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CASE REPORT

Duloxetine to treat chronic inflammatory low back pain in ankylosing spondylitis patients. Case reports*

Duloxetina no tratamento da dor lombar inflamatória crônica em pacientes portadores de espondilite anquilosante. Relato de casos

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SUMMARY

BACKGROUND AND OBJECTIVES: Ankylosing spondylitis (AS) is a chronic inflammatory autoimmune disease. Its major symptom is chronic inflammatory low back pain, which treatment and complications represent a considerable burden to society. New therapeutic options have been studied to treat refractory inflammatory low back pain in AS patients. The objective was to present two AS patients with low back pain refractory to non-steroid anti-inflammatory drugs (NSAIDs), who presented important clinical improvement with duloxetine.

CASE REPORTS: Two male patients with AS and chronic inflammatory low back pain refractory to NSAIDs, who used duloxetine (60 mg/day) and presented major clinical improvement.

CONCLUSION: Duloxetine was effective to decrease chronic inflammatory low back pain intensity in AS patients.

Keywords: Analgesics, Ankylosing spondylitis, Causalgia, Low back pain.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A espondilite anquilosante (EA) é uma doença inflamatória crônica de etiologia autoimune, cujo principal sintoma é a lombalgia crônica de caráter inflamatório, cujo tratamento e complicações representam um encargo considerável para a sociedade. Novas opções terapêuticas têm sido buscadas para o tratamento da dor lombar inflamatória refratária nos pacientes com EA. O objetivo foi apresentar dois pacientes portadores de EA com dor lombar refratária ao uso de anti-inflamatórios não esteroides (AINES), que apresentaram importante melhora clinica com a duloxetina.

RELATO DOS CASOS: Dois pacientes do sexo masculino com EA e dor lombar crônica inflamatória refratária ao uso de AINES, que usaram duloxetina (60 mg/dia) e apresentaram melhora clinica importante do quadro doloroso.

CONCLUSÃO: A duloxetina se mostrou eficaz para a redução da intensidade da dor lombar crônica inflamatória em pacientes portadores de EA.

Descritores: Analgésicos, Causalgia, Dor lombar, Espondilite anquilosante.

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory autoimmune disease preferably affecting the spine, which may evolve with stiffness and progressive functional limitation of the axial skeleton[1,2]. It is more frequent in young adults, in general starting between 20 and 40 years of age with prevalence in males (3:1), Caucasians and HLA-B27-positive individuals[2,3]. It is part of the spondiloarthrites complex to which HLA-B27 is strongly correlated with its positiveness varying from 80% to 90% of cases[4].

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Major clinical symptom is chronic inflammatory low back pain associated to morning stiffness[1,5] and its treatment is also based on symptoms relief. Although non-steroid anti-inflammatory drugs (NSAIDS) are proven to be effective in controlling pain and stiffness, the possibility of NSAIDS-induced chronic nephropathy may contribute to increased morbidity/mortality in this group of patients, which have led to the search of alternative therapies to control disease pain and activity.

Chronic pain prevalence is markedly increased in AS patients and the prevalence of symptoms compatible with fibromyalgia is increased as compared to general population[6], indicating that chronic pain treatment should be introduced even before anti-TNF agents. New therapeutic options have been studied to treat refractory inflammatory low back pain in AS patients[7]. Duloxetine has been widely studied to treat benign chronic pain, especially fibromyalgia pain, diabetic neuropathic pain and chronic musculoskeletal pain. Several studies have evaluated duloxetine in chronic low back pain and osteoarthritis patients and results have shown efficacy of 60-120 mg/day[8-10]. Benefits have been also documented in a longer study[11], however there are no studies proving the efficacy of duloxetine to treat inflammatory low back pain in spondyloarthritis and, particularly, in AS patients.

This study aimed at presenting two AS patients with inflammatory low back pain refractory to NSAIDS who presented major clinical improvement after duloxetine, associated or not to other common analgesics.

