REVIEW ARTICLE

Drug Use for Pain Management in Cancer Patients

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ABSTRACT

Cancer pain management is a multidisciplinary effort, where the use of drug is often greatly beneficial for the patient. Pain assessment using the visual analog scale (VAS) is very helpful. Mild pain can be managed using acetaminophen or non-steroid anti-inflammatory drugs (NSAIDs). Moderate pain can be treated using mild opioids, while severe pain is treated using strong opioids such as morphine. Administration of morphine is safe, with a dose that is titrated to reach the optimal dosage, and does not produce serious side-effects. Administration of laxatives to prevent constipation should commence since the first administration of morphine.

Keywords: Cancer pain, Drugs, Opioid, Morphine

INTRODUCTION

Pain relates to a discomfort sensation and a person's emotional experience associated with actual or potential tissue damage. Cancer pain is usually chronic, and over 90% of cancer pain can be treated with drugs. Only a small percentage of cancer pains cannot be treated with drugs, in which other modalities such as block anesthesia, nerve incision, radiation, etc., are used.

A third of all new cancer cases are accompanied by pain, and during advanced stages of cancer, approximately 70% of cases suffer from pain. Nuhonni SA from Dharmais Cancer Hospital reported that in home care patients, 68% had pain as a problem, aside from other problems.

Cancer pain is generally classified into 3 types: neuropathic pain, somatic pain, and visceral pain, and is thus managed according to each pathophysiology. It is not uncommon to find a combination of the three types of pain. Thus, pain assessment becomes crucial and greatly support the success of pain control.

Cancer pain is often undertreated, due to the following reasons:

- Patients often prioritize cancer-related complaints, thus disregarding pain
- Pain is often only stated when the patient is asked
- Physicians are generally scared of administrating opioids due to lack of knowledge on the types and dosage
- There is also a lack of understanding in the patients and their family, making them fear morphine.

PAIN MANAGEMENT

Pain management is a multi-disciplinary effort, where various fields are involved, all in accordance with the problem at that point. In general, cancer management is divided into 2 parts: non-drug pain management and pain management using drugs. Non-drug pain management includes the following:

- Anesthetic block
- Nerve incision
- Radiotherapy
- Physiotherapy
- Psychotherapy
- Etc.

These modalities are not discussed in this paper.

DRUG USE FOR PAIN MANAGEMENT

Up to now, the WHO stepladder has been still the gold standard for cancer pain management. To facilitate pain assessment, there are various pain assessment tools, one of which is practical and simple to understand Visual Analog Scale (VAS), with a 1-10 scoring. The scores are interpreted as follows: scores 1-3 mild pain, 4-6 moderate pain, 7-10 severe pain.

The treatment recommended by the WHO follows the following order:

First step: for mild pain, administer acetaminophen or NSAIDs with or without adjuvants.

Second step: for mild to moderate pain, administer mild opioids accompanied with acetaminophen or NSAIDs with or without adjuvants.

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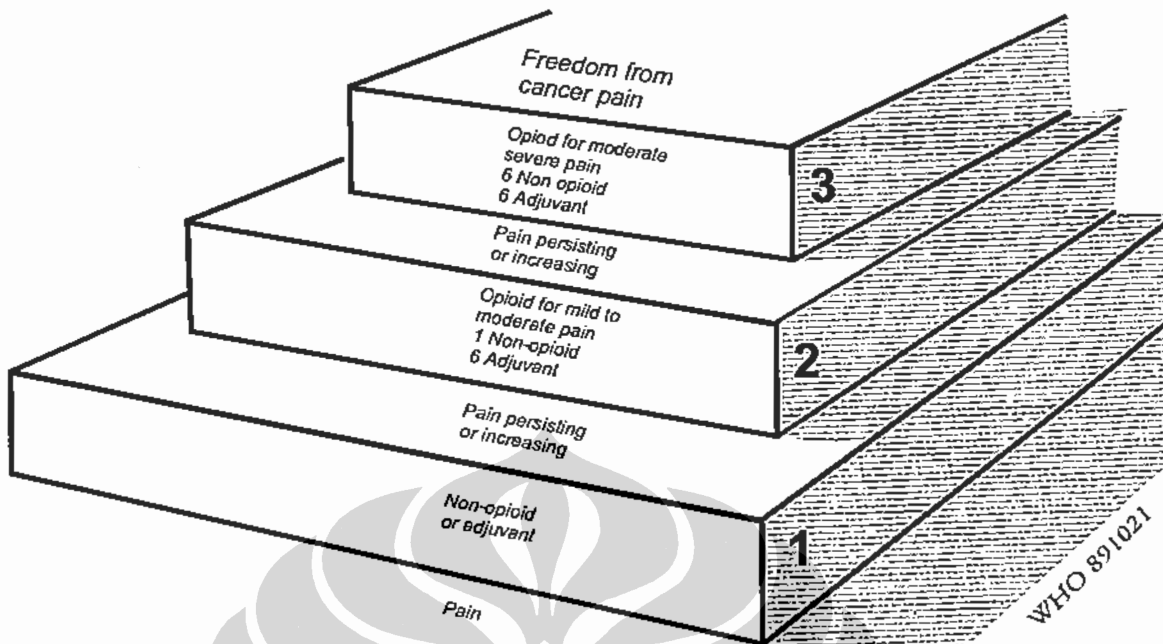

