Proceedings of the Pakistan Academy of Sciences 49 (4): 289-294 (2012)

ISSN: 0377 - 2969 print / 2306 - 1448 online

Pakistan Academy of Sciences

Review Article

Pain Management in Cancer Patients: A Review

Wasam Liaqat Tarar*, Sundus Sonia Butt, Fatima Amin and Mariam Zaka Butt

Department of Pharmacy, Lahore College for Women University, Lahore, Pakistan

Abstract: Pain management in cancer patients is a dire need which is often overlooked in the overall healthcare provided by oncologists. This review focuses on revealing the crucial trends and issues on effective pain management. The meta-analyses of previous research studies demonstrate that pain management in cancer patients is often suboptimal and there are many barriers which lead to poor pain management. According to the WHO guidelines there should be scheduled administration of drugs orally on the occurrence of pain, starting with non-opioid drugs such as acetaminophen, NSAIDs or COX-2 inhibitors following mild opioids and later strong opioids. Pain management in cancer patients is often inadequate due to the reasons as poor diagnosis of pain and reluctance of patient to take opioids or report pain. On physician's part reasons are reluctance to prescribe opioids and perceived excessive regulation. Most oncologists must be proficient of managing pain in cancer patients as the guidelines are available. Effective alliance with pain experts and experts on palliative care can also be helpful. There is a need for collaboration in the form of clinical teams including nurses, doctors and pharmacists rather than individual efforts to be involved in managing cancer pain.

Keywords: Pain management, cancer patients, oncologists, opioids

1. INTRODUCTION

A disagreeable sensory and emotional experience which is related with tissue damage either actual or potential, or expressed in terms of such damage is defined as pain. The causative factor of pain in cancer may by the tumor itself or by some medical interventions performed while diagnosing and treating the disease. Pain is divided into two sub-categories. The first category is the sensory input to the central nervous system (CNS) which results in identification of the sensation of pain. Pain is defined to be subjective. The second component is the reactive, subjective component. It deals with the meaning or interpretation of the pain which is in reaction to the first component. The setting in which the pain occurs influences it to a great extent (e.g., more fear may be induced by "crushing" chest pain than by the same pain intensity in any other part of human body). The experiences, behaviours and mind-set of cancer patients also influence it. The reactive component has wide variability from one individual to another [1].

2. PREVALENCE OF CANCER PAIN

Pain in cancer is widespread and its prevalence varies according to the stages of illness. Patients with early disease (48%), patients undergoing cancer treatment (59%) and 64-74% with advanced disease have cancer pain. Most of the time of cancer patients with pain is spent in the community settings until the last days of their lives. Overall, cancer pain pervasiveness in Europe is 72%. Elderly patients and those in care homes are particularly more prone to under-treatment of pain. Primary care teams along with palliative care teams are more likely to initiate and treat cancer pain, but the education of patients, caregivers and healthcare providers is of prime importance for improved patient outcomes [2, 3].

2.1. Age and Cancer Pain

Age is not found to have any correlation with the pain intensity but older patients are found to respond adversely to lower doses of drugs or potency of analgesic drugs in secondary care settings (out-

Received, September 2012; Accepted, November 2012
*Corresponding author: Wasam Liaqat Tarar; E-mail: wasam_tarar@hotmail.com

patient clinics and hospice inpatient units) [4, 5, 6]. A scantiness of research on community based patients having cancer pain is found. Cognitive impairment in older people is associated with greater intensity of cancer pain [7]. Their experience does not differ from younger people as they do not suffer from more adverse effects, and do not need increase in dose or the need for changing opioid [5, 8].

2.2. Pain Assessment Scale

Different categories of pain severity i.e. mild, moderate and severe pain, in terms of their interference with function were identified. Using a 0-10 point numerical scale aforesaid three distinct levels of severity of pain can be defined. 1-4 ratings correspond to mild pain, 5-6 to moderate pain, and 7-10 to severe pain based on extent of interference with cancer patient's performance and activity. It demonstrates that the pain severity-interference relationship is non-linear. There were only slight differences in the specific interference items which pain affects, whereas these cut-points were same for majority of nation-wide samples. The different pain levels are found to be useful in clinical trials, clinical evaluation and also epidemiology [9]. The hospitalized cancer patients report more pain intensity and in many it is under-treated. Patients at community settings have even greater intensity of pain than those in secondary care hence effective strategies for pain management in primary care must be implemented [10, 11] .