CASE REPORTS

Case 1: Male patient, 41 years old, with HLA-B27-positive AS with 15 years of evolution. He presented inflammatory low back pain with severe morning stiffness and progressive decrease in lumbar spine motility. Radiological exam has shown bilateral sacroiliitis (grade 3 to the left and 4 to the right), however there was no spinal ankylosis. He used several NSAIDs until 2008: sulfasalazine (3 g) for two and a half years and paracetamol, up to 3000 mg/day, without pain improvement. In June 2008 he presented BASDAI 5.6, BASFI 5.3, PCR 7.8 mg/dL, Shöber index 0 and tragus-wall ratio of 13 cm to the right and 12 cm to the left, without chest expansibility changes. In July 2008, an MRI has shown signs of bone edema in vertebral angles in L_3 and L_2 and degenerative disk changes in L_4-L_5 and L_5-S_1, without evidences of disk protrusions. After negative epidemiological evaluation for Tb, non-reactor PPD and normal chest X-rays, we started with subcutaneous anti-TNF agent adalimumab (40 mg/dL) with marked pain relief after 4 infusions. Until April 2011 he continued with clinical remission, seldom needing NSAIDS. In May 2011 inflammatory low back pain worsened with frequent night awakenings and ibuprofen (2800 mg/day) and continuous paracetamol (3 g/day) were reintroduced. Two weeks later, and without clinical improvement, codeine (90 mg/day) was associated and has decreased the number of night awakenings with severe morning stiffness and partially relieved pain during hydrogymnastic which worsened after physical activity interruption. Laboratory tests have not shown inflammatory activity worsening, with PCR 0.6 mg/dL and BASDAI 6.3. MRI dated June 2011, in T_1 and T_2 sequences with fat suppression, did not show bone edema, but only degenerative changes. Although discussing the change of the anti-TNF agent as a therapeutic possibility, duloxetine was introduced in the initial dose of 30 mg/day, which was increased to 60 mg/day one week later. Six weeks later, patient came back with marked low back pain improvement, BASDAI 3.2 and normal PCR. In August 2011, weak opioids were withdrawn and ibuprofen was reduced to 1200 mg/day. Patient is now under common analgesics, NSAIDS and 60 mg/day duloxetine.

Case 2: Male patient, 33 years old, with AS since he was 22, HLA-B27-negative. He came to the service with severe axial sequelae and skier posture, progressive inflammatory low back pain worsening and spinal ankylosis, reporting gastric intolerance to NSAIDS, without eye and skin complaints. Patient was under irregular use of solfasalazine (1 to 3 mg/day) without clinical improvement. For having highly altered metrics (tragus-wall ratio of 15 cm and Shöber index 0), BASDAI 7.3 and PCR 1.29 mg/dL by untrasensitive method, anti-TNF agent was introduced. Patient has no history of contact with tuberculosis and chest X-rays were normal, however PPD was a strong reactor with 25 mm of induration area. Chemoprophylaxis with isoniazid was started until anti-TNF could be introduced, in addition to paracetamol (3 g/day) associated to tramadol (150 mg/day). There has been intolerance to tramadol and duloxetine was started at 60 mg/day, divided in two doses and associated to paracetamol. Three weeks later patient presented significant pain improvement: BASDAI 4.2 with visual analog scale for spinal pain of 3.2.

DISCUSSION

Both patients have long evolution disease and major symptom for both was inflammatory low back pain, however just patient 2 had spinal fusion with typical bamboo aspect and patient 1 may be considered as having spondylitis without radiographic ankylosis.

Neurological complications are described in 2.1% of AS patients[12] and since none of our patients had neurological changes, low back pain was considered not neuropathic.

To evaluate disease clinical improvement and activity, inflammatory activity tests, such as PCR and VHS are commonly used and in the last decades other tools have been standardized to evaluate new drugs. BASDAI questionnaire (Bath Ankylosing Spondylitis Disease Activity Index) was used to evaluate duloxetine efficacy, which is currently considered one of the most important tools for clinical essays[13,14], with six questions addressing domains related to fatigue, spinal pain and joint symptoms, and pain due to entheses involvement, and two questions related to morning stiffness quality and quantity.

Score is measured by VAS from zero to 10 (zero = good; 10 = bad). BASDAI values above 4 indicate presence of disease activity. Anti-TNFα drugs are clinically effective for inflammatory low back pain and improve parameters such as BASDAI and BASFI[15,16], however they are very expensive and have major immunobiological adverse effects such as severe infections (especially disseminated tuberculosis), demyelinating disorders, worsening of congestive heart failure, appearance of systemic lupus erythematosus autoantibodies and hypersensitivity reactions.

Due to these problems, antidepressant drugs such as duloxetine may be useful as adjuvant therapy to treat inflammatory low back pain. Due to its low cost as compared to the cost of biological molecules, duloxetine may be used even before anti-TNF agents. Both patients had clinical indication for anti-TNF agents, however only patient 1 has used the biological drug before duloxetine. Patient 1 was refractory to pain during biological treatment and patient 2 used duloxetine before the anti-TNF agent. Both remain with good clinical lumbar pain control to date.

These reports evidence that duloxetine is an indication for chronic inflammatory low back pain in AS patients with or without indication for anti-TNF agents, however such results should be carefully interpreted. Controlled placebo studies are needed to evidence the efficacy of duloxetine and other antidepressant drugs on inflammatory low back pain of AS patients.

CONCLUSION

Duloxetine was effective to decrease chronic inflammatory low back pain intensity in ankylosing spondylitis patients.

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