Figure 1. The WHO Step Ladder Guideline for Pain Management

Third stage: for moderate to severe pain: administer strong opioids accompanied with acetaminophen or NSAIDs with or without adjuvants.

The WHO also recommends the following efforts for cancer pain management:

1. Oral administration
   Oral administration is effective, inexpensive, and efforts should be made to administer drugs orally if possible. This is a simple way to regulate drug titration, and should thus be prioritized.
2. Around the clock
   Patients should receive painkillers around the clock (during the whole day) with the same method or with the use of sustained release preparations.
3. By the ladder
   The type of painkillers used should correlate to the degree of pain, using the WHO stepladder as a guideline to optimize pain management.
4. Individualized
   Each patient should receive individualized treatment. Each patient requires different doses and/or interventions to reach painlessness.
5. Attention to detail
   The results of treatment and drug side effects in each patient should be carefully monitored during treatment. The WHO has taken an initiative to take aggressive action against pain. Physicians have been recommended to administer individualized cancer treatment for each patient, and that most cancer pain can be controlled with opioids.

Recently, a practical guideline for cancer pain management has been released. The need for continuous pain assessment and re-assessment should be emphasized. The guidelines are drug specific, and dosage depend on the severity of pain. For moderate to severe pain, short-acting opioids are recommended for initial treatment. The duration of administration should be tailored according to assessment results, and so should changes in dosage. In addition, continuous treatment should include assistance in educational activity and psychosocial support. Side effect prevention should also receive attention. Even though these guidelines have been validated, they state more specific and clear medications for various levels of pain.

DRUG USE

A. Non-opioids

1. Acetaminophen or salicylates
   For mild pain, the recommended dose is a maximum of 600 mg administered every 4-6 hours. For moderate pain, codein is usually added. The side effects of this drug should receive attention, and so should doses that can affect the liver and the kidneys.
2. Non-Steroid Anti Inflammatory Drugs (NSAIDs)
   There are many drugs in this group, with various strengths against pain. Since these drugs have many side effects, the risk and benefit should be the main consideration. These drugs are particularly used for

pain due to bone metastasis or somatic pain.

B. Opioids

1. Codein

Codein is a mild opioid that is quite effective in treating moderate pain, and is often administered along with Acetaminophen. The maximum dose is 30 mg every 4 hours every day. Administration of laxatives is recommended when using this drug, since constipation may be greatly disturbing for the patient.

2. Tramadol

This is a mild opioid and a relatively new drug that is often used for acute and chronic pain. A reference states that its strength to alleviate pain is almost the same as the combination between codein and acetaminophen. For cancer treatment, a maximum of 600 mg/day may be administered. This drug is not mentioned in the WHO stepladder. It causes less constipation than codein.

3. Morphine

Morphine is a strong opioid and is the main choice for pain that cannot be managed using Acetaminophen and NSAID combinations. Administration of morphine is usually commenced in the case of severe pain or pain that shows no response to prior medications, according to the WHO stepladder.

Morphine is a drug with a high dose tolerance, even to a reported 2 g per day.

Even though many cancer patients suffer from pain, the use of the proper opioid and adjuvant medication can control approximately 75-85% of pain when administered orally, rectally, or transdermally.

Besides the benefits of the use of morphine, its side effects should also receive attention, since many medical professionals such as physicians and nurses as well as patients and their family are afraid of or unwilling to receive morphine. These fears should be dealt with so that people have a better understanding. The dose of morphine used is relatively small, so there is inadequate reason not to increase the dose if the response to treatment has not been achieved. The necessary antidote in case of intoxication is Naloxone.

Morphine can be initially administered intravenously, by drip, or subcutaneously, followed by oral administration of short-acting drugs every 4-6 hours. After the appropriate dose is achieved, we can switch to slow-release morphines administered every 12 hours. Administration of morphine should be tailored according to the patient's condition.

