compensate for possible exclusion. These patients abruptly stopped their neuropathic pain medications that were not necessary anyway and were randomly enrolled in the study, received the allocated peripheral nerve blocks, completed the follow-up period, and included in the statistical analyses (Figure 1).

The patients were comparable in age, sex, weight, height, affected site, pain intensity, previous pharmacotherapy, and physiotherapy between groups (Table 1). Prior pharmacotherapy included paracetamol, nonsteroid anti-inflammatory drugs, and/or opioids in all patients. The duration for nerve injury and neuropathic pain was comparable between groups (11.5 ± 20 and 9.7 ± 20.2 months in group control and 14.7 ± 19.9 and 12.9 ± 20.2 months in group methylprednisolone).

The types of peripheral nerves that were blocked during the study period include thoracic paravertebral (N = 18), femoral (N = 18), common peroneal (performed at the site of fibular head and neck) (N = 17), sciatic (N = 15) (subgluteal approach in six patients, transgluteal approach in two patients, lateral proximal approach in seven patients), suprascapular (N = 6), popliteal (N = 7), and lateral distal sciatic nerve (lateral approach to sciatic nerve before the division in popliteal fossa) (N = 7) (Table 2).

Neuropathic pain due to transection and compression were the common etiologies that were observed in the study and originated from paravertebral, femoral, common peroneal, sciatic, lateral distal sciatic, and popliteal nerve (N = 53). Another etiology of neuropathic pain was due to tension of femoral, sciatic, and popliteal nerves and originated from painful scars (N = 11). Ischemia was the cause of neuropathic pain originated from common peroneal and lateral distal sciatic nerve (N = 11); accidental intraneural injection was the cause of neuropathic pain aroused from femoral and sciatic nerve (N = 2); and neuropathic pain due to repetitive microtrauma and entrapment was another etiology originated from suprascapular nerve (N = 6). The etiologies of nerve injuries for each type of nerve block, the localization and extension of neuropathic symptoms, and corresponding nerve blocks may also be found in Table 3.

Preblock NRS, postblock NRS, $LANSS_0$, accompanying symptoms, and analgesic requirements were comparable between groups. Three-month postblock NRS scores were significantly lower in group methylprednisolone in comparison to group control ($P < 0.0001$) (Figure 2). Postblock and 3-month postblock NRS scores were significantly decreased in both groups in comparison to preblock NRS ($P < 0.0001$, $P < 0.0001$, $P < 0.0001$, and $P < 0.0001$, respectively). Three-month postblock NRS and postblock NRS were comparable in group methylprednisolone but significantly different in group control ($P < 0.0001$). $LANSS_1$ scores after 3 months were significantly decreased in both groups ($P < 0.0001$ and $P < 0.0001$, respectively) but $LANSS_1$ scores in group methylprednisolone were significantly lower than $LANSS_1$ scores in group control ($P < 0.0001$) (Figure 3).

