Effectiveness and tolerability of tapentadol in very elderly patients with assessment of cognitive-behavioral aspects

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Abstract

Pain is a common complaint of the elderly and the prevalence of persistent discomfort increases with aging. Suffering may be underreported as some elderly patients incorrectly believe that pain is a normal process of aging. The aim of this study is to assess the analgesic effectiveness and tolerability of tapentadol in elderly patients with assessment of cognitive-behavioral aspects. During treatment with tapentadol, elderly patients experienced reduced pain intensity and improved physical and mental health.

Introduction

The prevalence of pain increases with each decade of life but pain, though frequent, is not part of physiological ageing.[1] In Italy persistent pain, or pain that lasts more than three months, is related to progressive non-neoplastic pathologies, affects from 40% to 85% of the very elderly population, and 2/3 of cases are caused by musculoskeletal diseases.[2,3] About 60% of older people in the country, and 80% of those residing in long term care facilities, suffer from pain.[3]

Managing pain in the elderly is not an easy challenge.[4] Cure is all the more effective when it takes into account the fragility of these subjects due to a large number of factors, including physical health, cognitive state, psycho-emotional state, functional state, socio-economic condition and lifestyle.[4,5] Further complicating the therapeutic choice is the fact that elderly patients are less tolerant of analgesics, anti-inflammatory drugs, and some adjuvant agents such as tricyclic antidepressants, and the way in which age affects various parameters of drug absorption and elimination, which varies from one subject to another.[5,6]

Tapentadol possesses an original and innovative mechanism of action: an agonist of opioid receptors μ (MOR) and noradrenaline reuptake inhibitor (NRI); both mechanisms of action contribute complementarily and synergically to its analgesic efficacy, demonstrated in various models of both nociceptive and neuropathic pain.[7,8] Furthermore, tapentadol is very safe in relation to the low risk of drug interactions due to reduced plasma protein binding, lack of impact on CYP450 enzymes, the major metabolic pathway through glucuronidation, and the absence of active metabolites.[8]

Aim

The aim of the study was to assess the analgesic effectiveness and tolerability of tapentadol PR (50-250 mg BID) in very elderly patients, with assessment of cognitive-behavioral aspects.

Materials and Methods

Forty patients were enrolled (mean age 78.9 years, SD 5.7, 88% women), with pain intensity greater than or equal to 4 on the numerical rating scale (NRS).

Analgesic therapy using tapentadol PR was begun at a dose of 50 mg twice a day (BID), increased if necessary to 50 mg twice a day up to total daily dose not exceeding 500 mg. The patients were examined upon joining the study (V0), and after 7 (V1), 30 (V2) and 60 days (V3).

Primary endpoints

- Percentage of responder patients, *i.e.* patients with a reduction of pain intensity of at least 30%, at the end of observation, compared to baseline, evaluated using NRS from 0 to 10.

Secondary endpoints

- Assessment of quality of life using the short form-12 questionnaire (SF-12).
- Assessment of cognitive status and functional autonomy was made using the mini-mental state examination questionnaire (MMSE), the BADL questionnaire (basic activity of daily living) and IADL (instrumental activity of daily living).
- Adherence to therapy evaluated by dropout number.

Tolerance assessment

During the observation period all side effects were recorded, specifically for their severity, duration and possible therapeutic measures.

Analysis of the main variable

The main variable, patient responder frequency, was analyzed by evaluating the number of responders compared to the actual number of patients admitted to the study. 95% confidence intervals were reported.

This assessment also applies to those dropout patients for whom an NRS scale is available beyond the baseline; to calculate the reduction percentage the last available survey was used.

Analysis on other clinical parameters

Intensity of pain, detected at intervals called for during the study period, was assessed by analyzing variance for repeated measurements without grouping with multiple comparisons *versus* baseline. The quality of life (questionnaire SF-12) was evaluated by test t for paired samples by comparing the value found at the end of the study with the baseline. Finally, cognitive-behavioral questionnaires (BADL, IADL and MMSE) were evaluated using the Wilcoxon test; also in this case a comparison was performed of the final value with the baseline.

Adverse events were reported in a descriptive manner.

The threshold value used to evaluate the significance of statistical tests is 0.05 (5%).

