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Original Article

Comparison of invasive and non-invasive treatment approaches in neuropathic pain

Sehand Debbagh[1], Nalan Ornek Celebi[1], Ozkan Onal[2], Altan Sahin[1]

[1]Department of Anesthesiology and Reanimation, Medical Faculty, Hacettepe University, Ankara, Turkey; [2]Department of Anesthesiology and Reanimation, Medical Faculty, Selcuk University, Konya, Turkey

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Abstract: Patients with neuropathic pain account for 30-50% of the patients referring to pain clinics. The treatment of neuropathic pain is a difficult clinical situation in which classical analgesics and treatment methods remain inadequate and which requires interdisciplinary treatment. Neuropathic pain is usually refractory to treatment and clinicians frequently use drug combinations and sometimes invasive interventions. The aim of the present study was to measure the efficacy of invasive and non-invasive methods in patients with neuropathic pain by comparing VAS scores at the baseline of treatment, at 1st month, 2nd months, and 6th months. A total of 127 patients older than 15 who were referred to the algology section of Hacettepe University Faculty of Medicine Anesthesiology and Reanimation Department between 2005 and 2008 and who underwent treatment with invasive and non-invasive methods were included in the study. Group 1: Non-invasive group (n: 76) includes patients undergoing treatment with non-pharmacological methods such as exercise and psychotherapy and pharmacological methods such as tricyclic antidepressants, anticonvulsants, SSRI, topical and I.V. lidocain, opioids, canabinoids, NSAI, and NMDA receptor antagonists. Group 2: Invasive group (n: 51): includes patients who underwent treatment with epidural or perineural injections of local anesthetics and corticosteroids, implantation of epidural intrathecal drug administration systems, and neural ablative systems (glycerol injection to gasser ganglion or gamma knife treatment. In the distribution of VAS levels according to group during follow up period, there was no statistically significant difference between medical and invasive groups at any time interval ($P>0.01$), while significant intra-group differences were found in both groups at all time intervals from the baseline to 2nd year ($P<0.01$). In the medical treatment group, VAS levels decreased compared to baseline in all time intervals. There was significant difference between all time intervals ($P<0.001$). In invasive treatment group VAS levels decreased compared to baseline at all time intervals. In addition, there was significant difference between all time intervals ($P<0.001$). Results of the present study indicate that pharmacological options exerting analgesic effect on pain and invasive methods are essential in relieving in neuropathic pain and improving functionality and quality of life by themselves with proper indications or in combination.

Keywords: Neuropathic pain, invasive treatment, medical treatment, VAS score

Introduction

Neuropathic pain (NP) is defined by International Association of the Studies on Pain (IASP) dysfunction of nervous system as pain initiated or caused by a primary lesion or dysfunction of the nervous system. Peripheral NP is a pain syndrome involving positive (spontaneous pain, paresthesia, dysesthesia, allodynia, prolonged and exaggerated pain due to noxius stimulant) and negative (loss of sensation) symptoms [1]. Unlike physiological pain, NP is characterized by increased spontaneous pain without external stimulant and/or with a stimulant normally harmless. Abnormal stimulation of somato-sensorial system is present [2-4]. NP should immediately be considered when autonomic dysfunction presenting with a different neurological lesion or paresthesia, dysesthesia occurs in motor and sensorial regions.

Injury of the brain, spinal cord, or peripheral nervous system (trauma, compression tumoral invasion, ischemia, inflammation, metabolic disturbance, nutritional deficit, cytotoxic agents, and degenerative diseases) may lead to NP syn-

drome [5-8]. Patients with NP account for 35% of patients presenting to pain clinics [9]. Treatment of NP is a challenging clinical condition requiring interdisciplinary approaches and with which conventional analgesics and treatment methods are mostly unable to cope. Neuropathic pains usually respond less to opioid drugs and neurolytic procedures than nociceptive pain. In treatment, adjuvant analgesic drugs should always be used [10]. NP is usually refractory to treatment and clinicians frequently employ drug combinations and sometimes invasive interventions. In order to increase quality of life for patients, new treatment mechanisms based on symptom and mechanisms increasingly become common. Multidisciplinary combinations of pharmacological options and invasive methods exerting analgesic effect on pain are essential in relieving NP, functionality, and improving quality of life [11-13].

The aim of the present study was to evaluate the efficacy of invasive and non-invasive treatment. Treatment modalities in patients with NP by comparing VAS scores at the onset, 1st month, 3rd months, and 6th months of treatment.