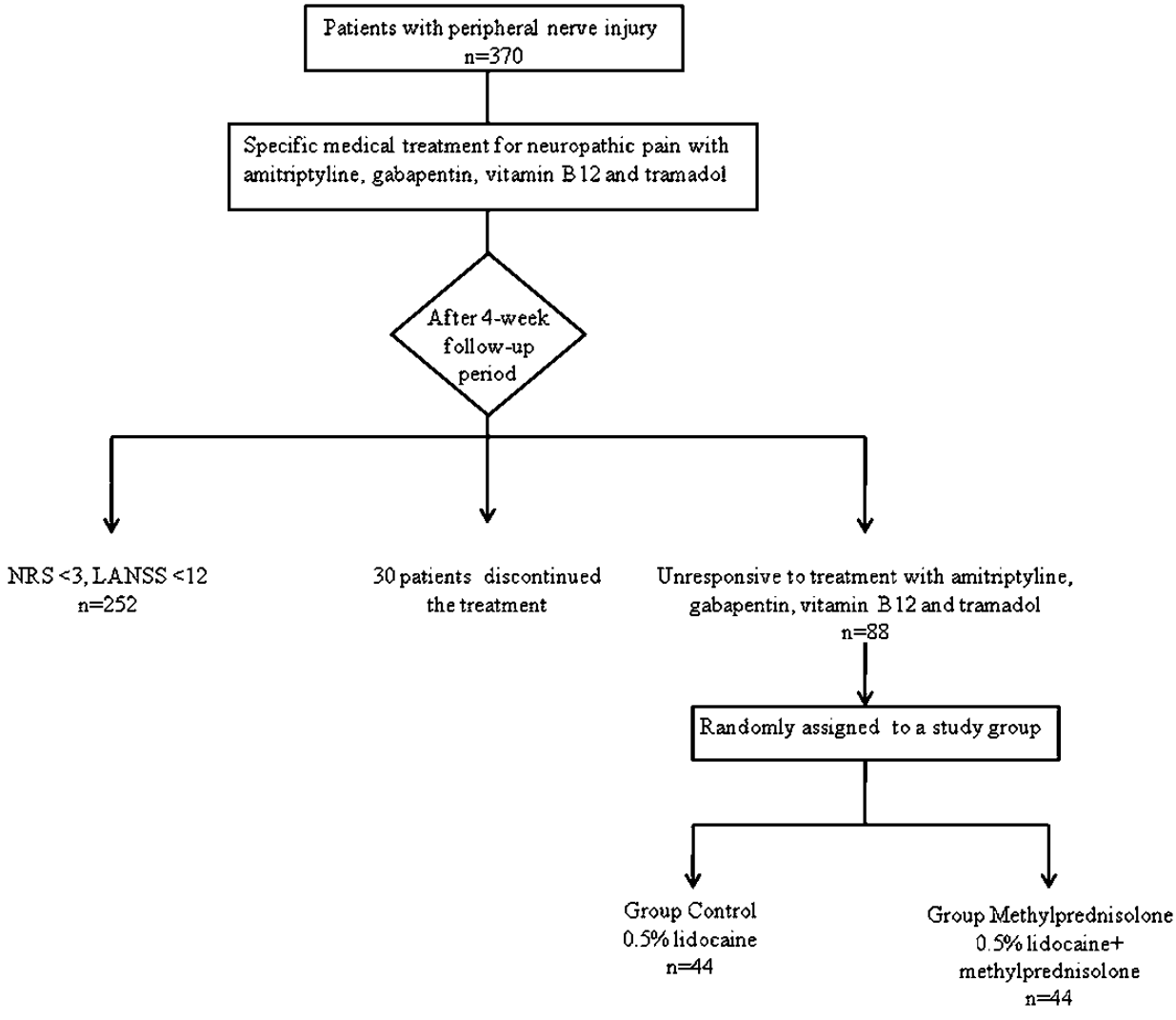

Figure 1 Flow diagram of patients through the phases of the trial. n, number of patients. LANSS = Leeds assessment of neuropathic symptoms and signs; NRS = numerical rating scale.

Numbness was recorded in 77.3% (N = 34) of the patients in group control and in all patients in group methylprednisolone at initial visit. At the end of 3-month follow-up, numbness did not recover in any patients in group control, whereas numbness improved in 95.4% (N = 42) of the patients in group methylprednisolone ($P < 0.001$). Burning sensation was recorded in 40.9% (N = 18) of patients in group control and 36.7% (N = 16) of patients in group methylprednisolone at initial visit. Burning sensation was no longer present in 27% (N = 5) of the patients in group control, and in all patients in group methylprednisolone ($P < 0.0001$). Hyperalgesia was recorded in 59.1% (N = 26) of patients in group control and 50% (N = 22) of patients in group methylprednisolone. Sensory test for hyperalgesia demonstrated that none of the patients were completely free of hyperalgesia, but 50% (N = 13) of the patients with hyperalgesia in group control reported distinctive levels in response to painful stimulus, while 96.4%

Table 1 Demographic data, affected site, and the number of the patients treated previously with pharmacotherapy and physiotherapy

	Group Control	Group Methylprednisolone
Age (year)	57.8 ± 13.9	51.8 ± 14.7
Sex (M/F)	29/15	27/17
Weight (kg)	75.2 ± 12.2	70.7 ± 9.8
Height (cm)	172.4 ± 9.7	169.4 ± 9.4
Affected site (R/L)	20/24	26/18
Pharmacotherapy (N)	41	40
Physiotherapy (N)	14	12

Data expressed as mean ± standard deviation.
F = female; M = male; R = right; L = left.

