Lidocaine 5% patch in the treatment of localized neuropathic pain due to nerve compression. Case reports

Emplastro de lidocaína a 5% no tratamento da dor neuropática localizada por compressão nervosa. Relato de casos

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DOI 10.5935/2595-0118.20230040-en

ABSTRACT

BACKGROUND AND OBJECTIVES. Neuropathic pain is a chronic condition with a significant burden for patients, society, and healthcare systems. Due to neuropathic complexity, its management must be different than the one for nociceptive pain. First-line systemic treatments may be associated with dose-dependent adverse events and drug-drug interactions. On the other hand, topical treatments have less systemic adverse events, with the 5% lidocaine transdermal patch being recommended for first- or second line of treatment for neuropathic pain according to various international guidelines. The aim of this study is to present three cases of localized neuropathic pain due to nerve compression managed with 5% lidocaine transdermal patch.

CASE REPORTS: The cases of three adult patients (>40 years old) with pain or tingling for a long period of time and their outcomes with treatment with 5% lidocaine transdermal patch for a prolonged duration were investigated. All three cases report a significant improvement in pain.

CONCLUSION: The results of the reported cases revealed that a 5% lidocaine transdermal patch represents an effective, safe and tolerable and noninvasive option for the management of localized neuropathic pain due to peripheric nerve compression.

Keywords: Lidocaine, Nerve compression, Neuropathic pain, Pain.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor neuropática é uma condição crônica com impactos significativos para o paciente, a sociedade e o sistema de saúde. Pela sua complexidade neuropática, a sua abordagem deve ser diferente da dor nociceptiva. Os tratamentos sistêmicos de primeira linha para a dor neuropática podem estar associados à incidência de eventos adversos dose-dependentes e interações farmacológicas. Por outro lado, os fármacos tópicos apresentam menor incidência de eventos adversos sistêmicos, sendo o emplastro de lidocaína a 5% recomendado como primeira ou segunda linha de tratamento para essa condição em diversos *guidelines* internacionais. O objetivo deste estudo foi apresentar três casos clínicos de dor neuropática localizada por compressão nervosa manejados com o emplastro de lidocaína a 5%.

RELATO DOS CASOS: Três pacientes com idade superior a 40 anos e queixas de dor ou parestesia de longa duração foram manejados com emplastro de lidocaína a 5% em tratamento prolongado, com melhora da intensidade de dor expressiva.

CONCLUSÃO: Os resultados dos casos reportados revelaram que o emplastro de lidocaína a 5% se apresenta como uma opção terapêutica eficaz, segura, bem tolerada e não invasiva no manejo da dor neuropática localizada por compressão nervosa periférica.

Descritores: Compressão nervosa, dor, dor neuropática, lidocaína.

INTRODUCTION

Neuropathic pain (NP) is a chronic condition that has significant impacts on the patient, society and the health system[1],

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Presented on August 5, 2022.
Accepted for publication on July 24, 2023
Conflict of interests: André Liggieri has received payment or honoraria for lectures, presentations, participation in speakers' bureaus, manuscript writing or participation in educational events from Grünenthal, Cristália and Hypera Pharma and has participated in the Data Safety Monitoring Board or advisory board of Cristália and Hypera Pharma. Mariana Palladini has received payment or honoraria for lectures, presentations, participation in speakers' bureaus, manuscript writing or participation in educational events from Grünenthal, Mundipharma and Zodiac and support for participation in meetings and/or travel from Grünenthal, participated in the Data Safety Monitoring Board or Advisory Board of Grünenthal and holds leadership or position of trust in another board, society, committee or advocacy group, paid or unpaid from SBED and IASP.
Other financial or non-financial interests: Paulista Pain Center (*Centro Paulista de Dor*).
Sponsoring sources: Editorial assistance was provided by Content Ed Net, with funding from Grünenthal.

HIGHLIGHTS

- Neuropathic pain significantly impacts the patient, society and the healthcare system.
- The approach to neuropathic pain should be different from the approach to nociceptive pain due to its complexity.
- In these case reports, lidocaine patch produced pain relief, with apparent long-term safety and tolerability, although it is not possible to extrapolate to the population itself due to methodological limitations.

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leading to compromised quality of life, increased number of visits to health services and drug prescriptions, and progression of morbidity, both from the pain itself and from the underlying disease[2].