Material and method

This retrospective study was conducted with the approval of Hacettepe University Ethics Committee and included 127 patients over the age of 15 who presented to Algology Department of Anesthesia unit between 2005 and 2008 and were diagnosed with NP and underwent invasive and non-invasive treatment. The aim of the present study was to evaluate the efficacy of invasive and non-invasive methods in patients with NP, by comparing VAS scores at onset, 1st month, 3rd months, and 6th months of treatment. In this study, archive of patients' files in our department was utilized. Patients who had not completed at least six months of follow up after the diagnosis of NP and who did not regularly attend follow up visits were excluded from the study. Of these, 127 patients were allocated into two groups according to their treatment modalities. Patients who did not complete at least six months of follow up after the diagnosis of NP and those who did not attend follow up visits regularly were excluded from the study. A total of 127 patients were divided into two groups according to treatment methods.

Group 1: Non-invasive group (n: 76) includes patients treated with non-pharmacological methods added to physical therapy. Patients were treated with tricyclic antidepressant (amitriptyline), SSRI (fluoxetine), anticonvulsant (gabapentin, pregabaline, carbamazepine), topical lidocaine, opioid (tramadol), and NSAID (dexketoprofen, paracetamol) as pharmacological treatments.

Group 2: Invasive group (n: 51) includes patients treated with interlaminar or transforaminal epidural steroid plus local anesthetic for low back pain and cervical radiculopathy, dorsal root ganglion block plus radiofrequency for low back pain and cervical radiculopathy, peripheral nerve steroid and ablation for intercostal neuralgia, glycerol injection to gasser ganglion or gamma knife treatment for trigeminal neuralgia.

In the present study, treatments were compared according to VAS scoring system. Visual Analog Scale (VAS) evaluation was used to transform some values that could not be measured numerically into numerical values. Two extreme definitions of the parameter that were evaluated were written to the two ends of a 10 cm line and the patient was asked to rate his own status any signing the points corresponding to his condition. In this test, the mean of the values obtained in patients was taken [14].

Statistical evaluation

Data analysis was made with SPSS (Statistical Package for Social Science) for Windows 11.5 program. Descriptive statistics are expressed with mean ± standard deviation (minimum - maximum) for age, with median (25th-75th percentage) for VAS levels, and with the number of cases and (%) for sex distribution. The significance of the difference between groups in terms of mean ages was evaluated with Student's t test and whether sex distribution was different with Pearson's Chi square test. The significance of the difference between groups at each time point was analyzed with Bonferroni corrected Mann Whitney U test. Whether there was a significant difference in VAS levels at different time points within groups themselves was evaluated with Bonferroni corrected Friedman test. $P<0.05$ was considered significant for all results. In all probable multiple comparisons, Bonferroni correction was made in order to control Type I error.

Table 1. Demographic characteristics of cases according to groups

Variables	Medication group	Invasive group	*p*-value
Age	59.7±15.8 (15-93)	57.9±13.7 (26-83)	0.514[a]
Sex			0.565[b]
Male	26 (34.2%)	20 (39.2%)	
Female	50 (65.8%)	31 (60.8%)	

[a]Student's t test, [b]Pearson Chi square test.

Table 2. The distribution of VAS levels at different time points according to groups

Variables	Medical group	Invasive group	*p*-value[a]
Onset	6 (6-7)	6 (6-7)	0.883
1st month	5 (4-6)	5 (4-5)	0.045
3rd month	4 (3-5)	4 (3-4)	0.056
6th month	3 (3-4)	3 (2-4)	0.098
2nd year	2 (1-4)	2 (1-3)	0.013
p-value[b]	<0.001	<0.001	

[a]Comparison between groups: according to Mann Whitney U test, Bonferroni correction, P<0.010 was considered significant for all results. [b]Comparison within groups: according to, Friedman test, Bonferroni correction P<0.025 was considered for all results.

Table 3. *P* values of comparisons between groups in terms of VAS values at different follow up time points

Follow up up time points	Medical group	Invasive group
Onset-1st month	P<0.001	P<0.001
Onset-3rd month	P<0.001	P<0.001
Onset-6th month	P<0.001	P<0.001
Onset-2nd year	P<0.001	P<0.001
1st month-3rd month	P<0.001	P<0.001
1st month-6th month	P<0.001	P<0.001
1st month-2nd year	P<0.001	P<0.001
3rd month-6th year	P<0.001	P<0.001
3rd month-2nd year	P<0.001	P<0.001
6th month-2nd year	P<0.001	P<0.001

Results

Among patients included in the present study with the diagnosis of NP, mean age was 59.7±15.8 in medication group, while it was 57.9±13.7 in invasive group. The youngest patients were at the age of 15 while the oldest was 93. There was no significant difference between groups in terms of mean age (p: 0.514) of the patients treated with medical methods, 26 was (34.2%) male and, 50 was (65.8%) female, while in the group treated with invasive methods, 20 was male (39.2%) and 31 female (60.8%). No significant difference was found between two groups with respect to sex distribution (P=0.565) (**Table 1**).

