Effect of prolonged-release tapentadol in the management of moderate-to-severe chronic pain in elderly patients. Case reports

Efeito do tapentadol de liberação prolongada no manejo da dor crônica de moderada a intensa em pacientes idosos. Relato de casos

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ABSTRACT

BACKGROUND AND OBJECTIVES: Prolonged-release (PR) tapentadol has demonstrated efficacy, safety, and good tolerability for the management of moderate to severe chronic pain in patients over 65 years of age. The objective of this study was to describe three clinical cases in which tapentadol PR was used as treatment of moderate to severe chronic pain in individuals aged 75 to 83 years old.

CASE REPORT: Two female patients (75 and 83 years old) and one male patient (78 years old) with chronic osteoarticular pain or low back pain of moderate to severe intensities and with functional limitation, who had undergone previous unsuccessful treatments and were functionally limited, underwent treatment with tapentadol PR. Tapentadol PR was associated with considerable improvement of pain in all three patients, leading to greater independence in performing daily activities. In addition, the use of tapentadol PR did not cause any significant adverse effects.

CONCLUSION: Treatment with tapentadol PR seems to be effective and tolerable in the management of moderate to severe chronic pain in senior patients.

Keywords: Analgesia, Chronic pain, Elderly, Tapentadol.

RESUMO

JUSTIFICATIVA E OBJETIVOS: O tapentadol de liberação prolongada (LP) demonstrou eficácia, segurança e boa tolerabilidade para o tratamento de dor crônica moderada a grave em pacientes com mais de 65 anos de idade. O objetivo deste estudo foi descrever três casos clínicos em que o tapentadol de liberação prolongada foi usado como tratamento para dor crônica de moderada a grave em indivíduos de 75 a 83 anos de idade.

RELATO DOS CASOS: Dois pacientes do sexo feminino (75 e 83 anos de idade) e um paciente do sexo masculino (78 anos de idade) com dor osteoarticular crônica ou dor lombar de intensidade moderada a grave e com limitação funcional, que haviam sido submetidos a tratamentos anteriores sem sucesso e estavam limitados funcionalmente, foram submetidos a tratamento com tapentadol LP. O tapentadol LP foi associado a uma melhora considerável da dor em todos os três pacientes, levando a uma maior independência na realização das atividades diárias. Além disso, o uso do tapentadol LP não causou nenhum efeito adverso significativo.

CONCLUSÃO: O tratamento com tapentadol parece ser eficaz e tolerável no tratamento da dor crônica moderada a grave em pacientes idosos.

Descritores: Analgesia, Dor crônica, Idoso, Tapentadol.

INTRODUCTION

In Brazil, chronic pain has a prevalence of 50% in the population over 65 years of age[1,2] and it negatively impacts mobility, autonomy and mental health, reducing the quality of life of affected individuals[3]. Opioid analgesics, although generally prescribed for the treatment of chronic pain of moderate to severe intensity, have their use limited by adverse effects[4], which may be exacerbated in seniors due to physiological peculiarities, drug metabolism and increased risk of drug interactions due to polypharmacy[5].

Unlike pure opioids, whose mechanism of action involves agonism of opioid receptors, tapentadol has a dual mechanism of

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HIGHLIGHTS
- Chronic pain is a highly prevalent condition in senior;
- Tapentadol presents a dual mechanism of action that can be considered an option in the management of mixed chronic pain;
- Tapentadol prolonged-release appears to be effective, tolerable and safe in the management of chronic pain of moderate to severe intensity in seniors.

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action (moderate opioid-receptor agonism and inhibition of noradrenaline reuptake)[6]. The prolonged-release version of tapentadol had its registration approved for the treatment of moderate to severe chronic pain in 2010 and 2011 in Europe and the United States of America, respectively. After being registered in Brazil in 2021, tapentadol PR has been used in the country as an additional option for the control of moderate to severe chronic pain in outpatient settings. Its efficacy and tolerability in individuals over 65 old have been demonstrated in several international clinical studies[6-10].

This article describes three clinical cases in which tapentadol PR was used in Brazil as treatment for moderate to severe chronic pain in individuals aged between 75 and 83 years old.

CASE REPORTS

All the patients are aware that the information obtained from their clinical cases has been registered and can be eventually used for scientific studies and publications. Their personal data are all preserved.

Case 1: Complex osteoarticular pain

A 75-year-old female patient, housewife, with systemic arterial hypertension, diagnosed with depression 35 years ago, overweight, and using an orthosis (cane), reported continuous pain in her hand and knee joints, occasionally associated with edema and heat. She reported a left knee arthroplasty 10 years ago and functional limitation in activities that require walking, besides expressing disappointment with the low effectiveness of previous treatments performed.