The estimated prevalence of NP is approximately 7% to 10%, with an expected increase in the future due to population aging, increased incidence of diabetes *mellitus* and increased survival rate of post-chemotherapy cancer patients[2,3].

NP is caused by a lesion or disease in the somatosensory system, including peripheral fibers (Aβ, Aδ and C) and central neurons[3]. Factors involved in NP include imbalances at several levels, such as excitatory and inhibitory signals, conformational changes in voltage-dependent ion channels, and variability in the way pain stimuli are modulated in the central nervous system (CNS)[3].

Although the causes and characteristics of pain vary, NP tends to have abnormal sensory perceptions in common, usually distinguished as positive symptoms (such as paresthesia, hyperpathia, hyperalgesia and allodynia) and/or negative symptoms, such as changes in thermal, mechanical or pain perception[4]. Such symptoms may occur in isolation or, more often, in combination. It is also common to attribute certain characteristics to this type of pain, such as burning, needling, tingling or electric shock[4].

The complexity of neuropathic symptoms, the unsatisfactory results obtained with treatments and the difficulty of therapeutic choice contribute to making NP a complex problem and difficult to diagnose[1], requiring a different approach to nociceptive pain[1]. In addition, only 2% of patients with chronic pain are treated by pain specialists[5]. Thus, the challenge of a correct and early diagnosis of this condition is most often under the responsibility of non-specialist physicians[5].

Because of its complexity, NP can remain undiagnosed and/or untreated for months or years. Moreover, even when treated, about 40% to 60% of patients obtain only partial relief of symptoms[5].

Localized neuropathic pain (LNP) is the most common form of NP, affecting about 60% of patients[2]. It is characterized by being a type of peripheral NP, with a consistent and circumscribed area of pain, limited in size to that of a sheet of A4 paper; its diagnosis is difficult due to the various signs and symptoms that can result from it[2].

Although the suspicion of LNP may be clearer when it manifests close to the pain region of origin, as in cases of postoperative LNP or post-herpetic neuralgia, for example, its diagnosis may become more challenging in less evident conditions, such as diabetic peripheral neuropathy (a situation in which patients may present distinct areas of localized pain) or low back pain with a neuropathic component (an etiology in which there is frequent concomitant nociceptive component)[6].

To facilitate diagnosis in patients with chronic pain by non-specialist physicians, a study proposed a tool consisting of four screening questions and a diagnostic algorithm for LNP, which is based on the patient's clinical history, the distribution of pain, the presence of positive or negative neurological symptoms at the site, and the size of the painful area (Figure 1)[5].

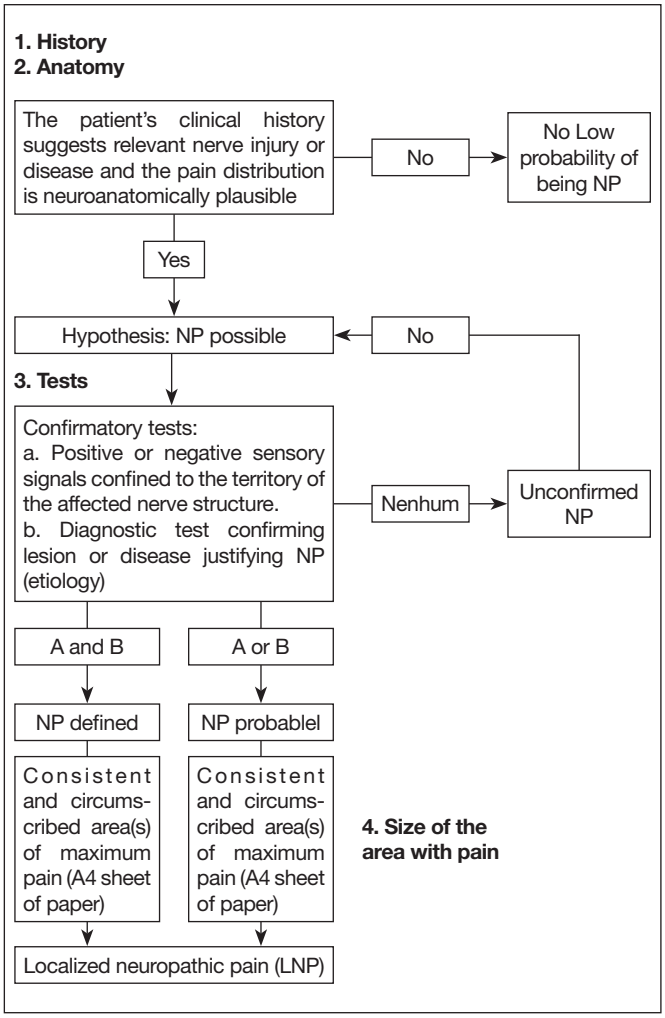

Figure 1. Diagnostic tool for neuropathic pain and localized neuropathic pain. Adapted[5]