2.3. Intensity of Cancer Pain

The patients having moderate pain occurring several times weekly often suffer from moderate-to-severe pain in a month. Many patients receive prescription analgesics and others receive strong opioids either alone or as combinations with milder opioids or NSAIDs. The patients undergoing prescription analgesics therapy still experience breakthrough pain. Many of the cancer patients with pain report difficulties in accomplishing daily life routine activities. Whereas many patients hold that the quality of life is not considered as a priority by their physicians in overall course of therapy. The treatment of pain in cancer is suboptimal as patients are not pain free. The management of pain should be given a prime importance and the pain should not be considered as part and parcel of cancer. The pain treatment guidelines should be revised by healthcare teams for effective pain control in cancer patients [12].

2.4. Concurrent Symptoms

Cancer patients suffer 3.3 symptoms as an average along with pain. These symptoms include anorexia, insomnia, constipation, sweating, nausea, vomiting, diarrhea, dysphagia, dyspnea, neuropsychiatric symptoms, urinary symptoms, dyspepsia, paresis, pruritus, and dermatological symptoms. The occurrence of these symptoms is associated with the site of tumor, intensity of pain, and opioid therapy. The association between symptoms and sex, age, or stage of tumor is not that significant. These symptoms must be addressed to improve patient's quality of life. Only highlighting the pain while treating cancer patients with pain is not going to serve the purpose for patients rather a more global and erstwhile approach is the need of hour for associated symptoms management [13].

3. TREATMENT GUIDELINES

Chronic pain in cancer is treated by opioid analgesics as they are drugs of choice. The dose equianalgesic to the previous opioid should be estimated first when a new opioid is to be started in a patient who has already been treated with opioids. Approximate equianalgesic dose for codeine is 120 mg and for hydromorphine is 2 mg. Patients taking appropriate dose of acetaminophen i.e., 1gm every four hours and still their pain is not controlled then another drug should be started rather than increasing acetaminophen dose. Hepatotoxicity, which is the major adverse effect of acetaminophen is often reported while treating cancer pain with acetaminophen. The dose of morphine varies. Continuous infusion is found to be helpful in patients who require frequent dosing or those who are unable to take medicine orally. Due regard must be given to infusion rates. Many guidelines have come to the forefront for continuous opioid infusions. Methadone should be avoided in elderly patients, patients suffering from severe liver dysfunction and in patients with retarded pulmonary function. Meperidine should be avoided when chronic frequent use is required and in patients

with renal dysfunction. Meperidine can lead to seizures as it's metabolism forms normeperidine which possesses CNS stimulatory activity. Orally administered heroin is same as morphine as it is metabolized to morphine. Parenteral heroin can b given in small volume as it has better solubility than morphine therefore more drug quantity can be delivered. Propoxyphene results in the same effects as all other opioid analgesics. However it is less potent as compared to other opioids, which makes it a suitable candidate to be administered along with non-opioid analgesics [1].

3.1. Effectiveness of Opioids when given Parenterally

It is established that it is easier to control pain by preventing it from recurring rather than treating it when it has recurred as we relate with the words 'precaution is better than cure'. Hence medication on frequent schedule basis is preferred rather than PRN for patients with persistent chronic pain. Also the anxiety level in patient increases as he knows the effect of last dose is to subside and he has to experience pain before the next dose. This aggravates the pain, making it difficult to manage. The parenteral route is more effective for all opoids due to the incidence of first pass effect when given by oral route. The ratio of oral:parenteral effectiveness of morphine is found to be 1:6. Thus, when drug switching from oral to parenteral route is to be done, doses can be made half or reduced to one-third, and when switching from parenteral to oral route, doses can be made double or triple [1].

3.2. Oncologists's Ability

When oncologists are interviewed about their cancer pain management ability they rate themselves high on a numeric scale of 0-10 {median, 7; interquartile range [IQR], 6 to 8}. They rate their peers and fellows as more conservative prescribers compared to themselves as they still follow long-established guidelines. The quality of pain management training conducted in medical school and during residency is rated as 3 and 5 respectively which is not sufficient [14].