No significant difference was found between medical and invasive treatment groups in terms of VAS scores at any follow up time point (P>0.01), while there was significant difference in VAS scores at different time points within the groups themselves from the onset of treatment until 2nd year of treatment (P<0.01) (**Table 2**).

There were statistically significant differences between groups in terms of VAS values at different follow up time points (P<0.001) (**Table 3**).

The horizontal line at the middle of each box indicates median value (50th percentage), while upper and lower borders of boxes indicates respectively 25th and 75th percentile values. Lines above and below the boxes indicate respectively minimum and maximum values (**Figure 1**).

In the medical treatment group, VAS level decrease compared to onset at all time points. There was significant difference between all time points (P<0.001) (**Table 4**; **Figure 2**).

Invasive treatment group VAS levels decreased compared to onset at all follow up time points. In addition, there is statistically significant difference between VAS scores at different time points (P<0.001) (**Table 5**; **Figure 3**).

Discussion

International pain association defines NP as the pain caused or initiated by a primary lesion or dysfunction or temporary disturbance in peripheral or central nervous system. The pathophysiology of NP has not been completely understood. So far, many human and animal studies have been carried out on this issue and its pathogenesis was attempted to be explained and treatment options developed. However, NP is still among pain syndromes difficult to treat and in some cases adequate treatment cannot be offered. Therefore, both the physiopathology and treatment of NP has increasingly be-

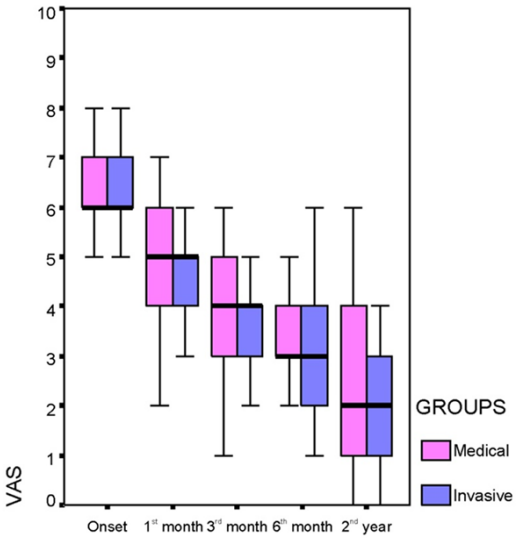

Figure 1. The distribution of VAS levels according to groups at different follow up time points.

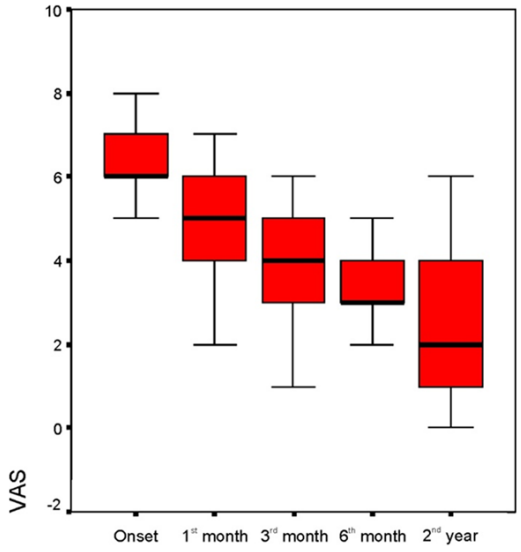

Figure 2. Medical group VAS levels at different follow up time points.

Table 4. VAS levels in medical groups at different follow up time points

Variables	VAS levels
Onset	6 (6-7)
1st month	5 (4-6)[a]
3rd month	4 (3-5)[a,b]
6th month	3 (3-4)[a,b,c]
2nd year	2 (1-4)[a,b,c,d]

[a]The difference with onset is statistically significant (P<0.001); [b]The difference with 1st month is statistically significant (P<0.001); [c]The difference with 3rd month is statistically significant (P<0.001); [d]The difference with 6th month is statistically significant (P<0.001).

Table 5. Invasive group VAS levels at different follow up time points

Variables	VAS levels
Onset	6 (6-7)
1st month	5 (4-5)[a]
3rd month	4 (3-4)[a,b]
6th month	3 (2-4)[a,b,c]
2nd year	2 (1-3)[a,b,c,d]

[a]The difference with onset is statistically significant (P<0.001); [b]The difference with 1st month is statistically significant (P<0.001); [c]The difference with 3rd month is statistically significant (P<0.001); [d]The difference with 6th month is statistically significant (P<0.001).

come a focus of attention for clinicians and investigators [15-18].