A validation study of this tool showed 80% sensitivity and 90.7% specificity in distinguishing LNP from other types of pain[7].

Another simple and validated resource to assist in NP diagnosis is the DN4 questionnaire, which consists of 10 items, 7 of which are related to the pain characteristics described by the patient, and 3 items associated with findings in the clinical examination (Figure 2). Each affirmative answer scores 1 point, and scores ≥ 4 indicate the suspicion of NP[8].

Despite several studies showing that many patients with NP do not receive adequate treatment, pharmacotherapy remains the treatment of choice[2].

The consensus recommends the use of gabapentinoids, antidepressants and topical drugs for NP treatment as first- or second-line choices, with opioids recommended as first- or third-line therapies[2,4,9].

First-line systemic treatments for NP can often be associated with the incidence of dose-dependent adverse events, such as gastrointestinal disturbances, sedation and cognitive changes, as well as the possibility of triggering pharmacological interactions[2,4].

On the other hand, topical drugs have a lower incidence of systemic adverse events and are more associated with cuta-

Questionnaire for neuropathic pain diagnosis - DN4
Please complete the four questions below by ticking one answer for each number:
Patient interview
Question 1: Does your pain have one or more of the following characteristics?

	Yes	No
1. Burning		
2. Painful sensation of cold		
3. Electric shock		

Question 2: Are one or more of the following symptoms present in the same area as your pain?

	Yes	No
4. Tingling		
5. Pins and needles		
6. Numbness		
7. Itching		

Patient examination
Question 3: Is the pain located in an area where physical examination may reveal one or more of the following characteristics?

	Yes	No
8. Hypoesthesia to touch		
9. Hypoesthesia to needle prick		

Question 4: In the painful area the pain may be caused or increased by:

	Yes	No
10. Brushing		

Score
Zero - For each negative item, 1 - For each positive item
Score above 4/10
( ) Neuropathic pain
( ) Nociceptive pain

Figure 2. Questionnaire for neuropathic pain diagnosis (DN4). Adapted[8]

neous adverse events, which are generally well tolerated[2,4]. They constitute a valuable class for LNP treatment, with 5% lidocaine transdermal patch being recommended as the first or second line of treatment for this condition in several international guidelines[2,4,9,10].

Studies in adults have shown that the use of 5% lidocaine transdermal patch in the treatment of LNP produces effective analgesia, with a satisfactory safety and tolerability profile, even in long-term use[9]. When necessary, the patch can be used in combination with other oral treatments, due to its low potential for pharmacological interactions[11,12]. Thus, the SFETD (French Society for the Study and Treatment of Pain) guideline, published in 2020, recommends its use as first-line treatment in LNP[9].

The 5% lidocaine transdermal patch exerts analgesic action through two mechanisms: pharmacological action, by irreversibly blocking voltage-dependent sodium channels, and mechanical protection conferred by the hydrogel layer, forming a barrier against stimuli capable of causing allodynia and/or hyperalgesia[2].

The dose of lidocaine absorbed depends on the covered skin area and the duration of application, with the maximum recommended dose being up to three patches simultaneously for a period of 12 hours per day[13].

The aim of this report was to present three clinical cases of localized neuropathic pain (LNP) due to nerve compression managed with 5% lidocaine patch.

CASE REPORTS

The CARE (CAse REport) guidelines were used as a framework for this article[14]. The CARE guidelines are a set of international standards developed to improve the accuracy, transparency and completeness of case reports in healthcare[14]. Adherence to these guidelines was in pursuit of ensuring that case reports provide relevant and valuable information to health professionals and researchers[14]. The use of the CARE guidelines in this article helped to ensure that the case reports presented were of high quality, provided relevant details about the patient's condition and treatment, and could be used to inform clinical decision-making and future research efforts.

