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SCIENTIFIC ARTICLE

Morphine as first medication for treatment of cancer pain

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KEYWORDS

Cancer pain;
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Abstract

Background and objectives: the medications used according to the recommendation of the World Health Organization do not promote pain relief in a number of patients with cancer pain. The aim of this study was to evaluate the use of morphine as first medication for the treatment of moderate cancer pain in patients with advanced and/or metastatic disease, as an option to the recommendations of the World Health Organization analgesic ladder.

Method: sixty patients without opioid therapy, with ≥ 18 years of age, were randomized into two groups. G1 patients received medication according to the analgesic ladder and started treatment with non-opioids in the first, weak opioids in the second, and strong opioids in the third step; G2 patients received morphine as first analgesic medication. The efficacy and tolerability of initial use of morphine were evaluated every two weeks for three months.

Results: the groups were similar with respect to demographic data. There was no significant difference between the groups regarding pain intensity, quality of life, physical capacity, satisfaction with treatment, need for complementation and dose of morphine. In G1 there was a higher incidence of nausea ($p=0.0088$), drowsiness ($p=0.0005$), constipation ($p=0.0071$) and dizziness ($p=0.0376$) in the second visit and drowsiness ($p=0.05$) in the third.

Conclusions: the use of morphine as first medication for pain treatment did not promote better analgesic effect than the ladder recommended by World Health Organization, with higher incidence of adverse effects.

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PALAVRAS-CHAVE

Dor oncológica;
Analgesia;
Morfina

Morfina como primeiro medicamento para tratamento da dor de câncer

Resumo

Justificativa e objetivos: Os medicamentos usados segundo a recomendação da Organização Mundial de Saúde (OMS) não promovem alívio da dor de uma parcela dos pacientes com dor oncológica. O objetivo deste estudo foi avaliar o uso de morfina como primeiro medicamento para o tratamento da dor oncológica moderada, em pacientes com doença avançada e/ou metástases, como opção às recomendações da escada analgésica preconizada pela OMS.

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Método: Sessenta pacientes sem terapia com opioide, com idade maior ou igual a 18 anos, foram distribuídos aleatoriamente em dois grupos. Os pacientes do G1 receberam medicamentos segundo a escada analgésica e iniciaram o tratamento com não opioide no primeiro degrau, opioide fraco no segundo e opioide potente no terceiro; os do G2 receberam morfina como primeiro medicamento analgésico. Foram avaliadas a eficácia e a tolerabilidade do uso inicial de morfina, a cada duas semanas durante três meses.

Resultados: Os grupos foram semelhantes quanto aos dados demográficos. Não houve diferença significativa entre os grupos quanto à intensidade da dor, qualidade de vida, capacidade física, satisfação com o tratamento, necessidade de complementação e dose de morfina usada. No G1 houve maior incidência de náusea ($p=0,0088$), sonolência ($p=0,0005$), constipação ($p=0,0071$) e tontura ($p=0,0376$) na segunda consulta e para sonolência ($p=0,05$) na terceira.

Conclusões: O uso de morfina como primeiro medicamento para tratamento da dor não promoveu melhor efeito analgésico do que a escada preconizada pela OMS e houve maior incidência de efeitos adversos.

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Introduction

The prevalence of cancer has increased, with an estimated projection for 2020 of 17 million new cases.¹ This means that there will be an increase in individuals with pain caused by the disease and by treatment.²

The World Health Organization (WHO) developed the analgesic ladder as a guideline for the treatment of cancer pain and recommended the use of nonsteroid anti-inflammatory drugs (NSAIDs) for mild pain on the first, weak opioids for moderate pain in the second, and potent opioids for severe pain in the third step. Adjuvant drugs may be involved in all steps.

In a retrospective study of 1229 patients with cancer pain, the author reports that the analgesic ladder is effective in 71%.³ Many patients do not get adequate pain relief.^{4,5}

Factors related to patients, healthcare institutions and regulatory policies on drug use contribute to the undertreatment of pain.^{6,7} Many patients with moderate to severe pain do not receive analgesics and only 24% of those with severe pain are medicated with a potent opioid. In one study, 32% of patients reported that the discomfort was so great that they preferred death.⁸ Despite the evolution of knowledge about pain, more than 80% of patients with advanced cancer suffer from pain.⁹ In a systematic review, the authors suggest that pain is undertreated in approximately half of patients.¹⁰

Few studies have proposed an alternative to the WHO ladder¹¹ and suggested that opioids are prescribed inappropriately.¹² In a review, the authors suggest that the WHO protocol does not use evidence-based recommendations.¹³ Some authors criticize the restriction of potent opioids for the third step.¹⁴ In a study of 5084 patients, 56% had moderate to severe pain at least monthly.⁸ Better pain control and patient satisfaction could be obtained with the use of potent opioids as first medication.¹⁴

Because of these controversies, further studies are needed. The aim of this study was to determine whether the use of morphine in the first step of the WHO ladder can improve the outcome.

Method

Model

Prospective randomized study.

Participants

After approval by the Ethics Committee and the informed written consent was obtained, the effectiveness of morphine used in the first step of the WHO ladder was investigated in patients with locally advanced and/or metastatic cancer. Patients with difficulty in maintaining clinical follow-up, cognitive impairment and previous treatment with opioids were excluded. The study was registered at [clinicaltrials.gov](#) under number NCT01541124.

Randomization, intervention and evaluation

The patients were divided into two groups with the use of envelopes containing the number of the patient and the group to which he (she) belonged. Patients were included in the sequence by allotment in the visit. G1 patients were treated according to the guidelines of the WHO analgesic ladder and started on the first step, with paracetamol 1 g every six hours (maximum dose 4g/day); in the second step, codeine (30 mg) every four hours (maximum dose of 360mg/day); and morphine 10 mg every four hours in the third step. G2 patients received morphine 10 mg every four hours. Whenever indicated, adjuvant drugs were associated to the treatment.

According to pain intensity, G1 patients switched drug in obedience to the analgesic ladder and G2 patients had adjusted the dose of the analgesic drug. The need for palliative cancer therapy, such as radiotherapy, chemotherapy or hormone therapy, was indicated by the oncologist.

Pain intensity every two weeks by using the visual analogue scale (VAS), quality of life every four weeks through the brief questionnaire of quality of life of the WHO,¹⁵ satisfaction with treatment, physical capacity as assessed by the Eastern Cooperative Oncology Group (ECOG) index,¹⁶ and

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