Table 2 The peripheral nerve blocks performed in the groups

Peripheral Nerve Blocks	Group Control (N)	Group Methylprednisolone (N)	*P* values
Thoracic paravertebral N.	8	10	0.396
Femoral N.	10	8	0.396
Common peroneal N.	8	9	0.5
Sciatic N.	7	8	0.5
Suprascapular N.	3	3	0.662
Popliteal N.	4	3	0.5
Lateral distal sciatic N.	4	3	0.5

(N = 21) of the patients in group methylprednisolone were completely free of hyperalgesia ($P < 0.0001$). Allodynia was recorded in 43.2% (N = 19) of the patients in group control and 56.8% (N = 25) of patients in group methylprednisolone. At the end of 3-month follow-up, 80.7% (N = 15) of the patients in group control and all patients in group methylprednisolone were completely healed from allodynia ($P = 0.028$).

All patients were managing pain with analgesic medications during the initial visit. Three months after the injections, 13 patients in group control and 31 patients in group methylprednisolone had discontinued taking tramadol. The average daily tramadol consumption throughout the 3-month period was 97.7 ± 76.2 mg in group control and 22.7 ± 39.5 mg in group methylprednisolone ($P < 0.0001$).

Discussion

Neuropathic pain is a common clinical outcome of traumatic peripheral nerve injury. The results of treatments for neuropathic pain are often unsatisfactory and indicate that underlying mechanisms might be an important factor in selecting an appropriate treatment. Our results show that corticosteroids improve 3-month outcomes in patients with neuropathic pain following nerve injury. This result is consistent with other studies suggesting that effective therapy for neuropathic pain due to nerve injury may be achieved by reducing production of inflammatory mediators at the site of nerve injury and suppressing afferent ectopic neural discharges from injured nerves [2–4,8,9]. Corticosteroids can reduce inflammatory mediator synthesis, inhibit neurogenic extravasations and edema formation, silence neural firing, reverse their input to central neurons, and change pain behaviors with their membrane stabilizing and analgesic effects [3,4,7,8,16].

Analgesic effects of systemic corticosteroid administration on neuropathic pain after surgical procedures that involve nerve injury have been proven in animal and human studies [7–9,17]. As demonstrated in these studies, systemic corticosteroid administration in the treatment of neuropathic pain due to nerve injury should be administered in the early period of the injury with high doses and sustained for long durations to improve the clinical response [16,18]. However, difficulty in assessing the patients in the acute phase of neuropathic pain, determining the amount and the duration of systemic steroid administration to improve pain response, and avoiding the possible serious side effects due to high dosage of steroids may be the main causes of preferring the administration of depot form of corticosteroids directly to the site of nerve injury. The duration of the *in situ* release period of the depot form of corticosteroids that is stated by the manufacturer as several weeks to several months might also prolong the improved neuropathic pain response [19].

The effect of locally applied methylprednisolone on the behavior of animals with painful peripheral mononeuropathy was examined and demonstrated that local application of methylprednisolone reduces the heat hyperalgesia and the mechanical allodynia but not the mechanical hyperalgesia [11]. Among a series of clinical reports, rapid and prolonged suppression of spontaneous discharge in chronic neuromas was reduced with corticosteroid therapy [20]. The mechanism was depended on the corticosteroids' well-known membrane stabilizing effects and might also depend on the fact that such an injection may shrink fibrosis at the site of the neuroma and thereby reduce mechanical pressure and torsion upon the injured nerve. The results of a pilot study also offered the beneficial effect of perineural injections of corticosteroids in postherpetic neuralgia and nerve entrapment syndrome [11]. The benefit of perineural injection for reflex sympathetic dystrophy was also demonstrated in a patient who primarily received corticosteroids systemically but discontinued after the occurrence of serious side effects such as weight gain, cushingoid habitus, and myopathy [21].