4. Transdermal fentanyl

This is an opioid that is specifically used for patches/ attached to the skin and is slow-releasing, and is thus more commonly used for maintenance, and not for initial treatment. This drug is particularly helpful for specific conditions, such as for patients that cannot swallow and those with poor general condition. This drug usually works for 3 days, and is available in various dosage.

C. Adjuvants

1. Gabapentin

Gabapentin is used as an adjuvant, and is more commonly used in neurogenic pain. The recommended dose is 100 mg three times daily, which can be raised to 300 mg three times daily.

2. Amytriptilline

This drug is greatly beneficial as an adjuvant for all types of pain, particularly for post-trigeminal herpes neuralgia. Since it affects the psychological state of the patient, the commonly used dose is 12.5 mg to 25 mg 2 to 3 times daily.

3. Carbamazepine

This is also commonly used for pain.

4. Corticosteroids

These drugs are also beneficial for pain management, and are particularly used to relieve edema and inflammation. Dexamethasone may be administered at a dose of 10 mg orally, intravenously, or subcutaneously 3 times daily.

5. Biphosphonate

This drug is only used for bone pain or somatic pain.

PRACTICAL GUIDELINES

After the type of pain is assessed, the drugs should be administered according to the severity of pain, where mild pain should receive Acetaminophen, etc. If the pain still cannot be controlled, the patient should be treated according to the following guidelines:

A. If morphine has not been used.

1. Maximum 600 mg of Acetaminophen plus maximum 30 mg of codein every 4-6 hours. If there is a sudden breakthrough pain, 300 mg of Acetaminophen may be administered every 2 hours for a maximum of 14 tablets (300 mg each), or
2. 30 mg of codein every 4-6 hours and if there is sudden pain, add 30 mg of codein, every 2 hours if necessary. Remember to administer laxatives since the initial administration of codein. Anti-vomiting agents are also recommended. After reassessment, if the patient is responsive, administration of the drugs should be continued for maintenance, or switched to sustained release morphine tablets.

If the pain is uncontrollable, strong opioids may be administered, such as 10 mg of oral short-acting morphine every 4-6 hours. And if there is breakthrough pain, 5 mg may be administered every 2 hours if necessary, or 5 mg of intravenous or subcutaneous morphine may be administered every 4-6 hours. If there is a sudden breakthrough pain, 2.5 mg of morphine may be administered every 2 hours.

After the pain is reassessed, if it is still uncontrollable, the dose is increased as much as 30%. Remember to administer laxatives. It is also recommended to administer anti-vomiting agents. If the drug is well tolerated and the pain is still uncontrollable, increase the dose 30%. If the pain is under control, sustained release morphine tablets are recommended. If it is still uncontrollable, reevaluate the possibility for the administration of adjuvants such as steroids, Gabapentin, Amytriptilline, Cabamazepine, etc., or perhaps using non-drug modalities.

B. If morphine has been used.

If the patient still feels pain, determine the dose of morphine per 24 hours. For example, if the patient is receiving 30 mg of morphine per 24 hours, increase the dose to 30% to 40 mg every 24 hours. If there is a sudden breakthrough pain, administer 10% of the 24 hour dose, in this case 4 mg every 2 hours if necessary.

To switch from injected morphine to oral morphine use a 1:2.5-3 ratio. For example, if a cancer patient's pain is controlled with 5 mg of injected morphine every 4 hours, or 30 mg every 24 hours, the drug should be switched to 90 mg of short acting oral morphine every 24 hours, but to avoid tolerance disturbance, the dose is reduced 30%, and 10 mg of morphine is thus administered every 4 hours. Such dose produces good results and is well tolerated. Afterwards, 30 mg of sustained release morphine tablets can be administered every 12 hours. Remember to administer laxatives from the initial use of morphine, since its use can cause constipation, which is relatively difficult to treat.

Continuous assessment should be performed. In cases of mild and moderate pain, assessments should be performed every 24-72 hours, but in cases of severe pain (VAS 7-10), assessments should be made within 24 hours, since the pain should be controlled immediately.

The administration of neuropathic adjuvant drugs such as Gabapentin, Amitryptilline, Carbamazepine, and Corticosteroids should not be combined in one capsule, and should thus be packaged in separate capsules.

CONCLUSION

Cancer pain is a complaint in new cancer cases, and particularly in advanced stages of cancer. Cancer pain management is a multi-disciplinary effort, consisting of the use of drugs and non-drug modalities, involving various fields working according to each expertise. Cancer pain management using morphine is still feared due to a lack of knowledge from medical professionals including physicians. The morphine-phobia needs to be dealt with. Even though cancer pain management is individualized, the guidelines for pain management should be understood, so that administration of painkillers can be adjusted according to the guidelines, to reach the aim of treatment, where cancer patients are free from pain.

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