Case 1

A 62-year-old female patient presented with complaints of pain and tingling in the thumb, index and middle finger of the right hand for 6 weeks, which worsened at night, with a pinprick sensation, burning and numbness, with an intensity of 6 by the visual analog scale (VAS), which ranges from zero to 10.

The patient underwent electroneuromyography (ENMG), which demonstrated a pattern compatible with moderate carpal tunnel syndrome, while ultrasonography revealed thickening of the median nerve.

She had positive Tinel's and Phalen's sign on physical examination, as well as hypoesthesia to needle prick and pain intensity. Applying these clinical data to the DN4 questionnaire, a score of 6 points was obtained (with values ≥ 4 suggesting neuropathic pain).

Using the diagnostic tool for LNP (Figure 1), it was concluded that the condition was compatible with confirmed LNP. Thus, the diagnosis of carpal tunnel syndrome with associated LNP was closed, and the patient was initially medicated with 5% lidocaine transdermal patch for four weeks.

After the first four weeks of treatment, the patient discontinued use and returned, presenting pain with VAS of 1 and DN4 equal to zero. She underwent corticosteroid (betamethasone) infiltration and at the follow-up visit reported no further symptoms.

Case 2

A 42-year-old male patient complaining of pain in the right upper limb for 4 months, characterized by tingling, numbness, burning and pinprick, with VAS of 5, in an area smaller than that of a sheet of A4 paper.

The patient tried initial treatment through physiotherapy with transcutaneous electrical nerve stimulation (TENS) and non-steroidal anti-inflammatory drugs (NSAIDs), without improvement of the condition.

On physical examination, he had hypoesthesia to the touch in the lateral region of the right arm, both rotator cuff and shoul-

der impingement tests were negative, with no changes in muscle strength. Shoulder MRI was unchanged and cervical MRI showed disc protrusion between C5 and C6, without radicular conflicts.

Clinical evaluation led to a DN4 of 6, suggestive of NP. Application of the diagnostic tool (Figure 1) was compatible with LNP diagnosis. The diagnosis was localized NP caused by possible C5-C6 nerve root compression.

Treatment with 5% lidocaine transdermal patch applied over the area of pain for 4 weeks was proposed. At reassessment, a 40% decrease in the burning area and hypoesthesia were observed.

After one month of using the patch, the patient was well and discontinued the medication. Six months later, during the COVID-19 pandemic period, he returned with a complaint similar to the initial one, associated with the change in the work environment, due to the home office, with VAS of 5 and again presenting neuropathic symptoms (DN4=5).

Treatment with 5% lidocaine transdermal patch was chosen for 3 months, with guidance and corrections of ergonomics, release of myofascial trigger points and physiotherapy. The patient showed significant pain improvement in the first month of treatment (VAS=2). He started to use nortriptyline 25 mg to sleep and has maintained its use since then, trying to start physical activity.

Case 3

A 46-year-old female patient, secretary, presented with pain and tingling in the region of the index and middle fingers of the right hand for 6 months, with nocturnal worsening in recent days, associated with burning sensations, electric shock, needles and numbness. She reported dropping objects from her hand and had VAS of 7.

The patient had a history of hypercholesterolemia (under treatment with atorvastatin), menstrual cycle changes typical of the climacteric period and allergies to numerous drugs from different therapeutic classes, including analgesics, all of which she could not name.

Physical examination revealed positive Tinel's and Phalen's signs in the right hand and hypoesthesia to needle prick in the painful area. He had a DN4 of 5 and application of the diagnostic tool (Figure 1) pointed to LNP diagnosis, secondary to carpal tunnel syndrome.

5% lidocaine transdermal patch (for 12 hours at night) associated with the use of night orthosis was indicated, in addition to referral for physiotherapy and acupuncture.

After four weeks of treatment, the patient showed a significant improvement in pain at night and when typing, with VAS decrease to 4, but still presenting some difficulty in picking up objects.

Conservative treatment was maintained and surgery was avoided. After four months of treatment, the patient was discharged with improvement of pain.

DISCUSSION

LNP is a condition characterized by a consistent and circumscribed area of maximal pain, associated with negative or positive sensory signs and/or spontaneous symptoms characteristic of NP, limited to the size of a sheet of A4 paper[15]. This real-life case report followed the evolution of two patients with carpal tunnel syndrome and one patient with cervical disc herniation. All cases were diagnosed with LNP secondary to the respective conditions after the DN4 questionnaire and the diagnostic tool were applied and the patients scored higher than 4.