Previous treatments included hyaluronic acid joint infiltration in the knees (transient improvement), topical anti-inflammatory for the hands (little improvement), duloxetine (no response), and pregabalin (no response). She also reported intermittent use of oral anti-inflammatory drugs, codeine, and tramadol. She reported dyspepsia and peptic ulcer after the usage of anti-inflammatory drugs and constipation, dry mouth, and nausea after codeine and tramadol.

On physical examination, She demonstrated depressed mood (score 8 on the geriatric depression scale), emotional lability, irritability, impaired mobility, and gait imbalance. She displayed Heberden nodules on her hands and joint deformity in her right knee, with no heat or edema. Pain intensity was 7 by the Visual Analog Scale (VAS) and 1 by the DN4 neuropathic pain questionnaire. Conventional radiological exams showed reduced inter-articular space, subchondral sclerosis and marginal osteophytes.

The patient was prescribed venlafaxine (progression from 37.5 mg to 75 mg in 7 days), tapentadol PR (50 mg) every 12 hours, physiotherapy, and a low impact physical activity program. After 7 days of treatment, the patient reported no physical activity, persistent depressed mood, modest improvement in pain (VAS = 6/10), and no adverse effects from pharmacotherapy. She was then advised to increase the doses of venlafaxine (150 mg, once a day) and tapentadol PR (100 mg, every 12 hours).

Seven days after adjusting the venlafaxine and tapentadol PR doses, the patient reported an improvement in mood, she started doing physical activities, physiotherapy, and also reported improvement of pain (VAS = 3/10), in addition to functional gain. She was advised to continue taking venlafaxine (150 mg/day) and tapentadol PR (100 mg, every 12 hours).

Three months after starting treatment, the patient remained in a good mood, with progressive improvement of functionality and pain (VAS = 2/10). She reported constipation in the first 4 weeks, but osmotic laxatives were prescribed and they had a good therapeutic response. The dose of tapentadol PR was reduced to 50 mg every 12 hours.

At the sixth month of follow-up, she had a flat mood and reported improvement of constipation, return to low-impact physical activities, and willingness to perform activities of daily living. She reported occasional episodes of worsening joint pain, which she managed with local heat, massage, and simple analgesics. It was then suggested to reduce the venlafaxine dose to 75 mg/day and maintain the tapentadol PR dose.

Case 2: Hip arthrosis

An 83-year-old female patient, retired, with hypertension, diabetes mellitus type II and advanced hip arthrosis. She was referred for clinical pain management in preparation for a total hip arthroplasty.

The patient used a wheelchair and reported impossibility of walking due to intense pain in the right hip and buttock region, with pain intensity of 7 at rest and 10 when moving, according to the Verbal Numeric Rating Scale (vNRS). She reported left hip arthroplasty 3 years ago and lumbar spine arthrodesis 15 years ago, in addition to acute myocardial infarction 15 years ago. The patient used paracetamol (500 mg) and codeine (30 mg) every 6 hours for pain management and complained of constipation.

During a physical examination, the patient presented significant contracture of the right buttock muscles, intense pain on palpation of the right trochanteric region and fascia lata. She also presented severe limitation of movement of the right lower limb. The observed changes were not accompanied by edema, paresthesia, hypoesthesia/anesthesia or loss of strength in the lower limbs.

Anesthetic infiltrations with lidocaine in 5 muscle trigger points of the right buttock, as well as lidocaine and corticosteroid deposit in the region of the right trochanteric bursa were recommended as treatment. It was recommended discontinuation of paracetamol and codeine and initiation of pharmacotherapy with tapentadol PR (50 mg) every 12 hours, dipyrone (1 g) every 12 hours, and pregabalin (50 mg) once a day. The use of lubiprostone (24 mcg) every 12 hours for constipation and half a tablet of the association paracetamol (325 mg) + tramadol (37.5 mg) as an analgesic rescue dose (up to 4/4 hours) was also recommended.

