Tapentadol extended-release as a therapeutic strategy for pain control in cases of osteoarthritis. Case reports

Tapentadol de liberação prolongada como estratégia terapêutica para o controle da dor em casos de osteoartrite. Relato de casos

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ABSTRACT

BACKGROUND AND OBJECTIVES: Osteoarthritis affects many individuals worldwide and is caused by multiple factors that lead to joint wear and tear, inflammation and, consequently, chronic pain that is difficult to treat. It is predominant in seniors, but not restricted to older age groups. Pain reduction is prioritized when facing crises, so that rehabilitation work and postural corrections can be applied later. The present study aimed to evaluate the analgesic potential of tapentadol extended-release (ER) in three patients with osteoarthritis who had undergone numerous previous treatments and had a history of moderate to severe chronic pain.

CASE REPORTS: Three women, aged 49, 75 and 86 years old, diagnosed with osteoarthritis, with complaints of severe pain and who had undergone numerous therapies including drug use, without significant pain control were included in the study. The use of tapentadol ER was recommended and adjusted to each patient according to the intensity of pain. All of them responded satisfactorily and returned to their daily activities. One of them presented nausea after two days of tapentadol use, which was controlled with an antiemetic drug only during the two days of nausea

CONCLUSION: Tapentadol ER was effective in controlling pain from osteoarthritis in the three cases evaluated, without serious adverse effects. The period and dosage of tapentadol ER must be in accordance with the clinical evolution of each patient.

Keywords: Analgesia, Case reports, Chronic pain, Osteoarthritis, Tapentadol.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A osteoartrite afeta muitos indivíduos em todo o mundo, é causada por múltiplos fatores que conduzem ao desgaste articular, a inflamações e, consequentemente, a dores crônicas de difícil tratamento. É predominante em idosos, mas não restrita às faixas etárias mais elevadas. A diminuição da dor é priorizada diante das crises, para que trabalhos de reabilitação e correções posturais possam ser aplicados posteriormente. O presente trabalho teve por objetivo avaliar o potencial analgésico do tapentadol de liberação prolongada (LP) em três pacientes com osteoartrite que já haviam passado por inúmeros tratamentos prévios, com histórico de dor crônica de moderada a intensa.

RELATO DOS CASOS: Três pacientes do sexo feminino, com idades de 49, 75 e 86 anos, diagnosticadas com osteoartrite, com queixas de dor intensa e que haviam passado por inúmeras terapias e uso de fármacos, sem controle significativo da dor. O uso do tapentadol LP foi recomendado e ajustado a cada paciente conforme a intensidade da dor e todas elas apresentaram resposta satisfatória e retomaram suas atividades diárias. Uma delas apresentou náusea após dois dias de uso do fármaco, que foi controlada com um fármaco antiemético somente durante o período de dois dias de enjoo.

CONCLUSÃO: O tapentadol LP foi efetivo para controlar as dores decorrentes da osteoartrite nos três casos avaliados, sem efeitos adversos graves. O período e a dose do tapentadol LP deve considerar a evolução clínica de cada paciente.

Descritores: Analgesia, Dor crônica, Osteoartrite, Relatos de casos, Tapentadol.

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HIGHLIGHTS

- Chronic pain as a result of osteoarthritis is highly present in the population, is caused by multiple factors and must be comprehended and treated safely.
- Tapentadol ER apparently is effective to manage chronic pain associated to osteoarthritis and seems to be safe in different aged individuals. Each patient must be examined carefully and the dosage adjusted according to the patient's perception of pain. In the present case reports, tapentadol ER (100mg every 12 hours) was maintained for the three patients due to the beneficial response of pain control, no important adverse effects and recovery of daily activities.

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INTRODUCTION

Osteoarthritis is the progressive degeneration of joints and is mainly associated with aging, although it is also related to obesity, repetitive motion, and strenuous, high-impact exercise[1-3]. Both a sedentary lifestyle and excessive and improper use of the joints can result in a progressive process of joint wear. Genetic predisposition, inflammatory processes, bone malformations and falls, which cause bone misalignment and alter the contact areas between the joints, are also factors that favor the appearance of the disease[4]. In addition, osteoarthritis is more common in women due to changes in bone metabolism after menopause[5].