In contrast to the results of previously described single cases, a follow-up study showed that patients diagnosed with neuropathic pain that had one to several peripheral nerve blocks performed with methylprednisolone and 28% of the patients had complete pain relief up to 1 month while 66% had partial pain relief [12]. In this study, the patients were not purely diagnosed with neuropathic pain, the maximal amount of methylprednisolone given on one occasion was 40 mg, and the adjuvant local anesthetic was bupivacaine at a dose of 100 mg. Also half of

Table 3 Etiologies of nerve injuries for each type of nerve block and localization and extension of neuropathic pain symptoms

Corresponding Nerve Blocks	The Causes of Nerve Injuries				Localization and Extension of Symptoms
	Postsurgical	Posttraumatic	Postamputation	Postischemic	
Thoracic paravertebral N.	Thoracotomy (N = 8) Cholecystectomy (N = 4) Nephrectomy (N = 2)	Falling down the stairs (N = 4)	—	—	Flank pain extends to chest and upper abdomen
Femoral N.	Femoral hernia repair (N = 2) Stabbing (N = 2) Femur nerve fracture (N = 3) Surgical exploration during femoral arterial repair (N = 3)	i.m. injection (N = 1) Femoral angiography (N = 1)	Stump pain after lower limb amputation (N = 6)	—	Upper limb pain extends to knee
Common peroneal N.	Tibial fracture under knee (N = 4) Injury with gunshot (N = 2) Peripheral vascular occlusion (N = 4)	Blunt trauma (N = 3)	—	Ischemia secondary to arterial thrombosis (N = 4)	Distal foot pain extends to fingers
Sciatic N.	Stabbing and shooting (N = 4) Femur shaft fracture (N = 2)	Prolonged lithotomy position during delivery (N = 1) i.m. injection (N = 1)	Crush syndrome (N = 2) Stump pain after lower limb amputation (N = 5)	—	Back leg pain extends to popliteal fossa
Suprascapular N.	—	Nerve entrapment syndrome due to repetitive microtrauma (N = 4) Sports injury (N = 2)	—	—	Shoulder pain extends to back or upper arm
Popliteal N.	—	Penetrating injury (N = 2)	Stump pain after lower limb amputation (N = 5)	—	Lower leg pain extends to foot
Lateral distal sciatic N.	Stabbing and shooting (N = 2)	Compression of lower back leg in engineering vehicle (N = 2)	—	Ischemia secondary to arterial thrombosis (N = 3)	Distal knee pain extends to ankle

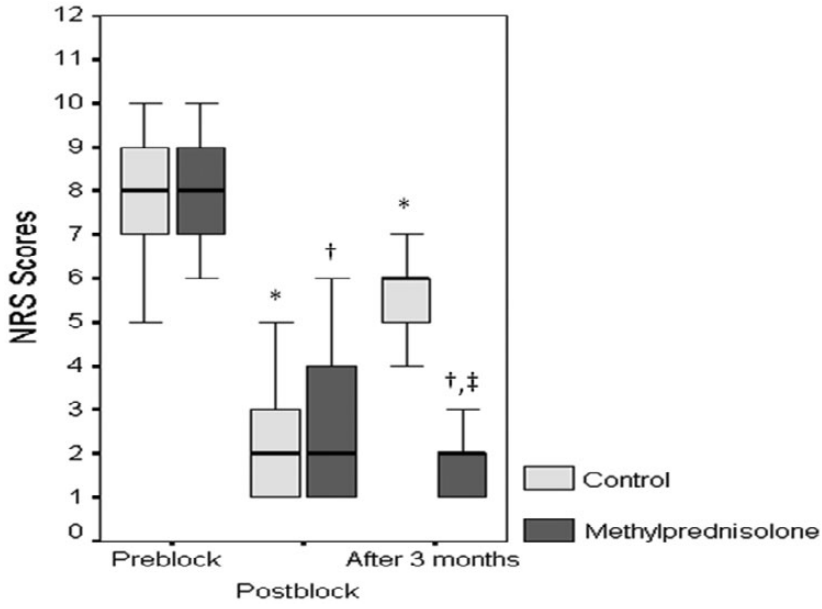

Figure 2 NRS scores (median, first and third quartiles). NRS = numerical rating scale. *P < 0.0001 compared with preblock NRS in group control. †P < 0.0001 compared with preblock NRS in group methylprednisolone. ‡P < 0.0001 comparison of 3-month postblock NRS scores between groups.

the patients with neuropathic pain benefited with complete pain relief but the duration was short lived. The heterogeneity of the patients and the nondepot form of methylprednisolone preference in 40 mg dosages might contribute to the distinctive results of this study.