Fifteen days after the beginning of treatment, the patient presented pain intensity 4-5 when resting and 8 when walking, according to the vNRS; however, she was not very active due to pain and fear of moving. She used an average of 2 rescue-doses of analgesic a day and presented improvement of constipation. The patient was then advised to increase the dose of tapentadol PR to 100 mg (every 12 hours) and reduce the frequency of lubiprostone use (24 μg, once a day), with maintenance of the other treatments. In addition, a new anesthetic infiltration with

lidocaine was performed in the muscle trigger points of the right buttock and trochanteric bursa.
Fifteen days after the adjustment of the drug, the patient presented significant pain reduction (intensity 0-2 at rest and 3-5 walking on the vNRS). She reported being more cheerful, spending more time out of bed, walking with a cane (without using a wheelchair), and defecating normally (even after suspension of lubiprostone). She used an average of 1 dose of rescue analgesic every 3 days, usually on the days she was on her feet the longest. The patient, whose total hip arthroplasty would occur in 20 days, was oriented to maintain the use of tapentadol PR (100 mg) and dipyrone (1 g) every 12 hours, suspend the use of pregabalin and return after surgery.

Case 3: Chronic low back pain
A 78-year-old male patient, former trader, with diabetes mellitus type II and depressed mood, reported a sudden onset of mild pain in the left hypochondrium 10 months ago. In the last 7 months this condition was associated with significant low back pain, intensity 9 on the visual numeric scale, of the burning type, worse at night, on waking up and on moving.
He also reported weakness, numbness in the lower limbs, and a clumsy gait, confirmed in the physical examination, in which pain was also observed at the compression of the left costal arches and posterior lumbar vertebral apophyses, positive Lasègue's sign on the right and left, and edema of the extremities (+/4+, soft, cold, and painless). His low back pain irradiated to the lower limbs and feet, following a lateral metameric pathway, and improved slightly with the use of paracetamol (500 mg), which he used every 8 hours. Previous treatments included various anti-inflammatory drugs, acupuncture, and physical therapy, with no improvement.
A magnetic resonance imaging of the lumbar spine and left costal arches was brought in for consultation, showing marked osteopenia, bone callus in the left costal arch (8th rib), and extensive extruded central herniated disc (L4-L5), in addition to stenosis of the low lumbar spinal canal (L3-L5).
He was found to have mixed chronic pain syndrome (nociceptive and neuropathic), spinal cord compression syndrome, osteoporosis with high fracture risk, and major depressive disorder. The patient was oriented to start physiotherapy and use duloxetine (30 mg) once a day, denosumab (60 mg) subcutaneously every 6 months, paracetamol (500 mg) every 6 hours and tapentadol PR in the following administration scheme: 50 mg every 12 hours for 5 days, 50 mg every 8 hours for another 5 days and 100 mg every 12 hours on subsequent days and further evaluation in 14 days.
Fourteen days after the start of treatment, the patient reported a significant improvement in pain (pain intensity 4 on the visual numeric scale), as well as greater independence in performing instrumental activities of daily living, moderate improvement in mood, and no adverse effects from the drug (except nausea in the first 3 days). He was instructed to maintain treatment with tapentadol PR (100 mg every 12 hours) and duloxetine (30 mg once a day) for another month.
Forty-five days after starting treatment, the patient showed further improvement in low back pain (intensity 2 on the visual numeric scale) and mood. The tapentadol PR dose was then reduced to 50 mg every 12 hours and duloxetine was maintained. The patient was advised to maintain the physiotherapy sessions.

DISCUSSION

The mechanism of action of tapentadol combines agonism of μ-opioid receptors (highly effective in the management of nociceptive pain)[11] and inhibition of noradrenaline reuptake (also effective in the treatment of neuropathic pain)[12]. This synergistic effect makes tapentadol an effective analgesic in the management of chronic nociceptive, neuropathic, or mixed pain. Because the pharmacologic effect of tapentadol is only partially dependent on conventional opioid mechanisms, sparing mu receptors may limit the appearance of certain adverse effects, such as gastrointestinal toxicities, compared to conventional opioids[11,13,14]. This was in line with what was observed in the cases reported here, with regard to the gastrointestinal tolerability profile.
Particularly important for seniors, the low percentage of binding to plasma proteins (20%)[15] and non-CYP4501-dependent glucuronidation metabolism[16] reduce the potential for drug interactions and facilitate pain management in polymedicated patients. Combined with this, the efficacy and favorable safety profile make tapentadol a good strategy in the treatment of moderate to severe chronic pain in senior patients.
Previous studies in the over-65 population show that tapentadol PR administration was effective and tolerable in the management of moderate to severe chronic nociceptive and neuropathic pain, including pain from chronic osteoarthritis[7,8,10,11], low back pain[8,9,11], musculoskeletal pain in the neck region[11] and diabetic neuropathy[11]. In these studies, the proportion of older adult patients who experienced at least a 50% reduction in pain was 63.6%[10] to 68%[6]. In one of the studies 100% of the patients had at least 30% pain reduction[11].
These results are in agreement with the reports presented here, since patients taking tapentadol PR showed a significant improvement in pain, functional gain, and improved quality of life. It is noteworthy that most patients over 65 years of age evaluated in previous studies reported being satisfied with the results obtained with tapentadol treatment[6-10]. Despite these positive outcomes, administration of any opioid should only be undertaken after a thorough screening of the patient in order to avoid unsafe and inappropriate use.