It is estimated that hundreds of millions of people in the world live with osteoarthritis[6], being more common in Europeans and North Americans than in Asians, Africans and Jamaicans[7], although obviously the lifestyle of each individual affects his or her risk of developing the disease. Although irreversible, its evolution can be controlled with movement adaptations, non-impact exercises, surgery, intra-articular therapies, and other strategies that maintain the functionality of movement. However, pain control must be the primary target[4,7]. In Brazil, the prevalence of osteoarthritis is 33% in individuals over 25 years of age, which leads to an estimate of almost 40 million people suffering from this disease[8].

Chronic pain, such as that caused by osteoarthritis, is very challenging and requires the use of analgesics, anti-inflammatory drugs, and adjuvant drugs, which usually cause significant adverse effects and further impact the quality of life of patients[9].

Tapentadol extended-release (ER) has been shown to be an effective drug for the control of moderate to severe chronic pain in a tolerable manner by patients, although some adverse effects are anticipated[10-12]. Its broad mechanism of action involves both noradrenaline reuptake and affinity for μ-type opioid receptors, thus acting on the neuropathic and nociceptive components that may be present in chronic osteoarthritis pain[10]. Additionally, in pre-clinical studies, evidence of control of visceral and inflammatory pains were also observed after treatment with tapentadol ER, besides the control of neuropathic and nociceptive pains[13].

The mean absolute bioavailability after a single dose of tapentadol ER, considering the fasting state, is approximately 32%. The maximum serum levels of tapentadol ER are observed 3-6 hours after administration. When consumed after a caloric breakfast, the area under the curve (AUC) and the maximum concentration of tapentadol ER raise 8% and 18% respectively. The molecule is widely distributed through the body, with a weak interaction with serum proteins[13,14].

Almost 97% of tapentadol is metabolized in humans and the most important metabolic pathway is the conjugation with glucuronic acid to produce glucuronides. After oral administration, approximately 70% of the drug (55% glucuronides and 15% of tapentadol sulfate) is excreted by the urine in the conjugated form and 3% is excreted in the unchanged drug form[13,14].

To a lesser extent, tapentadol is additionally metabolized to N-desmethyl tapentadol (13%) by CYP2C9 and CYP2C19, and to hydroxy tapentadol (2%) by CYP2D6, which are further metabolized by conjugation. The metabolites are almost exclusively (99%) excreted by the kidneys. Total clearance after intravenous administration is 1530 ± 177 mL/min. The terminal half-life is approximately 4 hours after oral administration of immediate release tablets and 5-6 hours after oral administration of extended release tablets[13,14].

In this study, three cases are described in which tapentadol ER was used as a treatment for chronic pain control of three patients diagnosed with osteoarthritis, with different ages (49, 75 and 86 years).

CASE REPORTS

Case 1: Chronic pain due to rheumatoid arthritis, with more intensity in the knee region

A 49-year-old female patient, accountant, reported pain crises in the right knee through the last ten years, with progressive intensity, already with less range of motion. She had undergone physiotherapy and joint infiltrations with triamcinolone with no improvement. There are no surgery options due to her age, KL grade and due to the lack of previous treatment with a specialist in pain. The patient has rheumatoid arthritis, with less intense pain in the cervical spine, hands, and ankles.

Tapentadol was prescribed due to the level of pain and due to its double effect, which would be ideal for the case associated with neuropathic pain. Tramadol specifically caused nausea and vomiting in the patient and she used methotrexate 25 mg/week; amitriptyline 75 mg/day and dipyrone 2 g every 6h. She quantified her pain at grade 8 by the DN4 questionnaire and grade 3 by the Visual Analog Scale[15]. She has a symmetrical valgus knee, range of motion of knee flexion 5º and 120º with swelling and effusion classified as 50% and moderate crepitus. As well as burning sensation, a twinge and hypoesthesia to needle prick. An MRI scan revealed degenerative changes in the medial meniscus and grade 3 chondral lesion in medial condyle by the ICRS classification. Tapentadol ER 50 mg was indicated every 12h for 7 days and only the arthritis drugs (methotrexate) was maintained. The patient reported nausea for 2 days, controlled with ondansetron, only necessary during the 2 days of discomfort. Her pain perception went down to 7 and the tapentadol ER dose was adjusted to 100 mg every 12 h for 21 days. Her pain perception became 3, with a neuropathic pain score of 4 by the DN4. She started to walk without support, since she used to depend on crutches with partial charge in times of pain crisis. The drug was maintained at the current dose until the next follow-up at 3 months, in conjunction with acupuncture and physiotherapy were recommended.