3.3. Inadequate Analgesia

There exists a discrepancy in treating patients as the patients at centers treating minorities more frequently suffer from under treatment of pain as compared to other hospital settings. The physician's inability to judge the pain intensity also leads to poor management of cancer pain. Other factor that contribute to inadequate pain management include physicians do not consider the pain to be associated with cancer, better performance status of patients, elderly patients and female patients. Thus, many patients report severe pain even after taking the analgesic therapy. This is pain is severe enough to hinder their daily life activities. The pain management in cancer patients is inadequate till date despite availability of cancer pain management guidelines [16].

3.4. Controlled Use of Opioids

Opioids have been used for the treatment of pain since ages but it has been recently (around past 60 years) brought under controlled use. The legitimate use of opioids is only under the supervision of licensed practitioners. According to current available guidelines the dose escalation and discontinuation of opioid drugs if treatment plan is not being accomplished, is to be carefully monitored. Unfortunately in busy practice settings this is not the scenario. Sometimes higher doses of opioids are being prescribed to cancer patients with chronic pain which is not the result of advanced cancer stage. Earlier there was a misconception that unlimited increase in dose of opioids is safe but now it has been established that unnecessary, prolonged and high dose opioid therapy is neither effective nor safe. Therefore the responsibility lies in the hands of physicians to control the prescribing of opioids even though when patients demand to increase the doses [17].

3.5. Cancer Therapy vs. Pain Therapy

Cancer therapy and pain therapy go hand in hand. The two important factors to be considered are cancer's treatability and cancer's "non pain" pathophysiology (pathophysiology that does not cause pain). Non-pain pathophysiology can give tough time by precluding oral administration of drugs, narrowing a patient's therapeutic index for analgesics, rendering psychologic pain therapies ineffective, and limiting the execution of invasive

pain-relieving procedures. Both cancer therapy and pain therapy exhibit influences on each other. Cancer therapy can hinder pain therapy by exacerbating pain or implicating other adverse effects. On the other hand it can be of help to pain therapy by reducing the proliferation of cancer, lending hand as co-analgesic, and by providing route for IV administration of drugs according to patients needs. Likewise pain therapy can improve cancer therapy by the performance status of patient and surgically performed interventions can help improve organ function [18].

3.6. Use of Multiple Opioids

No single opioid is completely safe. As drugs are only tools, it depends on our expertise how we use them to get the desired therapeutic outcomes. Dose escalation with many co-administered opioids leads to adequate pain relief along with many unwanted side effects in cancer patients with pain. Drug switching from one opioid to another is found to be helpful with no considerable correlation among the genetics and opioid response [19].

3.7. Morphine vs. Oxycodone

When intravenous dosing of two drugs i.e., morphine and oxycodone is compared, it is found that equal analgesic effect is achieved from both drugs. Their bioavailability is pretty much similar, only a little higher for oxycodone hydrochloride. The patients were able to readjust their oral dosings. While the IV dose for oxycodone hydrochloride to produce same amount of analgesia as morphine is 30% higher. Nausea and hallucinations are the drawbacks of morphine use. Otherwise both morphine and oxycodone are similar in their actions and there is no major difference in their side effects [20].

3.8. Spinal Administration of Opioids

The spinal administration of opioids may provide analgesia for longer duration to patients suffering from bilateral or midline lower abdominal or pelvic cancer pain. However, there are certain reasons which make the use of spinally administered analgesics obscure. Cross-tolerance to orally and parenterally administered narcotics is of significance. The rapid development of tolerance to spinal narcotics has also markedly limited their usefulness. Opioids extensively distribute in the CSF and plasma when administered through the epidural or intrathecal route. The drug reaching to brain stem sites may account for many of the toxic and therapeutic effects of spinal opioids [21].