In our double-blinded, controlled study, patients with neuropathic pain according to LANSS pain scale were selected, and administration of depo-methylprednisolone and lidocaine at the site of nerve injury demonstrated lower NRS and LANSS scores in clinical assessment for a 3-month duration, and complete pain relief was achieved for both mechanical allodynia and hyperalgesia according to sensory test evaluation. Also in our study, although the systemic distribution of perineurally injected corticosteroids might exaggerate the occurrence of systemic and local adverse effects which would complicate the treatment process, none of the patients reported local or systemic complications and did not experience degenerative lesions or nerve injury with steroid agents.

Glucocorticosteroids act through direct regulation of transcription, specifically inhibition of transcription mediated by nuclear factor κB and extragenomic effects [22]. These mechanisms are thought to have different dose–response curves and the selected dose in our study might affect all three mechanisms and cause the positive response to the treatment modality. Additionally, the results in our study

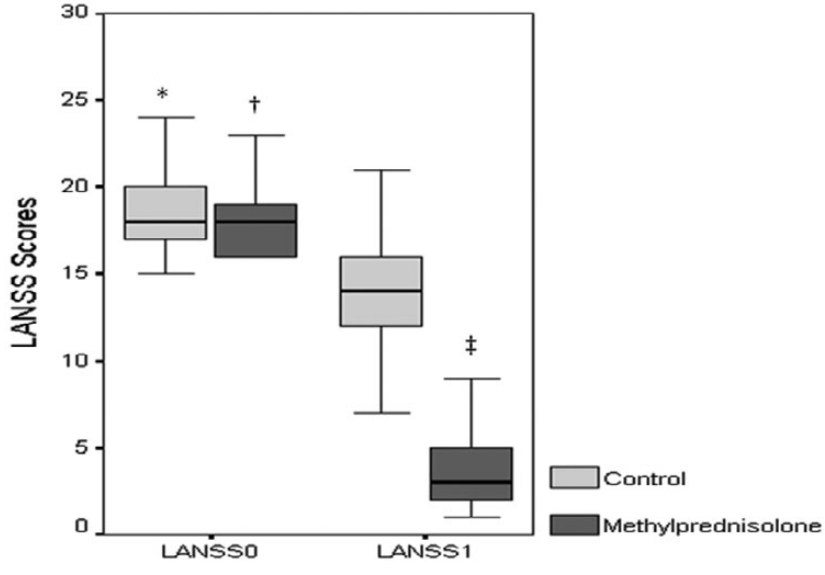

Figure 3 LANSS scores (median, first and third quartiles). LANSS = Leeds assessment of neuropathic symptoms and signs. *P < 0.0001 compared with $LANSS_0$ in group control. †P < 0.0001 compared with $LANSS_0$ in group methylprednisolone. ‡P < 0.0001 comparison for $LANSS_1$ between groups.

may also depend on adding local anesthetic lidocaine to depo-methylprednisolone solution, as NRS scores were significantly decreased after peripheral nerve block with lidocaine, and the decrease in NRS continued after 3-month follow-up. Additionally, sensory tests showed some improvement, and as a result LANSS pain scores were significantly decreased. Although lidocaine administration at the site of nerve injury was considered more diagnostic than therapeutic, study results represent a partial beneficial effect on the treatment of neuropathic pain.

It is generally believed that lidocaine alleviates pain by producing an impulse conductive nerve block and by decreasing the activity of spontaneous discharging of hyperactive neurons [20]. Local application of lidocaine exerts its anti-inflammatory effects by downregulating the proinflammatory cytokines IL-2, TNF-α, and interferon (IFN)-γ via nuclear factor-κB (NK-κB)-mediated inhibition of mRNA expression [23]. Therefore, the common proinflammatory signaling pathway for the inhibition of expression of a number of proinflammatory mediators by lidocaine and methylprednisolone might provide a synergistic effect on neuropathic pain treatment when administered together at the site of nerve injury. Also, this synergism at the cellular level may inhibit complete signal transduction pathways that play the main role in occurrence of neuropathic pain signs such as allodynia and hyperalgesia.

