

Pharmacological approach for the management of patient with carpal tunnel syndrome associated to diabetic polyneuropathy. Case report

Conduta farmacológica no tratamento de paciente com síndrome do túnel do carpo associada à polineuropatia diabética. Relato do caso

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ABSTRACT

BACKGROUND AND OBJECTIVES: Peripheral neuropathy and carpal tunnel syndrome are debilitating diseases associated to diabetes mellitus in 12 to 21% of cases. There are no significant evidences of the clinical differentiation between such painful syndromes and their specific management. This study aimed at reporting the clinical presentation of a patient with peripheral polyneuropathy associated to carpal tunnel syndrome, focusing on therapeutic approaches and discussing clinical differentiation between both diseases.

CASE REPORT: Male patient, 68 years old, married, retired, who looked for medical assistance complaining of burning pain, especially in left upper limb. He also referred pain in lower limbs with night exacerbation, in addition to numbness in extremities and pain intensity of 6 in the visual analog scale. Presence of trigger-points in trapezius and levator scapulae muscles. Patient was submitted to decompression surgery due to carpal tunnel syndrome diagnosis two years ago, however without postoperative improvement. Patient refers pain in upper and lower limbs, with nocturnal exacerbation, numbness and pain in extremities. He has history of hypertension, diabetes mellitus type 2 and leprosy. At physical evaluation: painful boot and glove hypoesthesia and possible motor deficit in C6 and C7. Electromyography showed mixed peripheral polyneuropathy of lower limbs and median carpal syndrome to the left. There has been movement amplitude improvement in myotomes C6 and C7. Pain decreased to 3 in the visual analog scale after two weeks under gabapentin and duloxetine.

CONCLUSION: It is difficult to clinically differentiate between neuropathy of different etiology and peripheral polyneuropathy. The proposed treatment has provided 50% improvement in the

visual analog scale two weeks later. Lidocaine infusion at 5% has provided acute improvement of patient's pain.

Keywords: Carpal tunnel syndrome, Diabetic Neuropathy, Pharmacotherapy.

RESUMO

JUSTIFICATIVA E OBJETIVOS: Polineuropatia periférica e síndrome do túnel do carpo são doenças debilitantes, associadas ao diabetes *mellitus* em cerca de 12 a 21% dos casos. Inexistem evidências significativas que direcionem sobre a diferenciação clínica entre essas síndromes dolorosas e o tratamento específico. O objetivo deste estudo foi relatar o quadro clínico de um paciente que apresentou polineuropatia periférica associada à síndrome do túnel do carpo, enfocando nas medidas terapêuticas e discutindo acerca da diferenciação clínica entre as doenças referidas.

RELATO DO CASO: Paciente do gênero masculino, 68 anos, casado, aposentado buscou atendimento médico por queixa de dor queimante, sobretudo em membro superior esquerdo. Refere dor também em membros inferiores, com exacerbção noturna, além de dormência nas extremidades, intensidade de 6 na escala visual analógica. Presença de ponto-gatilho nos músculos trapézio e elevador da escápula. Passou por cirurgia de liberação por diagnóstico de síndrome túnel do carpo há 2 anos, sem melhora pós-cirúrgica. Tem histórico de hipertensão arterial, diabetes *mellitus* tipo 2 e hanseníase. No exame físico: presença de hipostesia dolorosa em bota e luva e possível déficit motor em C6 e C7. Eletromiografia evidencia polineuropatia periférica mista de membros inferiores e síndrome do túnel do carpo mediana à esquerda. Houve melhora na amplitude de movimento nos miotomos C6 e C7. A dor foi para 3 na escala visual analógica após 2 semanas sob uso de gabapentina e duloxetina.

CONCLUSÃO: É difícil a diferenciação clínica entre neuropatia de outra etiologia e polineuropatia periférica. O tratamento proposto trouxe uma melhora na escala analógica visual de 50% após duas semanas. A infusão de lidocaína a 5% representou melhora aguda na dor referida pelo paciente.

Descritores: Farmacoterapia, Neuropatia diabética, Síndrome do túnel do carpo.