Case 2: Low back pain and knee osteoarthritis

Female patient, 75 years old, accompanied by her family, with great difficulty in walking and using a walker. She reported pain in the lumbar region and knees for ten years. Her perception of pain by the numerical verbal pain scale was 7 daily and, when in crisis, went up to 9. The pain radiated to the lower limbs, with shock sensation, burning sensation, and paresthesia. She presented mechanical claudication due to knee pain, and neurogenic claudication due to back pain. Obese, with an unbalanced and sedentary diet, the patient has hypertension, diabetes and anxiety, controlled with drugs. She had undergone cataract surgery

and plate fixation after a humerus fracture caused by osteoporosis 5 years ago. The patient reports previous consumption of oral anti-inflammatory drugs over the last ten years to minimize pain, which significantly compromised her renal function (creatinine = 1.2 mg/dL). Although there is a recommendation for surgery on her spine and knees, the patient hesitates. She underwent anesthetic blocks and radiofrequency in the lumbar region and knees, with no pain relief. For three months, she used codeine 60 mg every 6 hours, deflazacort 6 mg/day and dipyrone 1 g every 12 hours, with no improvement. She reports nausea, dizziness, and constipation using codeine. Under physical evaluation, there were no signs of loss of strength nor reflexes, with normal and symmetrical tropisms. Lasègue, Patrick and Gaenslen signs negative. Stable knees, valgus on the right, with limitation of movements, slight joint effusion on the right, with mild phlogistic signs and pain on movement. She presented a score of 5 on the neuropathic pain questionnaire (DN4 = 5). X-ray examination of the lumbar spine indicated decreased disc spaces from L1 to S1, with lordosis rectification and altered axis. Magnetic resonance imaging showed disc protrusion and arthrosis from T11 to S1, with lumbar canal stenosis, with modic I and grade 1 listhesis at L5-S1. On radiography and MRI of the right knee, decreased joint space, osteophytes, and evidence of osteoarthritis were seen. Electromyography indicated mild peripheral polyneuropathy. The patient was therefore diagnosed with low back pain and knee arthralgia due to osteoarthritis. Tapentadol ER 50 mg every 12 h for 30 days was prescribed without the previous anti-inflammatory drugs. The patient was instructed to lose weight, start an acupuncture treatment, physiotherapy, and viscosupplementation in the knees. Due to the COVID-19 pandemic, it was considered convenient to avoid frequent visits to the clinic. On her return, after 30 days of treatment, her pain perception was 5 by the Visual Analog Scale and neuropathic pain was 2 by the DN4. The tapentadol ER dose was adjusted to 100 mg every 12 hours for another 3 months, when perception of pain became 2 and neuropathic pain 1 (DN4=1). She started hydro gymnastics and weight training, no longer needed the walker, and reported no side effects of the drug. A gradual withdrawal was recommended in 30 days, however, the pain started to increase (score 5 by the Visual Analog Scale). The patient received guidance on risks and benefits of knee arthroplasty and lumbar spine decompression. Due to the pandemic of COVID-19 (from July 2021 to April 2022), the patient and family members chose to maintain treatment with tapentadol ER. She has been using the same dose of 100 mg every 12 hours for the past 9 months, doing hydrogymnastics and weight training, with the same pain perception of 2 and score of neuropathic pain of 1, and no adverse events.