In the present study, medical and invasive treatment methods were compared using VAS scoring in patients referring to our clinics and diagnosed with NP. Furthermore, no difference was found between medical and invasive treatment groups in terms of VAS scores at different time intervals. The results of the present study indicate that NP requires individualized treatment in addition to multidisciplinary approach and that clinical experience is also warranted. Because there is no single drug or drug group which has been proven to be effective for all patients, it is difficult to determine a pharmacological treatment which will be effective in any individual patient. This is due to the fact that pain symptom may originate from different mechanisms, individual factors play part in the perception of pain and underlying mechanisms may give rise to variable symptoms.

However, according to pharmacological treatment guide of NP issued by European Neurology Associations Federation, although there are drug options with priority according to primary cause, drug choice may depend on many factors ranging from the age of the patient to the side effects of the drug and psychological and physical condition of the patients. In various studies [19-21] it was revealed that although the drugs used in the treatment of NP treatment are usually beneficial, they do not exert the same effect in all patients.

In the study of Nanna et al. [19], the indispensable element of treatment against neuropathic

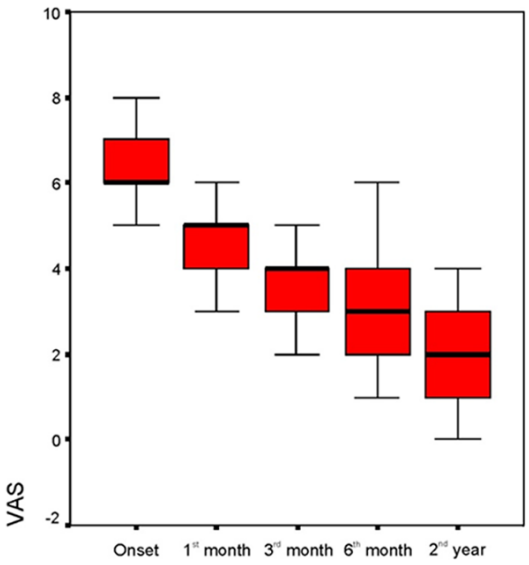

Figure 3. VAS levels at different follow up time points in invasive treatment group.

treatment, i.e. tricyclic antidepressants was effective in post stroke NP, post-therapeutic neuropathy, and diabetic non diabetic neuropathy. In contrast, it was not effective in phantom pain and HIV associated neuropathy, which was attributed to dose intervals and methodological conditions. In the study of Gorson et al. [22] 1/3 of the previously used does of gabapentin was used in all kinds of NP, suggesting that drugs and methods used in the treatment of NP should be evidence based, should have few side effects, decrease pain for a long time and have low cost [19].

As in medical treatment, multidisciplinary approach is also imperative in invasive interventions. Psychological help will be beneficial prior to spinal cord stimulation or implantation treatment [23]. While sympathetic nervous system blockage may be used in the treatment of NP presenting with the involvement of sympathetic paths, radiofrequency method may be used in peripheral nerve injury or radicular pain. Spinal cord stimulation is a method frequently used in the treatment of NP refractory to treatment. It may be employed in complex regional pain type 1 syndrome, refractory radicular pain and other conditions causing refractory NP. As in the medical treatment of NP, the aim of invasive treatment methods are to minimize pain and to Improve functional capacity and quality of life as much as possible.

The limitations of the present study are as follows: it is a retrospective study, not a blinded randomized one. The patients were not equally distributed to groups. In addition, higher numbers of patients could make the study statistically more robust. Medical and invasive methods were not classified in themselves, which could have shed more light on the treatment of NP.

Conclusion

Recently interest has increased in mechanism and treatment of NP. Therefore, important developments may be expected in treatment in the near future. Treatment of NP is an important public health problem with an important economic burden. In order to increase quality of life in patients, rapidly developing symptom and mechanism based treatment approaches have assumed importance in the treatment of NP. In the present study, a multidisciplinary combination of pharmacological options and invasive methods was demonstrated to exert analgesic effect on pain or the use of these options by themselves with proper indications was essential in relieving NP, functionality, and improving quality of life.

Disclosure of conflict of interest

None.

Address correspondence to: Ozkan Onal, Department of Anesthesiology and Intensive Care, Medical Faculty, Selcuk University, Konya, Turkey. E-mail: drozkanonal@selcuk.edu.tr

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