INTRODUCTION

Peripheral polyneuropathy (PPN) is a condition affecting more than one peripheral nerve, which induces sensitive and/or motor changes, being a complication secondary to diabe-

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tes mellitus (DM) in approximately 12 to 21% of patients, being in this case called diabetic polyneuropathy (DPN)^{1,2}. Symptoms are in general symmetrically distributed in “boot or glove” pattern, with exacerbation at night. Carpal tunnel syndrome (CTS) is the most common affection among those related to peripheral nerves compression and DM is knowingly a risk factor for CTS, which affects approximately 45% of diabetic patients as compared to 12% of general population^{3,4}. Clinical association between median neuropathy at the wrist, the electromyographic study of which in general reveals CTS, and DPN is present in about 29% of patients in whom it is presented as early manifestation of diabetic polyneuropathy⁵.

The literature satisfactorily addresses indications and recommendations for pharmacological treatment of neuropathic pain. For this purpose tricyclic antidepressants, selective inhibitors of 5HT and norepinephrine reuptake, gabapentin, pregabalin and topic lidocaine infiltration may be used⁶. However, there are not significant evidences directing a specific pharmacological management to patients in whom DPN and CTS are associated.

So, this study aimed at reporting a case of a patient with DPN associated to CTS, focusing on clinical differentiation, and at discussing most effective therapeutic measures in the pharmacological field.

CASE REPORT

Male patient, 68 years old, married, retired three years ago and who worked as industrial cook, with major complaint of left hand pain starting six years ago. Pain was diffuse, burning, being constant along the day (especially in left upper limb) and associated to night exacerbation and numbness in extremities. Intensity was classified by the visual analog scale (VAS) as 6/10 for lower limbs (LLLL) and upper limbs (UULL).

Patient was submitted to surgery due to CTS diagnosis two years ago, however without postoperative improvement. Patient has history of leprosy for eight years, is hypertensive and has DM type II. Patient was under previous use of losartan, metformin and gabapentin, being the latter discontinued by him due to no pain improvement.

At physical evaluation patient was conscious and oriented with painful hypoesthesia in boot and glove, signs of motor deficit in C6 and C7 and presence of trigger-points in trapezius and levator scapulae muscles. Electromyography has shown mixed peripheral polyneuropathy of LLLL and marked CTS to the left. We have also asked for magnetic resonance (MR) of cervical spine which has not shown significant changes.

Initial pharmacological approach to treat baseline diseases was to maintain losartan and metformin. For the former, a dose of 50mg/day was prescribed. For the latter, initial dose, which was one 850 mg/day tablet, was adjusted to two 500 mg/day tablets. Losartan was maintained to treat hypertension. Metformin, a biguanide which increases sensitivity to insulin, is justified to control DM, factor which triggers peripheral nerves changes culminating with DPN.

Although gabapentin is the most widely indicated first line to treat neuropathic syndromes, patient has reported that its previous use for six months had not improved pain. So, we decided to reintroduce gabapentin in the dose of 30 mg/day associated to 30 mg/day of duloxetine.

Pain, induced both by DPN and CTS, was managed with the association of gabapentin (which was reintroduced in the dose of 300 mg/day) and duloxetine (30 mg/day).

In addition to prescribed drugs, we also decided for a local injection of 5% lidocaine in painful areas, performed at consultation time.

Two weeks later, and adhering to proposed treatment, patient returned and reported major improvement and further amplitude of movements which before could not be performed due to recurrent pain. Pain intensity in LLLL and UULL, which initially was approximately 6/10 has improved to 3/10 according to VAS.

DISCUSSION

Painful, hypoesthetic and paresthetic symptoms of CTS are induced by medial nerve compression which may be caused by issues such as tenosynovial proliferation, tumor, wrist joint abnormality or muscle anomaly⁷, as well as any other situation increasing pressure of decreasing volume of the carpal tunnel. Major risk factors for this disease include pregnancy, hypothyroidism DM, obesity, renal failure, wrist fracture and occupation. With regard to the latter, it is known that CTS affects approximately 1% of retired workers and is the major reason of pain in hands of those performing manual work⁸. Diabetic polyneuropathy is a complication of diabetes (1 and 2), being characterized by progressive distal axonal degeneration, in addition to demyelination and axonal loss⁹. The pathway leading to painful symptoms is the injury of sensory and motor fibers, or both, caused by high glycemia levels, which may occur in local fibers in case of mononeuropathy, or in several fibers in case of polyneuropathy. Most common symptoms are painful paresthesia and sensory ataxia, which may affect up to 50% of DM type 2 patients. From the general picture, approximately 90% are represented by Diabetic Painful Distal Symmetrical (DSPN), disease which is often associated to CTS^{10,11}.