The patients in our study represented a group who may be considered as less centrally sensitized and more affected by peripheral mechanisms as they did not respond to the drugs acting on central mechanisms. The central effects of perineural corticosteroid injection may be demonstrated in future studies by including both the peripherally and centrally sensitized patients without pretreatment.

In our study, although adding methylprednisolone to peripheral nerve blocks containing lidocaine achieved encouraging results, an additional study group could be included to differentiate the pure effect of methylprednisolone on neuropathic pain symptoms and to examine the duration of pain relief or controlling for systemic effect to interpret the results as pure local or systemic. Thus, we would be able to identify the specific locally applied corticosteroid that relieved neuropathic pain due to nerve injury. In this study, we tried to block the nerves possibly indicated by dermatomal sensory impairment of the patients. We also tried to limit the blocks to the potential nerve which was injured primarily, and all individual blocks were performed by the most proximal approaches of the indicated block reported in the literature. The uncertainty about how close to the site of pain the injection has been placed might remain as a limitation of the method as we only depended on complaints and the expression of patients about their pain and visible traumatic site. On the other hand, we abruptly stopped neuropathic pain medications in patients who had unchanged average pain scores after a 4-week treatment period and did not consider the effect on our results. Although there is no scientifically established guideline for withdrawing antineuropathic pain drugs, it is considered important to stop one at a time, starting with those which may cause abstinence syndromes. In our study, none of the patients complained about any withdrawal symptoms; but not stopping neuropathic pain medications gradually is another methodological limitation of the study.

Conclusion

In patients with postinjury neuropathic pain symptoms unresponsive to oral analgesics and adjuvant analgesics, we demonstrated that adding 80 mg depo-methylprednisolone to 0.5% lidocaine solutions and injecting via peripheral nerve blocks at the proximal site of the nerve injury improved outcomes at 3 months more than injecting 0.55 lidocaine alone. This combination may be a simple alternative treatment for relief of persistent neuropathic pain due to selective nerve injury.

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Appendix 1 The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale

A. Pain Questionnaire

1. Does your pain feel like strange, unpleasant sensations in your skin? Words like pricking, tingling, pins and needles might describe these sensations.
   a) No (0) b) Yes (5)
2. Does your pain make the skin in the painful area look different from normal? Words like mottled or looking more red or pink might describe the appearance.
   a) No (0) b) Yes (5)
3. Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations when lightly stroking the skin, or getting pain when wearing tight clothes might describe the abnormal sensitivity.
   a) No (0) b) Yes (3)
4. Does your pain come on suddenly and in bursts for no apparent reason when you are still? Words like electric shock, jumping and bursting describe these sensations.
   a) No (0) b) Yes (2)
5. Does your pain feel as if the skin temperature in the painful area has changed abnormally? Words like hot and burning describe these sensations.
   a) No (0) b) Yes (1)

B. Sensory Testing

1. **Allodynia:** Examine the response to lightly stroking cotton wool across the nonpainful area and then the painful area. If normal sensations are experienced in the nonpainful site, but pain or unpleasant sensations (tingling, nausea) are experienced in the painful area when stroking, allodynia is present.
   a) No (0) b) Yes (5)
2. **Altered Pin-prick threshold:** Determine the pin-prick threshold by comparing the response to a 23-gauge needle mounted inside a 2 ml syringe barrel placed gently on to the skin in a nonpainful and then painful areas. If a sharp pin-prick is felt in the nonpainful area, but a different sensation is experienced in the painful area, e.g., none/blunt only or a very painful sensation, an altered pin-prick threshold is present. If a pin-prick is not felt in either area, mount the syringe onto the needle to increase the weight and repeat.
   a) No (0) b) Yes (3)

Total score (maximum 24):

If score < 12, neuropathic mechanisms are unlikely to be contribution to the patient's pain.

If score ≥12, neuropathic mechanisms are likely to be contribution to the patient's pain.