Hyperprolactinemia and galactorrhea associated with the use of duloxetine to treat chronic neuropathic pain. Case report

Hiperprolactinemia e galactorreia associada ao uso de duloxetina para tratamento de dor neuropática crônica. Relato de caso

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ABSTRACT

BACKGROUND AND OBJECTIVES: The association of the use of some drugs with hyperprolactinemia and galactorrhea has been reported in the literature, but information on the role of duloxetine in these alterations is scarce. Therefore, the aim of this study was to highlight this adverse effect and discuss the pathophysiological causes of galactorrhea associated with the use of duloxetine in a patient undergoing treatment for chronic pain.
CASE REPORT: Female patient, 70 years old, with herpetic neuropathy diagnosis. She developed refractory pain after drug treatment and was referred to the pain clinic. Duloxetine (60mg) taken once a day was maintained and associated with blocks with local anesthetic in regions of herpetic pain. The patient complained of galactorrhea and changes in weight and showed an increase in serum prolactin. Then, the possibility of hyperprolactinemia due to duloxetine was raised. Duloxetine was suspended, and after one month, a significant reduction in serum prolactin levels and end of galactorrhea were observed.
CONCLUSION: The treatment of patients with neuropathic pain is extremely challenging and the detailed understanding, especially of the pharmacological strategy and its possible adverse effects, is fundamental for the better management of patients and their well-being. Therefore, it is concluded that duloxetine, although rarely, can cause an increase in serum prolactin and galactorrhea in users.

Keywords: Duloxetine hydrochloride, Galactorrhea, Hyperprolactinemia, Pain.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A associação do uso de alguns fármacos com hiperprolactinemia e galactorreia tem sido relatada na literatura, mas são escassas as informações sobre o papel da duloxetina nestas alterações. Portanto, o objetivo deste estudo foi destacar este efeito adverso e discutir as causas fisiopatológicas da galactorreia associada ao uso de duloxetina no tratamento da dor crônica.
RELATO DO CASO: Paciente do sexo feminino, 70 anos, com diagnóstico de neuropatia herpética. Evoluiu com refratariedade álgica após tratamento farmacológico, sendo encaminhada à clínica de dor. Optou-se por manter a duloxetina (60 mg) uma vez ao dia e associar bloqueios com anestésico local em regiões de dor herpética. A paciente queixou-se de galactorreia e alteração de peso e apresentou elevação da prolactina sérica. Foi aventada, então, a possibilidade de hiperprolactinemia pela duloxetina. Foi, então, realizada a suspensão da duloxetina e, após um mês, foi observada redução expressiva dos níveis séricos da prolactina e cessação da galactorreia.
CONCLUSÃO: O tratamento de pacientes com dor neuropática é extremamente desafiador e a compreensão detalhada do processo, em destaque para a estratégia farmacológica e seus possíveis efeitos adversos é fundamental para o melhor manejo dos pacientes e manutenção do bem-estar. Diante disso, concluiu-se que a duloxetina, apesar de acontecer raramente, pode causar aumento da prolactina sérica e galactorreia em usuários.

Descritores: Dor, Cloridrato de duloxetina, Galactorreia, Hiperprolactinemia.

INTRODUCTION

The increased level of prolactin hormone in the blood is known as hyperprolactinemia, and the most common symptom is galactorrhea, in which there is spontaneous milky secretion from the mammary glands. In the absence of conditions such as pregnancy or lactation, it's caused by increased secretion of prolactin. This can occur due to a number of reasons, including the use of antidepressant drugs[1], such as duloxetine. Data on increased serum prolactin levels associated with use of duloxetine are limited, and there is no consensus in the literature regarding its prevalence.
The present study's objective was to report a case of hyperprolactinemia with galactorrhea due to the use of duloxetine for the treatment of chronic neuropathic pain.

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CASE REPORT

CARE guideline (Case REport) was used for the preparation of this case report in order to increase accuracy, transparency, and usefulness to the community[2,3].

The patient was a 70-year-old female living in Belo Horizonte, Minas Gerais, Brazil, with a diagnosis of intercostal herpetic neuropathy.

The patient developed pain located in the right hypochondrium and posterior chest to the right, with intense burning and 'stabbing' sensation, without associated allodynia or hyperalgesia, in the intercostal region between dermatomes T4 and T6 to the right. She was evaluated by the orthopedics and the internal medicine, who performed various exams for propedeutics.

The patient had systemic arterial hypertension under adequate clinical control and was taking losartan 25 mg regularly. The father had a diagnose of Parkinson's disease.

During the physical examination, the patient had no associated allodynia or hyperalgesia and had preserved strength.

The patient developed, after a long trip, pain in the right intercostal area.

Before the appearance of the classic lesions of herpes-zoster (Shingles), the patient developed pain in the right hypochondrium and dorsum and sought medical help from an orthopedist. The possibility of an acute muscle injury was considered, and physical therapy was prescribed. After one week, the vesicles, classic of herpes-zoster, appeared.