CONCLUSION

The results presented in the 3 case reports suggested that the treatment with tapentadol PR seems to be effective and tolerable in the management of moderate to severe chronic pain in senior patients.

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REFERENCES

1. Ferretti F, Silva MR, Pegoraro F, Baldo JE, Sá CA. Dor crônica em idosos, fatores associados e relação com o nível e volume de atividade física. BrJP. 2019;2(1):3-7.
2. Dellaroza MS, Pimenta CA, Matsuo T. Prevalence and characterization of chronic pain among the elderly living in the community]. Cad Saude Publica. 2007;23(5):1151-60.
3. Dueñas M, Ojeda B, Salazar A, Mico JA, Failde I. A review of chronic pain impact on patients, their social environment and the health care system. J Pain Res. 2016;9:457-67.
4. Kalso E, Edwards JE, Moore AR, McQuay HJ. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. Pain. 2004;112(3):372-80.
5. Ali A, Arif AW, Bhan C, Kumar D, Malik MB, Sayyed Z, Akhtar KH, Ahmad MQ. Managing chronic pain in the elderly: an overview of the recent therapeutic advancements. Cureus. 2018;10(9):e3293.
6. Kress HG. Tapentadol and its two mechanisms of action: Is there a new pharmacological class of centrally-acting analgesics on the horizon? Eur J Pain. 2010;14(8):781-3.
7. Schwittay A, Sohns M, Heckes B, Elling C. Tapentadol prolonged release for severe chronic osteoarthritis pain in the elderly-a subgroup analysis of routine clinical practice data. Pain Res Manag. 2020;2020:5759265.
8. Mateos RG, Bernal DS, Morera LMT, Ferri CM, Escobar AE. Long-term effectiveness and tolerability of pain treatment with tapentadol prolonged release. Pain Physician. 2021;24(1):E75-85.
9. Freo U, Furnari M, Ambrosio F, Navalesi P. Efficacy and tolerability of tapentadol for the treatment of chronic low back pain in elderly patients. Aging Clin Exp Res. 2021;33(4):973-82.
10. Kern KU, Sohns M, Heckes B, Elling C. Tapentadol prolonged release for severe chronic osteoarthritis pain in the elderly: improvements in daily functioning and quality of life. Pain Manag. 2020;10(2):85-95.
11. Aurilio C. Tapentadol prolonged release in fragile geriatric patients > 70 years with chronic severe musculoskeletal pain: an open-label, prospective, observational study. Eur Rev Med Pharmacol Sci. 2019;23(4 Suppl):40-4.
12. Carter GT, Sullivan MD. Antidepressants in pain management. Curr Opin Investig Drugs. 2002;3(3):454-8.
13. Zannikos PN, Smit JW, Stahlberg HJ, Wenge B, Hillewaert VM, Etropolski MS. Pharmacokinetic evaluation of tapentadol extended-release tablets in healthy subjects. J Opioid Manag. 2013;9(4):291-300.
14. Biondi DM, Xiang J, Etropolski M, Moskovitz B. Tolerability and efficacy of tapentadol extended release in elderly patients ≥ 75 years of age with chronic osteoarthritis knee or low back pain. J Opioid Manag. 2015;11(5):393-403.
15. Tzschentke TM, Christoph T, Kögel B, Schiene K, Hennies HH, Englberger W, Haurand M, Jahnel U, Cremers TI, Friderichs E, De Vry J. (-)-(1R,2R)-3-(3-dimethylamino-1-ethyl-2-methyl-propyl)-phenol hydrochloride (tapentadol HCl): a novel mu-opioid receptor agonist/norepinephrine reuptake inhibitor with broad-spectrum analgesic properties. J Pharmacol Exp Ther. 2007;323(1):265-76.
16. Kneip C, Terlinden R, Beier H, Chen G. Investigations into the drug-drug interaction potential of tapentadol in human liver microsomes and fresh human hepatocytes. Drug Metab Lett. 2008;2(1):67-75.