Results

Within the first 60 days (visit V3) of treatment with tapentadol, 28 patients out of 39 (72%) were responders to therapy (95%: CI 55% - 85%). In the period between the initial visit and the one after 7 days, the intensity of pain diminished by 22%, down from an average value of 7.2 on the NRS scale to an average of 5.6. After 30 days, it decreased by 39% (NRS=4.4) while, after 60 days, the reduction was 58% (NRS = 3.0). The reduction in pain intensity was

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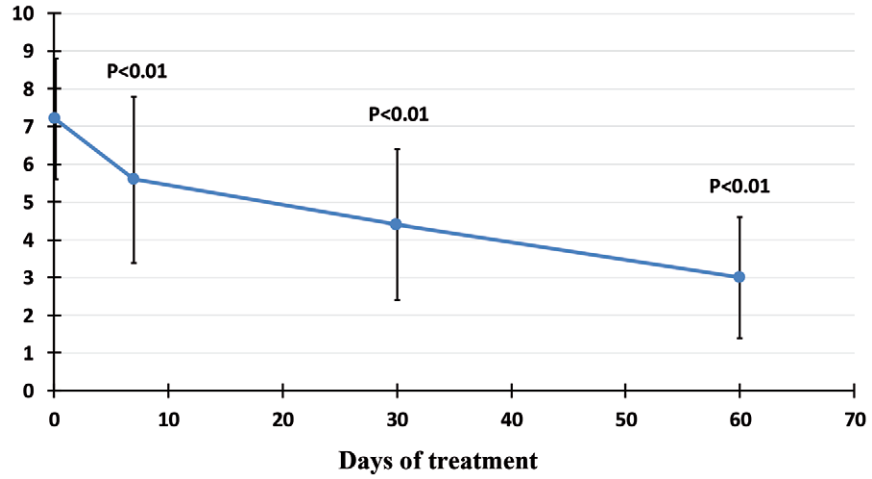

Figure 1. Pain intensity, median ± SD (N=27).

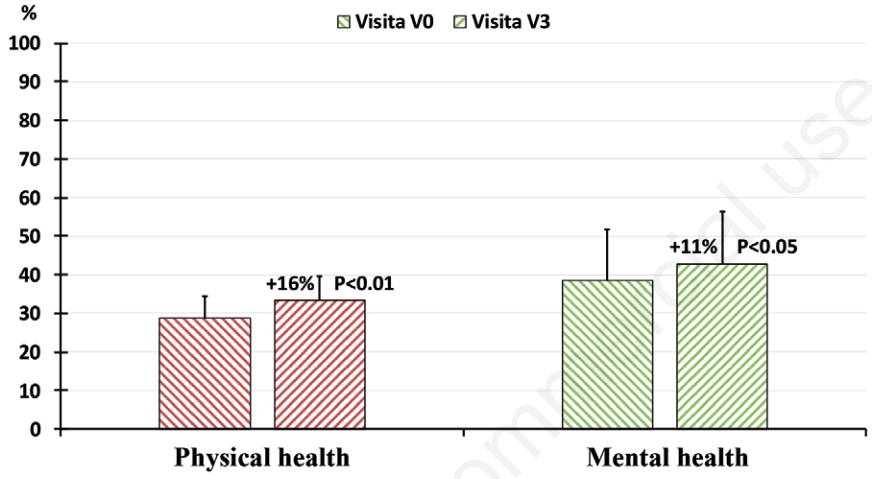

Figure 2. Short form-12 questionnaire median±SD (N=23).

statistically significant for all follow-up visits (P<0.01) (Figure 1).

Physical and mental health improved significantly (P<0.01 for physical health and P<0.05 for mental health) (Figure 2).

No significant changes in functional autonomy and cognitive status were detected during follow-up.

Before the end of the study, 13 out of 40 patients (32%) discontinued treatment with tapentadol; seven suspensions (18%) were due to adverse reactions to therapy while two (5%) occurred as a result of adverse events unrelated to tapentadol. Three patients (8%) decided to suspend therapy while one patient (2%) changed therapy, from tapentadol to ossicodone + naloxone, on the advice of the primary physician.

Besides constipation, a substantially constant side effect (around 30%) and only slightly higher than at the initial visit (22%), 20 side effects were reported by 12 patients (30%): the most frequent were headache, drowsiness, mental confusion and dizziness.

Conclusions

The analysis shows pain in elderly patients was reduced by administering tapentadol. The reduction in pain intensity was associated with a significant improvement in the physical and mental health.

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