

Evidence-Based Standards for Cancer Pain Management

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Abstract

Cancer pain management is the most problematic when found in patients who have a malignant tumor, and represents the most feared consequences for patients and their families. A thorough literature review was conducted using the electronic databases of CINAHL, EBSCO, MEDLINE, and PUB MED, for articles published between 2007 and 2013. We developed quality standards; using a research study, and selected domains based on the framework of the type of cancer pain management into both types of treatment, pharmacological and non-pharmacological cancer pain management, in order to manage cancer related pain through multidisciplinary aspects and holistic approach. Pharmacological and non-pharmacological modalities give the opportunity for effective care to be provided to cancer patients. Also, these techniques may help in reducing pain and it must be encouraged as a part of the holistic cancer pain management efforts.

Key words: Cancer Pain, Pain Management, pharmacological and non-pharmacological cancer pain management.

References

Cancer pain management is the most problematic when found in patients who have a malignant tumor, and represents the most feared consequences for patients and their families (Alexopoulos, et al. 2010). Cancer related pain management remains a challenge in cancer patients, their families, and oncology nurses due to lack of knowledge and assessment of pain which causes inadequate pain management (Winslow, Seymour, & Clark, 2005). However, there is inadequate pain management in different settings, especially in vulnerable populations and in low income countries. (Sydney, et al. 2008).

The most common problem facing cancer patients is bone metastases from lung, prostate, and breast cancer, that causes severe uncontrolled pain and need for multi methods of pharmacological and non pharmacological intervention to manage cancer related pain (Stenseth, Bjornnes, Kaasa, et al, 2007). The prevalence of pain among cancer patients is high worldwide: 64% in patients with metastatic or terminal disease stage, 59% in patients receiving anticancer treatment and 33% in patients who had been cured of cancer (Everdingen, Rijke, Kessels, Schouten, Kleef, & Patijn, 2007).

According to the American pain society if the plan of pain management includes both pharmacological and non-pharmacological interventions, it is considered effective and gives a positive effect on quality of life for patients and their families in order to decrease pain and remove suffering. Health care providers in this situation of performing holistic care have sustained interaction with patients and their families throughout the continuum of cancer care (American Pain Society, 2005). Thus, it is important for health care providers and decision makers to understand the updated knowledge on pain management strategies and relay their clinical services on evidence based practice in order to overcome all barriers to effective pain management among cancer patients, and select the most appropriate method to treat cancer related pain.

The purposes of this paper are to review and analyze the existing research studies on evidence based cancer pain management and to summarize the findings into evidence-based recommendations. Also, this paper is intended to answer the following questions: (1) what are the pharmacological methods that manage cancer related pain in patients with malignant tumor? (2) What is the relative efficacy of current adjuvant (non-pharmacological/non-invasive) physical or psychological (e.g., relaxation, massage, heat and cold, music, and exercise) interventions to help in managing cancer related pain?

Methodology

A thorough literature review was conducted using the electronic databases of CINAHL, EBSCO, MEDLINE, and PUB MED, and COCHRANE DATABASE for articles published between 2007 and 2013. The following key words were used to search the electronic databases: cancer pain, pain management, pain symptoms, pharmacological and non-pharmacological cancer pain management.

Many articles were obtained and reviewed, but only 15 research articles achieved the inclusion criteria for the purpose of this study. The inclusion criteria were the following: (1) it is a research-based study; (2) written in the English language; (3) investigated the cancer pain management; (4) used either pharmacological and nonpharmacological techniques to manage cancer related pain. Based on the inclusion criteria, a total of 15 articles was selected and formed the basis for this review; a total of 14 research studies of randomized control trials (RCTs) and only one systematic review.

RCTs are considered to be the most reliable form of scientific evidence in the hierarchy of evidence that influences healthcare policy and practice because RCTs reduce spurious causality and bias (Schulz, Altman, & Moher, 2010). The articles that were included in this study were quantitative studies randomized control trials (RCTs) that were published in peer reviewed nursing and medical journals.

Countries within which the studies for this review were conducted include the United States, Australia, Canada, China, India, Greece, Egypt and Taiwan. The sample sizes in the 14 studies in this review ranged from 24 to 318 adult cancer patients aged between 18 and 60 years, and randomly assigned.

Finding

We developed quality standards; using a research study, and selected domains based on the framework of the type of cancer pain management into both types of treatment, pharmacological and non-pharmacological cancer pain management, in order to manage cancer related pain through multidisciplinary aspects and with a holistic approach.

