Review Article

Tapentadol in the Management of Pain in Cancer Patients

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Abstract

Addressing cancer pain requires real analysis and reflection. Successful management of pain through medical therapy requires a balance between effective analgesia and good tolerability, which is often difficult to achieve with conventional opioids. Treatment with tapentadol for oncologic pain results in successful pain relief, good tolerability and improvement in overall quality of life. This indicates that it is also a therapeutic option in pain of oncological origin. The combination of two mechanisms of action, which interact synergistically to produce analgesia, is a promising approach to generate effective analgesics. Tapentadol combines the agonistic activity of the μ opioid receptor (MOR) with the inhibition of noradrenaline reuptake (NRI) and thus provides highly effective analgesia comparable to strong opioids, but with favorable tolerability.

Keywords: Pain; Oncology; Tapentadol

1. Introduction

When a medical oncologist encounters a new patient, he has three main objectives: to increase overall survival, to improve the quality of life and, if possible, to keep the cost reasonable for the patient and for civil society. Often, the oncologist focuses his action on survival and puts well-being, like pain, in second place. Frequently the patient also associates cancer with the presence of pain and feels that he is obliged to suffer. Because of this, both physician and patients frequently disregard pain, neglect and subvert this symptom that has a significant impact on the daily life activities and decreases the ability to tolerate targeted cancer treatments, worsening the prognosis of the disease.

Due to the increasing incidence of cancer, the consequent pain is a major public health problem throughout the world. Several meta-analyzes have revealed a 50% prevalence of pain in cancer patients, and more than 90% of patients present pain in all stages of their illness [1]. Pain in cancer patients is a complex, multidimensional phenomenon with a strong impact on quality of life, posing a challenge for health professionals who deal with it daily. The approach of oncological pain implies to know the bio-psycho-social context of the patient, in order to perceive the changes that emerge there [2].

2. Methods

Review of the literature by searching articles in scientific databases, namely MEDLINE-PubMed, Directory of Open Access Journal (DOAJ). In a first phase, the selection of articles was carried out based on the title and, later, the summaries or complete articles were revised when necessary for the final selection. The search for magazines or the language of publication was not restricted. Descriptive synthesis of the data and narrative analysis of the results were performed.

3. Clinical Evidence of Tapentadol in the Treatment of Cancer-Related Pain

According to the International Association for the Study of Pain, pain is "an unpleasant emotional sensation or experience, associated with actual or potential tissue damage, or described in terms of such harm." It is a unique and individual experience, modified by prior knowledge of an injury that may be existing or presumed, that is, in any situation the pain is what the patient refers and describes. To guide the sequential use of drugs, the WHO (World Health Organization) has developed a four-step analgesic ladder. Pain should be treated according to an ascending scale of drug potency related to its intensity. All medicinal products may be accompanied by other adjuvants, either by the specificity of action in some types of pain or by their indication for the control of adverse effects of opioids. They may also decrease the need for increased dose of opioids, thus favoring a treatment with a lower risk of toxicity. For mild pain, the preferred analgesics are non-opioids, such as acetaminophen, aspirin, and other non-steroidal anti-inflammatory drugs (NSAIDs). In the case of mild to moderate pain, it is necessary to introduce lighter opioids, such as codeine or tramadol, in combination with non-opioids. Finally, moderate and severe pain is controlled by stronger opioid derivatives, such as morphine and fentanyl, with or without the aid of NSAIDs. Opioids are the basis of analgesia management. They are subdivided according to their action into recipients mμ as pure agonists, pure antagonists and mixed agonists / antagonists and according to their duration of action of long and short duration. Morphine is the prototype opioid drug. It is considered the standard for comparison and is mainly used for moderate or severe oncologic pain. Based on the recommendations of the European Association of Palliative Care (EAPC) on opioid analgesics and their undesirable effects, the anesthetic, neurolytic and neuraxial procedures represented on the fourth step of the WHO analgesic ladder were associated with opioid escalation [3].

In addition to the pharmacological approach, there are many techniques which can be used as adjuvants in the sense of providing improved pain relief in cancer patients. Physical activity, relaxation, or acupuncture, among others, are also therapeutic weapons for pain relief [4].

Pain is a common and highly debilitating complication for cancer patients, affecting their quality of life. Like many medical conditions, it is multi-pathophysiological and, therefore, from a theoretical perspective, it can be better treated by drugs that act on multiple mechanisms of action. Tapentadol is a central acting analgesic with two mechanisms of action (opioid agonist and noradrenaline reuptake inhibition), with an improved side effect profile and may represent a significant advance in the treatment of pain in oncology. The efficacy and safety of tapentadol for the treatment of pain was expressed in phase III clinical studies demonstrating that tapentadol provides comparable efficacy to morphine, but is associated with improved gastrointestinal tolerability [5, 6, 7].

In clinical practice, tapentadol is of particular interest, particularly in patients who may have some element of hyperalgesia associated with prolonged treatment with opioids at relatively high doses. Also, in patients with bone metastasis, since the bone pain has been associated with a masked state of hyperalgesia. Thus, it is a therapeutic alternative for pain resulting from bone metastasis.

Because of its characteristics, it was assumed that its use would be associated with a reduction of opioid-related adverse effects, but with analgesic potency equivalent to typical opioid agonists. In contrast to classical opioids, this drug combines two mechanisms of action into one molecule: μ opioid receptor (MOR) binding and noradrenaline reuptake inhibition (NRI). Both mechanisms have been shown to contribute synergistically to the analgesic efficacy of tapentadol, while reducing the typical side effects of opioids, such as nausea and vomiting. This synergistic effect of MOR-NRI may, however, be highly important from a clinical standpoint, since the therapeutic window for the treatment of severe oncologic pain is often limited by the adverse effects associated with the administration of opioids [8].

Given the significant contribution of the non-opioid mechanism of tapentadol (NRI) in the analgesic action, and its low μ-load for the estimated adverse effects, it may be worth considering that it is more accurately called a "strong analgesic" instead of "Strong opioid". The results of a published analysis suggest that for a drug to be a "strong analgesic" it does not have to be a strong opioid and that this distinction is particularly important when considering the side effects of strong analgesics [9].

Comparisons in animal models between morphine and tapentadol show a lower tendency to develop tolerance, presumably due to MOR-NRI action. It has been suggested that tapentadol is the first representative of a proposed new class of MOR-NRI analgesics.

4. Conclusion

The analgesic efficacy of tapentadol was shown to be equivalent to controlled release of oxycodone or morphine, and demonstrated a more favorable gastrointestinal tolerability profile. In addition to pain control, the restoration or preservation of quality of life, particularly in the advanced stages of cancer, needs to be taken into account. Therefore, its use in cancer patients has been shown to be effective with concomitantly good tolerability. Tapentadol

may be considered as a flexible therapeutic weapon to be acknowledge in the treatment of moderate to severe oncologic pain.

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