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CASE REPORT

Sildenafil to control neuropathic pain after nephrectomy. Case report*

Uso do sildenafil no controle de dor neuropática após nefrectomia. Relato de caso

Thiago Robis de Oliveira[1], Tatiana Vaz Horta Xavier[1], Tereza Cristina Bandeira Silva Mendes[2]

* Received from the Pain Treatment Outpatient Setting Dr. Josefino Fagundes da Silva, Clinicas Hospital, Federal University of Minas Gerais. Belo Horizonte, MG.

SUMMARY

BACKGROUND AND OBJECTIVES: Neuropathic pain is defined as pain started or caused by somatosensory system injury, which leads to major functional loss and limitation. Its treatment is critical to improve quality of life. This study aimed at reporting neuropathic pain control with sildenafil in a patient refractory to normal therapy.

CASE REPORT: Male patient, 40 years old, evolving with very severe neuropathic pain after lumbar nephrectomy to treat renal neoplasia. Adequate pain control was not reached with normally used first, second or third line drugs. Sildenafil for six months has provided adequate pain control, importantly decreasing its intensity and greatly improving functional limitation presented by the patient.

CONCLUSION: Sildenafil has provided important pain intensity decrease, emerging as an option to treat neuropathic pain not controlled by normal therapy.

Keywords: Neuropathy, Nitric oxide, Pain, Phosphodiesterase inhibitors.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor neuropática é definida como aquela iniciada ou provocada por lesão no sistema somatossensorial, que causa importante perda funcional e limitação para o paciente. O seu tratamento é fundamental para a melhoria da qualidade de vida dos pacientes. O objetivo deste estudo foi relatar o controle de dor neuropática utilizando sildenafil em paciente refratário a terapêutica habitual.

RELATO DO CASO: Paciente do sexo masculino, 40 anos, evoluiu com dor neuropática de grande intensidade após nefrectomia por via lombar para tratamento de neoplasia renal. O controle adequado da dor não alcançado com o uso dos fármacos de primeira, segunda ou terceira linha habitualmente usada. O sildenafil usado durante seis meses propiciou adequado controle da dor, diminuindo de modo importante sua intensidade permitindo diminuição importante da limitação funcional apresentada pelo paciente.

CONCLUSÃO: O sildenafil propiciou grande diminuição da intensidade da dor, despontando como opção para tratamento de dor neuropática não controlada com a terapêutica habitual.

Descritores: Dor, Inibidores de fosfodiesterase, Neuropatia, Óxido nítrico.

INTRODUCTION

Neuropathic pain is defined as pain started or caused by injury or dysfunction affecting the somatosensory system and its prevalence is of approximately 8% of the world population[1]. Diagnosis is done by symptoms description by patients, clinical signs evaluation, complementary exams and a positive response after adequate therapy. In general, the treatment is complex and response to medication is not always satisfactory. There are several treatment lines being antidepressants with norepinephrine and serotonin reuptake inhibition, calcium channels alpha-2-delta ligants and local anesthetics

1. Student of the School of Medicine, Federal University of Minas Gerais; Trainee of the Pain Treatment Outpatient Setting Dr. Josefino Fagundes da Silva, Clinicas Hospital, Federal University of Minas Gerais. Belo Horizonte, MG, Brazil.
2. Anesthesiologist, Master and Physician of the Pain Treatment Outpatient Setting Dr. Josefino Fagundes da Silva, Clinicas Hospital, Federal University of Minas Gerais. Belo Horizonte, MG, Brazil.

Correspondence to:
Thiago Robis de Oliveira
Rua dos Guaranis, 241/401 – Centro
30120-040 Belo Horizonte, MG.
Phone: (31) 8307-5762
E-mail: thiagorobis@gmail.com

the first line drugs. Tramadol and opioids are second line drugs. Third line drugs are other anticonvulsants and other categories of antidepressants[1].
This study aimed at reporting the treatment of post-nephrectomy neuropathic pain refractory to common therapy with sildenafil as major therapy.