Pharmacological Cancer Pain Management

Tetrodotoxin (TTX) is a potent neurotoxin that blocks voltage-gated sodium channels (Lee & Ruben 2008). Tetrodotoxin plays a crucial role in neuronal function under both physiological and pathological conditions, and is used to manage chronic pain conditions (Nieto et al., 2012).

Tetrodotoxin claims to provide effective cancer pain management and it is considered a strong analgesic that is characterized in the prolonged period to manage pain and is used in managing neuropathic pain, and improving the quality of life (Hagen et al., 2008).

Nonsteroidal anti-inflammatory drugs (NSAIDs) are used more effectively to manage cancer related pain when combined with opioids in order to give more effective pain management or to reduce the dosage of opioids that are given to cancer patients. Therefore the WHO ladder has added NSAIDs to step III to manage cancer related pain more effectively (Nabal et al., 2011).

In the study conducted by Mohamed and colleagues (2012) on patients undergoing major abdominal cancer surgery, they investigate the efficacy of intrathecally administered dexmedetomidine combined with fentanyl in control of cancer pain after surgery of 90 cancer patients.

The researcher recruited 90 cancer patients who were randomly assigned to receive intrathecally either 10 mg bupivacaine 0.5% (control group, n = 30), 10 mg bupivacaine 0.5% plus 5 u g dexmedetomidine (dexmedetomidine group, n = 30), or 10 mg bupivacaine 0.5% plus 5 ?g dexmedetomidine and 25 ?g fentanyl (dexmedetomidine= group, n = 30). The findings showed that Dexmedetomidine 5 u g given intrathecally, improves the quality and the duration of postoperative analgesia. It also provides an analgesic which indicates the usage of this drug to reduce pain in patients undergoing major abdominal cancer surgery.

Ketamine is a drug used in the induction and maintenance of general anesthesia. Other uses include sedation in the intensive care unit, especially in emergency cases (Peck et al., 2008). A study was done by Hardy and colleagues (2012) to determine whether ketamine is more effective than placebo when used in conjunction with opioids and standard adjuvant therapy in the management of cancer pain. The researcher recruited 185 participants and used randomized, double-blind, placebo-controlled design. The findings of the study found that ketamine does not have net clinical benefit when used as an adjunct to opioids and standard co analgesics in cancer pain. However current evidence is insufficient to assess the advantage and disadvantage of ketamine as an adjuvant to opioids for the relief of cancer pain.

Bisphosphonates are an antiresorptive medicine, which means they slow or stop the natural process that dissolves bone tissue, resulting in maintained or increased bone density and strength that reduces the risk of broken bones. Bisphosphonate increases bone thickness and lower the risk of fractures (Wong et al., 2002).

A randomized controlled trial was conducted on 256 patients with painful bone metastasis with solid tumors, to compare the effectiveness of the pain management effect of Bisphosphonates on incidence of skeletal-related events (Choudhury et al., 2011). The researcher found that use of Bisphosphonates for 6 months or more lead to significant improvement in relief of bone pain, and supports the effectiveness of Bisphosphonates in providing some pain relief for bone metastases that are the result of cancer spread.

Several advantages to improve quality of life and reduced chronic pain in a patient suffering from cancer related pain is when a combination of two analgesic agents was used. Most cancer types had metastasis properties to pain. (Sima et al., 2012) conducted a study of 246 patients and used a multicenter, randomized, double-blinded, placebo-controlled trial to investigate the efficacy of oxycodone/paracetamol for patients with bone-cancer pain. The researcher found that effective pain management in patients with bone-cancer pain, already on opioids, obtained clinically important, additional pain-control, with regular oxycodone/paracetamol dosing to the plan of cancer pain management.

A randomized controlled clinical trial of 153 women undergoing laparotomy for a gynecologic cancer disorder was used to establish the effect of perioperative patient-controlled epidural analgesia (PCEA) compared to postoperative intravenous (IV) patient-controlled analgesia (PCA) on postoperative recovery parameters after major open gynecologic cancer surgery. Patients were randomized to postoperative IV morphine PCA (control arm) or to postoperative morphine-bupivacaine PCEA (treatment arm). The researcher found that patients in the PCEA group had significantly less postoperative pain at rest on day 1 and during the first 3 postoperative days when coughing compared to the PCA arm ($P < 0.05$). The mean pain score at rest on Day 1 was 3.3 for the PCEA group compared to 4.3 for the PCA group ($P = 0.01$).