Oral treatments considered first-line for NP are commonly associated with dose-dependent systemic adverse events, which may compromise therapeutic adherence[15]. Thus, 5% lidocaine transdermal patch is an interesting alternative due to its good tolerability and safety profile[2]. 5% Lidocaine non-selectively blocks the sodium channels of injured C and Aδ sensory fibers, which generate ectopic discharges and propagation of the pain signal. As only 3% to 5% of lidocaine is absorbed into the bloodstream, its systemic action is assumed to be negligible or nil[12,15].

Unlike treatments with gabapentinoids and antidepressants, which can cause sedation, constipation and cognitive dysfunction, so far there are no reports of toxicity reported with the use of 5% lidocaine patches, nor the need for dose adjustment in patients with hepatic or renal insufficiency[12,16]. The most frequent complaints associated with its use are local, such as erythema, itching, burning and edema at the application site.

The patch can be used in combination with other oral therapeutic options in patients requiring a multimodal approach, allowing for a reduction in the doses of systemic drugs and, consequently, in the likelihood of adverse events[12,16,17].

In the real-life cases reported here, all patients had a reduction in pain intensity, as measured by the VAS scale, after treatment with 5% lidocaine. Cases 1 and 2 went from pain intensity 6 and 5 to pain intensity 1 and 2, respectively. The patient of case 3 went from a pain of intensity 7 to a pain of intensity 4. Thus, it can be seen that these real-life results are in line with what is reported in the literature, confirming the results of studies during the experimental research of the drug.

In a study[18] comparing the efficacy of 5% lidocaine transdermal patch with naproxen 500 mg twice daily for the relief of pain associated with carpal tunnel syndrome, it was found that with both treatments patients achieved a significant decrease in mean pain intensity (lidocaine 5%, $p<0.0001$; naproxen 500 mg, $p=0.0004$), with no statistical differences between treatments ($p=0.083$). However, patients treated with 5% lidocaine transdermal patch had a statistically significant higher overall impression of clinical improvement compared with patients treated with naproxen 500 mg twice daily, with 71.8% of patients in the 5% lidocaine group reporting being "satisfied" to "very satisfied" with the treatment *versus* 63.2% of patients in the naproxen group.

The aforementioned study also reported that patients treated with 5% lidocaine reported a lower incidence of adverse events than patients in the naproxen group, being 3.8% and 12.5%, respectively. Another study published in the same year[19] compared the use of 5% lidocaine transdermal patch

with local infiltration of 0.5 mL of 1% lidocaine + methylprednisolone 40 mg in individuals with carpal tunnel syndrome, and found that 80% of patients in the 5% lidocaine group reported being "satisfied" or "very satisfied" with the treatment, while 59% of patients in the other group reported the same level of satisfaction.

Thus, the results showed in the present reports demonstrate the efficacy and good tolerability of 5% lidocaine patches for non-invasive LNP treatment in general clinical practice, confirming the results already observed by other authors and the recommendations of recent guidelines, such as the SFETD, for the use of 5% lidocaine as first-line treatment for this condition[2,9].

CONCLUSION

In agreement with the descriptions in the scientific literature, the results of the reported cases revealed that 5% lidocaine transdermal patch presented itself as an effective, safe, well-tolerated and non-invasive therapeutic option in the management of LNP due to peripheral nerve compression.

ACKNOWLEDGMENTS

Editorial assistance was provided by Content Ed Net with funding from Grünenthal.