Case 3: Bilateral chronic osteoarthritis of the knee

Female patient, 86-year-old, retired teacher, with bilateral osteoarthritis in the knees and indication for arthroplasty 8 years ago, already with functional loss, but hesitant to undergo surgery. She had submitted to several previous treatments such as physiotherapy, hydrogymnastics, Pilates, and joint infiltrations with corticosteroids. She used analgesics (dipyrone), non-hormonal anti-inflammatory drugs, ointments, herbal remedies, and plasters, all of which did not provide satisfactory pain control. Her pain perception by the visual numeric scale was 5 for the right knee and 7 for the left knee. She was positive for neuropathic pain screening (DN4 = 5) in the right knee and (DN4 = 3) in the left knee[15]. She had restful sleep, a balanced diet with adequate macro and micronutrients, no mood swings, and had interrupted acupuncture and physiotherapy sessions due to the onset of the COVID-19 pandemic on March of 2020. She was using pregabalin 75 mg at night, dipyrone 1 g (1 to 2 times a day) and started transdermal buprenorphine 5 mg (5 mcg/h), with partial improvement. On clinical examination she presented bilateral varus of the knees, amyotrophy of the thighs, preserved reflexes and strength, difficulty walking, decreased range of motion, and pain in the bilateral gluteal and bilateral adductor trigger points. X-ray examination revealed bilateral severe osteoarthritis (bilateral Kellgren and Lawrence IV). Tapentadol ER 50 mg was introduced every 12 hours for 7 days. After 7 days, the transdermal buprenorphine was removed, and the tapentadol was increased to 200 mg/day, for more 14 days, when she was reassessed. After this period, the patient's pain perception became between 2 and 3 in both knees, according to the visual numeric scale, with no complaints of adverse effects and tapentadol ER 200 mg was maintained for 3 more weeks every 12 hours. Then, tapentadol ER was reduced to 100 mg for 4 weeks. After this period, she felt well, the pain was controlled, and she even reported to be able to take walks. She is still on tapentadol ER 100 mg 12/12h and pregabalin 75 mg at night. She continues sporadic use of dipyrone (2-3 g/day), but with significant improvement in functionality. The patient underwent physiotherapy treatment since the beginning of the treatment with tapentadol ER.

DISCUSSION

The three cases reported involve complaints of long periods of pain (between eight to ten years) with numerous attempts of pharmacological treatments without success, in addition to rehabilitation procedures and exercises that, although essential, become unfeasible in the face of pain. The patient in case 1, 75 years old, is overweight and has used drugs for a long period and developed renal damage, which reinforces the need for proper guidance to patients about the consequences of being overweight, sedentary, and long-term use of drugs. Many patients resist changes in lifestyle habits, but it is up to the physicians and/or professionals involved in care to emphasize the importance of recovering the functionality of movements so they can live with the disease in the long term, since osteoarthritis has no cure[16,17]. Tapentadol ER has been shown to be effective in clinical studies involving patients with osteoarthritis and has been well tolerated due its dual mechanism of action to control neuropathic and nociceptive pain[11,12,18-20]. In all three cases, the patients were able to respond satisfactorily to the treatment after titration of the drug, going from severe pain (from 7 to 9 on the numerical scale) to mild (from 2 to 3). One of them reported nausea during two days of drug use, and the others did not report any adverse effects. The dosage adjustment was in accordance with each individual perception of pain until it was under control. The adopted

withdrawal procedure was 50% weekly reduction of tapentadol ER until the maintenance of pain control was reached. The use of tapentadol ER has been maintained in 100 mg every 12 hours in all of the patients due to the effective analgesic effect without important adverse events.

All patients recovered their daily activities as well as their rehabilitation activities to control the progression of the disease. Due to the necessity of chronic use of opioids, other non-pharmacological therapeutic strategies must have been attempted before without any success. Once prescribed, such pharmacological therapy, it is important to monitor the patient closely[21]. The follow up period differed through patients since the COVID-19 pandemic was an atypical period that prevented many medical visits.

CONCLUSION

Tapentadol ER seemed to be effective and well tolerated in all three cases with no significant adverse effects. All patients recovered their normal activities with good pain control and were able to associate it with other non-pharmacological rehabilitation treatments.

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AUTHORS' CONTRIBUTIONS

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Data Collection, Conceptualization, Research, Writing - Review and Editing, Validation, Visualization
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