CASE REPORT

Male patient, 40 years old, 76 kg, African-Brazilian, single, away from labor function and with great social and affective life impairment. Patient was referred to the Pain Treatment Outpatient Setting, Clinicas Hospital, Federal University of Minas Gerais due to pain not controlled by common therapy. Patient had been submitted to lumbar nephrectomy due to renal neoplasia.
Patient evolved with very severe lumbar pain, with intensity 8 by the visual analog scale (VAS) and decreased local sensitivity since late postoperative period, with major functional limitation due to pain not controlled with sertraline (50 mg/day), pregabalin (75 mg) twice a day, clonazepam (2 mg/day), amitriptyline (25 mg) twice a day, paracetamol (500 mg) four times a day, nimesulide (100 mg) twice a day and cyclobenzaprine (10 mg/day). Tumor recurrence was discarded after clinical evaluation and complementary propaedeutics. Therapy was started with weekly sympathetic neuraxis blockade for two months, without significant improvement. We decided to introduce sildenafil (25 mg/day), associated to risperidone (1 mg/day) to control associated psychiatric symptoms. Other previously used drugs were withdrawn. Pain and side effects were weekly evaluated. After three months, pain intensity by VAS was 4 with significant improvement of functional limitations. Six months later, patient was discharged with pain intensity 3 according to VAS, under risperidone (1 mg/day) and with less frequent visits to the service.

DISCUSSION

Nitric oxide (NO) is a major chemical mediator of several physiological reactions, including relaxation of smooth muscle cells, platelet activity inhibition and peripheral and central nervous systems transduction. It is known that nitric oxide activates the guanylate-cyclase enzyme, which leads to cyclic guanosine monophosphate synthesis (cGMP)[2]. The NO/cGMP has a well established role in nociceptive pathways, as flags[3], being also part of the pathway were morphine and its derivatives act[5,6].
Sildenafil, a potent phosphodiesterase-5 specific and selective inhibitor, has antinociceptive effects in several animal models, such as carrageenan-induced pain, writhing test[4] and in the second phase of the formalin test[5,6], in addition to humans. Its use is already validated for erectile dysfunction, which is its most common indication, and to treat pulmonary hypertension[7]. The drug has a good pharmacokinetic profile with 41% of oral bioavailability, half-life of 3-8 hours and mostly hepatic clearance. It is counterindicated for patients under nitrates, with severe renal and/or liver failure or recent history of hemorrhagic stroke or myocardial infarction.
So far, its explained mechanism is the intracellular build up of cGMP, caused by phosphodiesterase-5 inhibition and leading to protein kinase G (PKG) activation. This process induces potassium channels opening, which leads to neuronal hyperpolarization responsible for the antinociceptive effect[8]. Other drugs, such as dibutiril-cGMP and 8-bromine-cGMP[9], which increase intracellular cGMP content, have shown, alone or synergistically, antinociceptive potential, whereas drugs degrading intracellular cGMP have caused hyperalgesia and alodínia in experimental models, confirming the explained mechanism.
Part of this process is also present in antinociception induced by morphine and its derivatives, with studies showing synergistic results of the use of both drugs. These same studies have shown that with opioid antagonists such as naloxone, sildenafil antinociceptive effects are attenuated or inhibited[5]. In addition, it has been observed that sildenafil also acts on the central nervous system, especially in the posterior horn of the gray spinal cord[10,11].
Neuropathic pain is still a therapeutic challenge because not all patients obtain a good pain control with available drugs. This clinical case allowed us to infer that sildenafil may be an alternative to control neuropathic pain not controlled by common first, second or third line drugs.
Sildenafil and other specific phosphodiesterase inhibitors may be important coadjuvants to treat neuropathic pain refractory to common therapy. This is the first report available in the literature about success obtained with sildenafil to control neuropathic pain. However, more baseline and clinical studies are needed to define the role of sildenafil to control neuropathic pain.

CONCLUSION

Sildenafil has provided significant pain intensity decrease, and emerges as an option to treat neuropathic pain not controlled with normal therapy.

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