After one week, vesicular eruptions developed along the dermatome where she had pain complaints. The patient was then diagnosed with herpes-zoster and given antivirals and analgesics. After 90 days of the skin rash onset, significant pain persisted, characterizing a scenario of post-herpetic neuralgia.

The diagnostic methods used were: blood biochemistry exam, urine tests, MRI of the total abdomen, cervical and thoracic spine and skull, colonoscopy, and endoscopy, all of which showed no alterations.

The following diagnoses were given: muscle damage after repeated exertion, herpes-zoster and post-herpetic neuralgia.

Oral therapies were started with pregabalin 450 mg/day (suspended due to dizziness possibly associated with the gabapentinoid), transdermal buprenorphine 5 mg/day (also suspended because the patient developed edema, erythema and skin itching). In addition, duloxetine 60 mg/day, supposedly associated with hyperprolactinemia and galactorrhea, was maintained.

The following were associated with the oral therapies: intercostal block at T3 to T8 levels with local anesthetic, venous sympathetic block with lidocaine 1% without vasopressor (2 mg/kg), and spinal erector plane block (ESP Block), after consultation with the pain specialist.

Drugs such as duloxetine, pregabalin and transdermal buprenorphine were prescribed. However, the patient developed refractory pain and adverse effects associated with the drugs, and was referred to the pain clinic after 1 year and 2 months of the herpes-zoster episode.

After admission to the pain clinic, the use of duloxetine 60 mg once a day was associated with blocks. During this period, the patient complained of galactorrhea and weight changes. She sought the endocrinologist, who detected elevated serum prolactin, and the values found were 47 ng/mL, considered double the reference values. Thus, the possibility of hyperprolactinemia due to duloxetine was raised. Duloxetine was discontinued and, after one month, there was a significant reduction in serum prolactin levels and cessation of galactorrhea. The new serum prolactin values were 28.5 ng/mL.

Due to the great challenges in managing this pain scenario, the decision was to not prescribe any antidepressant drug in this profile. A reduction in serum prolactin levels and cessation of galactorrhea were observed after suspension of duloxetine. Galactorrhea as an adverse effect associated with the use of duloxetine was verified.

DISCUSSION

Pain management in peripheral neuropathies is greatly complex, and duloxetine is an option considered by several international guidelines[4].

Although all management strategies should strive to improve pain, the functional consequences and possible adverse effects of their management should be taken into account.

Tricyclic antidepressants (TCA), selective serotonin reuptake inhibitors (SSRIs), gabapentanoids, tramadol, lidocaine, and capsaicin are the most effective options for the treatment of neuropathic pain.

Most of these first- and second-line options come with considerable potential for adverse effects. Duloxetine is also an important drug in the pharmacological arsenal for neuropathic pain treatment. Therefore, this report adds to the statistical data of this rare association, as well as highlighting the importance of this knowledge directed to the diagnosis and treatment of its possible complications by pain specialists and physicians in general

Antidepressant drugs with serotoninergic activity can cause hyperprolactinemia, which is associated with galactorrhea, gynecomastia, menstrual irregularities, and sexual dysfunction[5].

Prolactin is a protein-based lactogenic hormone produced by the adenohypophysis gland, and its regulation is controlled by the hypothalamus. The main physiological mechanism that controls prolactin secretion is the action of dopamine, secreted the hypothalamus neurons, which inhibits prolactin. Besides other complementary mechanisms, such as gamma aminobutyric acid (GABA) (stimulant effect), somatostatin (inhibitory effect), acetylcholine, norepinephrine and serotonin (stimulant effect)[5].

There are two main hypotheses to explain these dopamine-related mechanisms. Firstly, serotonin modulates prolactin secretion via postsynaptic receptors. The pathways connecting prolactin and serotonin secretion are several. Furthermore, in the central nervous system, the serotonin and dopamine neurotransmitters can also interact[6]. Thus, drugs that block dopamine receptors, such as antipsychotics, or those that increase serotoninergic neurotransmission, such as duloxetine, may contribute to increase prolactin secretion.

Secondly, serotonin inhibits GABA-producing interneurons, which may lead to decreased dopaminergic inhibition with increased prolactin secretion. The prevalence of antidepressant-induced hyperprolactinemia is 10.9 to 17.4%[7], and SSRIs, mainly sertraline, have been reported as the most frequent cause. Data related to duloxetine are more controversial.

CONCLUSION

In the present case of association between hyperprolactinemia and galactorrhea, increased prolactin levels due to the use of duloxetine were found.

AUTHORS' CONTRIBUTIONS

Carolina Mendonça de Goffredo Costa dos Santos
Writing - Preparation of the original
Joana Angélica Vaz de Melo
Data Collection, Writing - Review and Editing
Gustavo Márcio Silvino Assunção
Data Collection, Research

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