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Integrative Strategies for Cancer Pain Relief: A Contemporary Review

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Mini Review

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ABSTRACT

Cancer incidence has been increasing in recent years, making it the most prominent disease of our time. Its treatment is as crucial as managing the associated symptoms of the disease. Consequently, numerous research studies on these topics are currently being proposed. Opioids are known to be the primary choice for pain management in cancer patients. However, in some cases, adequate control cannot be achieved with a single medication, leading to the development of combination treatments. In this context, a systematic review was published on the subject of cancer pain, discussing relevant studies and considering all potential interventions for the management of oncological pain. This is, therefore, a mini-review on the same topic, focusing on certain aspects that were not highlighted in the initial publication but are still relevant in promoting further research in the same direction, contributing to the existing body of knowledge.

Keywords: Cancer pain; Pain management; Complementary therapies; Medical oncology; Interdisciplinary research

INTRODUCTION

Cancer incidence has been increasing in recent years, and therefore, it requires new studies and constant updates [1]. In this regard, new research is being conducted, both for the treatment of various types of cancer and for their short and long-term consequences. Among these consequences, one of the most relevant for oncology patients that significantly impacts their quality of life is pain.

For these and other reasons, reviews, meta-analyses, and clinical trials are essential to improve clinical practice and influence the treatment of cancer pain. In this context, the review titled "Treatment of Cancer Pain: A Systematic Review" sought to be the most diverse forms of oncology pain treatment, attempting to demonstrate which are the most current studies and the benefits of the treatments proposed at present [2]. However, due to the quality of the articles and the deficiency in unambiguously demonstrating the effects of medications and analgesic procedures, many studies still struggle to prove the effectiveness of the procedures, even though they may seem appropriate in practice. Some studies that were not included in the initial research but have the potential to demonstrate quality in clinical practice are discussed below.

LITERATURE REVIEW

Studies on cannabinoids have been explored for quite some time, but the results remain controversial. A study on cannabidiol for cancer pain showed a moderate level of evidence for this type of treatment, not only for pain symptoms but also for outcomes such as nausea, increased appetite, improved sleep patterns, and reduced anxiety, although with low evidence [3]. It is still unknown whether cannabidiol has carcinogenic effects when smoked, similar to tobacco, or if it has anticancer effects in addition to its analgesic effects and symptom improvement that justify its use. Further, more in-depth research with a larger population and longer study duration is essential to confirm these effects.

Another study [4], conducted after the production of our article, provides a review of the use of cannabinoids in pain management, including cancer pain [1]. One of the main points mentioned is post-operative pain, where a dose of 5 to 15 mg of Cannador® was introduced, demonstrating pain reduction. However, it was found that the effects are dose-dependent, with the ideal dose for use being 10 mg. On the other hand, medications such as dronabinol and nabilone did not show satisfactory results in this target population. Another medication studied is the THC:CBD extract (Sativex®), which was used for two weeks and significantly reduced pain in cancer patients compared to a placebo, although more side effects were observed. This drug did not demonstrate dose dependency. Another form of administering this drug, *via* oromucosal spray, also used for two weeks, showed a reduction in the pain intensity, as well as improvements in insomnia and fatigue.

Another medication mentioned in this study is Nabiximols®, which, when used for 5 weeks in chronic oncological pain, showed positive results even at moderate to low doses [4]. Its use in oromucosal spray also yielded positive results when used for an extended period of 3 to 5 weeks. Although not used as a first-line or sole treatment for cancer pain, cannabinoids can be beneficial when used as an adjuvant treatment. Additionally, the use of cannabidiol serves not only for pain symptoms but also for other symptoms such as nausea, increased appetite, anxiety reduction, and improved sleep patterns, among others. New studies need to be conducted to provide evidence for its use as an adjuvant treatment and to assess both its positive and negative side effects.

Other studies conducted after data collection have also significantly influenced the literature, particularly those related to physical exercise, as demonstrated in the following studies: A study evaluating the effect of exercise on pain and functional capacity involved 31 breast cancer patients and lasted for 12 weeks, showing benefits in pain

intensity, mood, and sleep [5]. It was also effective in improving flexibility, strength, and increasing patients' VO2. Moreover, fatigue and pain were directly proportional in the exercise group, suggesting a limit to the amount of exercise. The exercises were of three different types: aerobic, resistance exercises, and flexibility exercises. The small sample size affected the evidence in this study, so new studies with larger sample sizes may yield more significant results.

Another systematic review study on this topic showed benefits for all patients with cancer pain, demonstrating effects from small to large in pain reduction [6]. The exception was aerobic exercises when used in isolation, which were not significant. The results were consistent for a specific target audience: women with breast cancer or with two or more types of cancer. Additionally, there was a significant outcome for patients undergoing treatment and after chemotherapy and radiotherapy, but not for cohorts with mixed patients. However, the results were quite controversial, as they depended on the scale used, with one showing the effectiveness of exercise in pain improvement and other not demonstrating benefits (EORTC QLQ and SF-36). There was also a significant improvement in unspecified pain, but no effectiveness in specific pains such as body pain, musculoskeletal pain, and neuropathic pain.

Some medications have also received updates for use in cancer pain, such as tetrodotoxin. A meta-analysis showed an average 30% improvement in pain compared to placebo with the use of 30 µg administered twice daily [7]. This study also demonstrated that the medication is dose-dependent, with the best response at 30 µg. For oncological pain findings, 47% of patients reported pain relief. Side effects were associated with improved quality of life and reduced opioid consumption.

One of the studies [8], added to our review referred to the use of morphine-PGB (pregabalin) or morphine-PL (placebo) combination, demonstrating reduced morphine usage in the groups that combined PGB, along with improvements in sleep disturbances [2].

Another study [9], from the search period, although not added to the review, involving 70 patients compared the use of pregabalin and oxycodone in reducing pain to attempt to decrease the daily opioid dose [2]. It showed that there was no significant difference in the average daily dose of oxycodone until the first month, but there was a reduction starting from the third month. The secondary effects included a decrease in symptoms of nausea, vomiting, and constipation.

Lastly, a review on the complementary therapies found in the initial search, despite the heterogeneity of information and the short intervention time in the studies, revealed interesting findings on the most commonly used therapies. Regarding MR-IGI therapy (progressive muscle relaxation and interactive guided imagery), it achieved relief from the pain symptoms and altered immune system responses, leading to increased activated T cells and natural killer cell activity. As for acupuncture, the results were mixed: some studies showed a significant difference, while others did not demonstrate any differences in its use. However, the studies related to auricular acupuncture appeared to be more efficient. One of them showed a reduction in pain intensity and a decrease in medication consumption. Additionally, they also modulated natural killer cells by releasing nitric oxide, which stimulates the hypothalamic production of endorphins [10].

DISCUSSION AND CONCLUSION

Although acupuncture is one of the most studied complementary treatments for oncology pain, few definitive pieces of evidence are available. The use of this therapy appears to be essential, but with greater care regarding the treatment duration, sample size, and all the symptoms it can improve, in addition to the various application

methods associated with it. Studies require more robust methodology with higher levels of evidence and more specific data on this therapy.

Standard and complementary therapies related to pain in oncology patients are continually being updated. New treatments are tested daily and demonstrate improvements in pain management. It is estimated that even more articles will be produced, particularly related to complementary and adjuvant therapies, as primary opioid treatment is increasingly necessary and effective in managing moderate to severe pain but often insufficient on its own in many cases.

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