A major point of clinical differentiation between both diseases is that in CTS patients in general precisely describe the distribution of sensory disorders from the palm to finger tips (frequently middle finger), predominantly in the dominating hand (80% of cases), irradiating to shoulder. In DPN, symptoms have a uniform bilateral distribution, both in LLLL and UULL extremities in a distribution pattern known as boot and glove. While CTS symptoms are frequently associated to repetitive mechanical effort patterns, DPN symptoms are more related to exacerbation at night^{1,2,7-9}.

In our patient, the history of leprosy could be a risk factor, in addition to DM and occupation, leading to further morbidity of neuropathic painful syndromes, which could be explained by the trend of such patients to develop thin fibers neuropathy. In addition, Von Gierke et al.¹² have reported a

curious case of CTS as leprosy complication, which seems to have been caused by a possible latency of decades of the leprous neuritis¹². However, there are no further evidences in the literature to confirm such relationship.

In addition to history and physical evaluation, electroneuro-myography is the standard method for diagnostic confirmation of peripheral neuropathies. However, it is not uncommon to find changes in asymptomatic patients, however such changes are an additional risk factor for the development of the disease. With regard to CTS, evidences suggest that positive electromyography in asymptomatic diabetic patients represents increased risk factor for the development of other neuropathies, including DPN. Ultrasound is also a useful tool to help in the differential diagnosis of patients with CTS associated or not to DPN, by measuring the cross-sectional area (CSA) of the medial nerve. CSA cutoff value favoring the association between both diseases varies from 10.5 mm² to 11.6 mm², with sensitivity and specificity of up to 73 and 90%, respectively¹³.

Final clinical treatment for CTS is in general decompression surgery. Postsurgical improvement rate for DM patients is around 68% and it seems to be clinically lower as compared to a non-diabetic control group¹⁴. Another option is pharmacological therapy to control pain. Among options, a mean dose of 1800 mg/day of gabapentin has resulted in 40% decrease in symptoms pain intensity and functional level improvement of patients at the end of six months¹⁵. There are few studies on the efficacy of duloxetine and other drugs to treat CTS.

In case of DPN, treatment consists in controlling the baseline disease (DM) by controlling glycemia aiming at preventing the progression of damage to neuronal fibers, and in controlling pain induced by already established injuries. Analyzing most recent guidelines of the American Academy of Neurology (AAN)¹⁶, of the European Federation of Neurological Societies (EFNS)¹⁷ and of the National Institute for Health and Clinical Excellence (NIHCE)¹⁸, it was observed that both gabapentin and duloxetine are recommended as first or second choice drugs to treat such patients, as shown in table 1.

In our case, patient was refractory to decompression surgery and to gabapentin, which are first line therapies for CTS and

DPN, respectively. Since there is no formal indication in the guidelines for the treatment of both associated syndromes, we decided to maintain gabapentin in the dose of 30 mg/day because it is formally indicated to treat DPN and has beneficial results with regard to improving CTS pain, although in a significantly lower dose. Following guidelines recommendations, duloxetine in the dose of 30 mg/day was associated.

Topic 5% lidocaine infusion is justified due to its efficacy (65%) for acute neuropathic pain control, effect which is comparable or even better than the use of pregabalin. Pain control duration is approximately 7-8 hours and its efficacy may be maintained to up to one week^{12,19}.

CONCLUSION

It is difficult to clinically differentiate between neuropathy of a different etiology and PPN. However, with specific diagnosis and treatment patient had a positive response.

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Table 1. Guidelines to treat painful diabetic neuropathy

	EFNS (2010)	AAN (2011)	NIHCE (2013)
Pregabalin	1 st	1 st	1 st or 2 nd
Gabapentin	1 st	2 nd	1 st or 2 nd
Duloxetine	1 st	2 nd	1 st or 2 nd
Tricyclic antidepressants	1 st	2 nd	1 st or 2 nd
Opioids	2 nd or 3 rd	2 nd	-
5% Lidocaine	-	3 rd	-
Carbamazepine	NI	-	-

1st, 2nd and 3rd = first, second and third choice, respectively. EFNS = European Federation of Neurological Societies; AAN = American Academy of Neurology; NIHCE = National Institute for Health and Clinical Excellence; NI = not indicated. - = not mentioned.