Overall, postoperative pain at rest and while coughing in the first 6 days was less in women treated with PCEA compared to PCA ($P < 0.003$). PCEA offers superior postoperative pain control after laparotomy for gynecologic surgery compared to traditional IV PCA. Women requiring major open surgery for gynecologic cancer should be offered PCEA for postoperative pain management if there are no contraindications (Sarah et al., 2009)

On the other hand, in the study conducted by (Yeon et al., 2012) to evaluate the effectiveness and complications of continuous epidural analgesia in terminal cancer patients the researcher found that epidural analgesia was an effective pain management method in patients with terminal cancer stage. (Hong et al. 2008) conducted a study on 40 women with cervical cancer and found that the pain scores at 6 and 12 hours after surgery in the preemptive group were significantly lower than in the control group and preemptive epidural analgesia is a reasonable approach for potentially controlling perioperative immune function

and preventing postoperative pain in patients undergoing cancer surgery.

One hundred and eight cancer patients were included in a study conducted to compare the analgesic and adverse effects, doses, as well as cost of opioid drugs, of supportive drug therapy and other analgesic drugs in patients treated with oral sustained-release morphine, transdermal fentanyl, and oral methadone to manage cancer pain. Opioid escalation index was significantly lower in patients receiving methadone ($p < 0.0001$), although requiring up and down changes in doses. At the doses used, methadone was significantly less expensive ($p < 0.0001$) while the use and costs of supportive drugs and other analgesics were similar in the three groups. No relevant differences in adverse effects were observed among the groups during both the titration phase and chronic treatment. Methadone was significantly less expensive, but required more changes, up and down, of the doses, suggesting that dose titration of this drug requires major clinical expertise (Mercadante et al., 2008).

World Health Organization devised a medication algorithm known as the "3-step analgesic ladder" (WHO, 1986). The medications are required to treat mild cancer pain, non-opioids (acetaminophen, acetylsalicylic acid) and should first be introduced. If pain persists, or if at presentation it is moderate to severe, opioids should be introduced. Initially, "weak opioids" (codeine, tramadol) should be prescribed; if maximum doses are reached, the weak opioids should be rotated to "strong opioids." The strong opioids include morphine, oxycodone, hydromorphone, fentanyl, and methadone.

On their own, the strong opioids have no maximum dose. But it is important to note that, although oxycodone is a strong opioid, dosing for combination products containing both short-acting oxycodone and acetaminophen is limited by the maximum allowable daily dose of acetaminophen. Such combination agents are therefore considered appropriate for step 2 of the analgesic ladder. Although meperidine is considered a strong opioid, it is not used in the cancer pain setting, because consistent use leads to the accumulation of normeperidine in the body and a lowering of the seizure threshold (Inturrisi, 2002).

Non-Pharmacological Cancer Pain Management

Transcutaneous electrical nerve stimulation (TENS) is a non-pharmacological agent, based on delivering low voltage electrical currents to the skin. TENS is used for the treatment of a variety of pain conditions (Bennett et al., 2010).

TENS is applied to the site of bone pain by a medical researcher for a continuous 60 minute period after 2 to 7 days placebo or active, then applied for 60 minutes. The researcher found satisfaction with patient in patients in reduced pain level, and TENS is easy to use, and has most impact on patients at rest or on movement, which application provides more benefit, and which outcome scale best represented the experience of pain intensity and relief of cancer pain.

Controversially (Robb et al., 2007), recruited 41 women with chronic pain following breast cancer treatment, and outcome measures included pain report, pain relief, pain interference, anxiety and depression.

There was little evidence to suggest that TENS or TSE were more effective than placebo. All three interventions had beneficial effects on both pain report and quality of life, a finding that may be due to either psychophysical improvements resulting from the personal interaction involved in the treatment or a placebo response, and concluded the TENS or TSE needs more research to prove the effectiveness of this method in managing cancer related pain in breast cancer.

To effective pain management among health care provider the patients play a crucial role in their pain management team because pain management consists of a multidisciplinary team that focuses on patients who are suffering from cancer related pain. (Chou et al., 2011) the researcher recruited 122 patients to evaluate the effectiveness of a pain education program to increase the satisfaction of patients with cancer and to examine how patient satisfaction with pain management mediates the barriers to using analgesics and analgesic adherence. The experimental group showed a significant improvement in the level of satisfaction they felt for physicians and nurses regarding pain management. For those in the experimental group, satisfaction with pain management was a significant mediator between barriers to using analgesics and analgesic adherence.