3.9. Use of Benzodiazepines

Benzodiazepines can be used to indirectly manage cancer pain and have been found effective. It is related to their psychotropic effects including reduction of anxiety and depression in many instances. Benzodiazepines can serve the purpose for treating chronic pain, acute muscle spasm and associated anxiety, and neuropathic pain. Alprazolam and clonazepam have been found to be drugs of choice. They should not be always considered as first-line choices even for the above mentioned indications. Their potential benefits are associated with potential harmful effects sometimes such as physical and psychological dependence, cognitive impairment, worsening depression, overdose, and many other side effects [22].

4. BARRIERS TO CANCER PAIN MANAGEMENT

The various obstacles including behaviours which prevent successful management of pain are referred to as barriers. The list of significant barriers includes fear of addiction and tolerance of analgesics, poor assessment of pain, communication barrier among healthcare professionals and patients and some religious and cultural norms which all cumulatively lead to poor pain control. [23] [24] Reluctance of patients to report pain and utilization of analgesics stand at the top of the list. The patients are concerned about the addiction causing factor of analgesics and their side effects. There is also a wrong notion in patient's minds that pain is part and parcel of cancer and 'good patients do not whine about pain'. It should be eradicated from patient's minds. A major percentage of patients including older, less educated and patients belonging to lower income group have these sorts of concerns. Higher pain intensity and under treatment of pain leads to more concerns. [25] Other barriers included in effective pain management are poor assessment of pain, physicians are reluctant to prescribe opioids and perceived excessive regulation. The barriers and

limitation in pain related knowledge and practice norms within the oncology settings have not been duly addressed for past few decades, though cancer pain has been highlighted [14].

5. QUALITY IMPROVEMENT PROGRAMS

Quality improvement programs have been designed and implemented for the treatment of chronic and acute cancer pain. The five basic objectives of QI programs are; unrelieved cancer pain grabs physician's attention by raising a 'red flag', readily providing information regarding analgesics when orders require so, gaining patient's trust that they will be provided analgesic care hence they should report pain, implementing effective policies for the use of new era analgesic technologies, and coordinating and monitoring implementation of aforesaid measures. Though QI approach is helpful in improving patient's satisfaction and also helps identifying many underrated obstacles to optimal pain management, yet it is not an answer and solution to all undertreated pain problems. QI programs are multidimensional in nature and can provide a cornerstone that includes physician and patient education, minimizing errors in drug use process by designing informational tools, and overall improved process of assessing and treating cancer pain [26].

6. KNOWLEDGE AND BEHAVIOURS OF HEALTHCARE PROVIDERS

The knowledge and behaviours of healthcare providers towards pain management in cancer plays a key role in effective management and it varies widely. Nurses possess better pain assessment expertise than do doctors or pharmacists. As nurses are on the bedside of patients and they are more likely to observe changes in behaviour pattern of patients. Doctors have better knowledge of clinical pharmacotherapy. As pharmacists are experts on drugs therefore they have most knowledge about opioids pharmacology and kinetics. As these professionals nurses, physicians and pharmacists possess expertise in many areas they also lack sufficient skills in few areas. These comparisons help us identify the need for collaborative clinical teams instead of individual efforts to be involved in managing cancer pain [27, 28].

7. CONCLUSIONS

Drug therapy is the key to management of pain in cancer patients. Despite the availability of guidelines for pain management, many cancer patients still experience considerable pain and receive insufficient analgesia. Pain relief in cancer patients is often inadequate and suboptimal. This can be accredited to many reasons; pain is not given priority in overall healthcare, lack of education, inappropriate pain assessment and the appropriateness of opioid therapy i.e., restricted use of strong opioids among health care providers, patients, and patients' families. There is a right away need of effective methods of training oncologists and holding them accountable for their actions and ample pain relief. Most oncologists should be able to control cancer pain in the majority of the patients with cancer. There should be alliance with pain experts in relieving pain and implementing modern analgesic technologies. Improving the pain management in cancer patients can benefit hundreds of patients and their families. It will also provide a model for better healthcare of the even larger number of patients who have undertreated pain due to diseases other than cancer.

8. ACKNOWLEDGMENTS

We express gratitude to our Head of Department, Dr. Hafeez Ikram, for his kind guidance. We also express profound appreciation to our honorable teachers for their thoughtful guidance and sagacious advices. We are greatly indebted to our parents for their continuous support, encouragement and supplications at all stages.

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