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REFERENCES

1. Cruccu G, Truini A. A review of neuropathic pain: from guidelines to clinical practice. Pain Ther. 2017;6(Suppl 1):35-42.
2. Pickering G, Martin E, Tiberghien F, Delorme C, Mick G. Localized neuropathic pain: an expert consensus on local treatments. Drug Des Devel Ther. 2017;11:2709-18.
3. Colloca L, Ludman T, Bouhassira D, Baron R, Dickenson AH, Yarnitsky D, Freeman R, Truini A, Attal N, Finnerup NB, Eccleston C, Kalso E, Bennett DL, Dworkin RH, Raja SN. Neuropathic pain. Nat Rev Dis Primers. 2017;3:17002.
4. Likar R, Demschar S, Kager I, Neuwersch S, Pipam W, Sittl R. Treatment of localized neuropathic pain of different etiologies with the 5% lidocaine medicated plaster – a case series. Int J Gen Med. 2015;8:9-14.
5. Mick G, Baron R, Correa-Illanes G, Hans G, Mayoral V, Frías X, Sintes D, Keller T. Is an easy and reliable diagnosis of localized neuropathic pain (LNP) possible in general practice? Development of a screening tool based on IASP criteria. Curr Med Res Opin. 2014;30(7):1357-66.
6. Mick G, Baron R, Finnerup NB, Hans G, Kern KU, Brett B, Dworkin RH. What is localized neuropathic pain? A first proposal to characterize and define a widely used term. Pain Manag. 2012;2(1):71-7.
7. Mayoral V, Pérez-Hernández C, Muro I, Leal A, Villoria J, Esquivias A. Diagnostic accuracy of an identification tool for localized neuropathic pain based on the IASP criteria. Curr Med Res Opin. 2018;34(8):1465-73.
8. Santos JG, Brito JO, de Andrade DC, Kaziyama VM, Ferreira KA, Souza I, Teixeira MJ, Bouhassira D, Baptista AF. Translation to portuguese and validation of the Douleur Neuropathique 4 questionnaire. J Pain. 2010;11(5):484-90.
9. Moisset X, Bouhassira D, Avez Couturier J, Alchaar H, Conradi S, Delmotte MH, Lanteri-Minet M, Lefaucheur JP, Mick G, Piano V, Pickering G, Piquet E, Regis C, Salvat E, Attal N. Pharmacological and non-pharmacological treatments for neuropathic pain: Systematic review and French recommendations. Rev Neurol (Paris). 2020;176(5):325-52.
10. Allegri M, Baron R, Hans G, Correa-Illanes G, Mayoral Rojals V, Mick G, Serpell M. A pharmacological treatment algorithm for localized neuropathic pain. Curr Med Res Opin. 2016;32(2):377-84.
11. Goddard JM, Reaney RL. Lidocaine 5%-medicated plaster (Versatis) for localised neuropathic pain: results of a multicentre evaluation of use in children and adolescents. Br J Pain. 2018;12(3):189-93.
12. Nair AS, Mantha SSP, Azharuddin M, Rayani BK. Lidocaine 5% patch in localized neuropathic pain. Indian J Palliat Care. 2019;25(4):594-5.
13. Derry S, Wiffen PJ, Moore RA, Quinlan J. Topical lidocaine for neuropathic pain in adults. Cochrane Database Syst Rev. 2014;2014(7):CD010958.
14. Gagnier JJ, Kienle G, Altman DG. Moher D, Sox H, Riley D; CARE Group. The CARE guidelines: consensus-based clinical case reporting guideline development. Gob Adv Health Med. 2013;2(5):38-43.
15. Kocot-Kępska M, Zajączkowska R, Mika J, Kopsky DJ, Wordliczek J, Dobrogowski J, Przeklasa-Muszyńska A. Topical treatments and their molecular/cellular mechanisms in patients with peripheral neuropathic pain-narrative review. Pharmaceutics. 2021 Mar 26;13(4):450.
16. Gudin J, Webster LR, Greuber E, Vought K, Patel K, Kuritzky L. Open-label adhesion performance studies of a new lidocaine topical system 1.8% versus lidocaine patches 5% and lidocaine medicated plaster 5% in healthy subjects. J Pain Res. 2021;14:513-26.
17. Hans G, Robert D, Verhulst J, Vercauteren M. Lidocaine 5% patch for localized neuropathic pain: progress for the patient, a new approach for the physician. Clin Pharmacol. 2010;2:65-70.
18. Nalamachu S, Crockett RS, Gammaitoni AR, Gould EM. A comparison of the lidocaine patch 5% vs naproxen 500 mg twice daily for the relief of pain associated with carpal tunnel syndrome: a 6-week, randomized, parallel-group study. Med Gen Med. 2006;8(3):33.
19. Nalamachu S, Crockett RS, Mathur D. Lidocaine patch 5 for carpal tunnel syndrome: how it compares with injections: a pilot study. J Fam Pract. 2006 Mar;55(3):209-14.