It is important for health providers to consider patient satisfaction when attempting to improve adherence to pain management regimes in a clinical setting. Moreover (Thomas et al., 2012) recommended nursing staff use an educational program to manage cancer pain based in this study where patients show more control of pain and reduced demand for opioids to control pain or to reduce side effect of opioids. There is a need for more research on educational programs to manage cancer pain in order to determine the type of intervention that helps patients to manage cancer pain in different types of cancer disease.

The level of evidence for the use of acupuncture and massage for the management of preoperative symptoms in cancer patients is encouraging but inconclusive.

We conducted a randomized, controlled trial assessing the effect of massage and acupuncture added to usual care vs. usual care alone in postoperative cancer patients. Cancer patients undergoing surgery were randomly assigned to receive either massage and acupuncture on postoperative Days 1 and 2 in addition to usual care, or usual care alone, and were followed over three days. Patients' pain, nausea, vomiting, and mood were assessed at four time points. Data on health care utilization were collected. Analyses were done by mixed-effects regression analyses for repeated measures. One hundred and fifty of 180 consecutively approached cancer patients were eligible and consented before surgery. Twelve patients rescheduled or declined

after surgery, and 138 patients were randomly assigned in a 2:1 scheme to receive massage and acupuncture (n=93) or to receive usual care only (n=45). Participants in the intervention group experienced a decrease of 1.4 points on a 0-10 pain scale, compared to 0.6 in the control group (P=0.038), and a decrease in depressive mood of 0.4 (on a scale of 1-5) compared to +/-0 in the control group (P=0.003).

Providing massage and acupuncture in addition to usual care resulted in decreased pain and depressive mood among postoperative cancer patients when compared with usual care alone. These findings merit independent confirmations using larger sample sizes and attention control. (Mehling et al., 2007).

Moreover to compare the efficacy of massage therapy (MT) in control of pain intensity, mood status, muscle relaxation, and sleep quality in a sample (n = 72) of Taiwanese cancer patients with bone metastases the researcher used a randomized clinical trial and found that it was statistically and clinically significant in control of pain among patients and in adding improvements in mood and relaxation over time, this study results support employing MT as an adjuvant to other therapies in improving bone pain management (Jane et al., 2011)

Beaton et al, in their systematic review found strong, high-quality evidence in favor of exercise interventions (aerobic exercises and strength training given alone or as part of a multimodal physical therapy intervention) in patients with metastatic cancer for improving physical and quality of life measures. (Beaton et al., 2009)

Summary and Conclusions

Cancer related pain is still a permanent feared consequence for patients, their families, and health care providers. Thus, they need to be more effective method by a combination of pharmacological and non-pharmacological modalities; by using new methods to manage cancer related pain by providing a new opportunities for the patients to be more comfortable, improve quality of life, die with dignity and respect, and the health care provider needs to pay more attention and have familiarity with, and responsibilities toward these modalities for cancer patients.

The role of non-pharmacological modality in cancer pain management has an increasingly important contribution to provide holistic patient care as co-analgesics. There is evidence to support the use of patient education, cognitive behavioural therapy, relaxation, and music etc. Research on non-pharmacological modalities to cancer pain management is very important and essential.

Regarding pharmacological modality for cancer pain management many research studies recommended use of the WHO step ladder; research studies have shown effective pain management can be achieved in 90% of patients by using the WHO step ladder system. (Barakzoy and Moss, 2006).

Also, ketamine guideline, 2010 provides good opportunities to using ketamine as a third line to manage cancer related pain. (Palliative Care Guidelines: Ketamine in Palliative Care, 2013).

Pharmacological and non-pharmacological modalities give the opportunity for effective care to be provided to cancer patients. Also, these techniques may help in reducing pain and it must be encouraged as a part of the holistic cancer pain management efforts. From this point of view, it should be underlined for the patients and health care providers that these are used together as two modalities of treatment for management of cancer related pain.

Recommendation

From this point of view, it is recommended to use various non-pharmacological methods for pain management but we need more research study results that support the efficiency of these methods. They need to conduct randomized controlled experimental studies, to examine the efficiency of these methods in cancer pain management. Also, it is recommended to use the WHO stepladder for pharmacological modality as a first line to manage cancer related pain.

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