

Mini Review

An Overview of Current Drug Advancement for Acute and Chronic Pain

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Abstract

This short review focuses on medication for the management of pain along with guidelines for the use of the prescribed medicines. WHO has suggested the pain ladder for the management of the acute and chronic pain. The use of the non-opioid and opioids are reviewed. Also, the use of acetaminophen together with non-selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and COX-2 selective are described. Several other medicines which were originally invented for the cure of other diseases, but now they are well employed for pain treatment. The anticonvulsant, gabapentin and pregabalin are in use for treatment of active pain. In the same way, for the treatment of osteoporosis, calcitonin was initially discovered but now it is in widely use for management of pain. The anesthetic ketamine is also used to treat pain. For the topical treatment, Lidocaine and capsaicin patches are being used to cure the localized pain. The applications of localized patches also help to avoid the maximum systemic adverse effect. Overall several drugs are being used for the treatment of the pain with the multi-component approaches for the acute and chronic pain relief.

Keywords: Pain management; Opioids; Pain ladder; Analgesics

Introduction

It is always a challenging task for a medical practitioner to manage the acute and chronic pain of patients. The people suffering from pain have the higher hurdle in their social, biological, and economical lifestyle. Scientific researchers have adequately handled the pain management issues, and since past two decades, leading improvements have established in this area. On a global impact, acute or chronic pains affect the fundamental social life of a patient and consequently, he might be separated from the main link of human welfare [1]. It has well noted that due to the effect of severe pain, patients are losing their mental stability and become anxious over the time. Usually, chronic pain develops a silent depression in the patient that severely affects the human life in the United States as well as all over the world [2]. In some case, the strength of pain urges the patient for suicidal behavior [3]. Methodological and holistic lines of therapies have much appreciated for pain management for patients who are experiencing either acute or chronic pain or in many cases, both [4,5]. That's why the pain management requires a multidisciplinary approach for its diagnosis and treatment. There are many alternatives available for the clinical treatment of pain, and most of them are on the pharmacological criteria. Conversely, the applications of medications for the pain management are often very confusing and contradictory.

Considering these points, WHO has introduced a pain ladder or analgesic ladder to set guidelines for the pain management. The pain ladder has formerly used for the pain caused by cancer, but now a day's medical practitioners are using this ladder for the management of any pain [6]. The general principle of this ladder is to start medication with the first line drugs for pain management and if pain persists then move on to the second and third line of drugs. According to this set protocol, if the patient is not in severe pain, it is recommended to

start the oral administration of the drug with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) including COX-2 inhibitors for pain relief [7]. However, if the pain still persists due to the expansion of disease, then more efficient treatment will be required. The second line of weak opioid can be used for the suppression of pain, and if it is also inefficient, then the third line of strong opioid can be utilized. The use of a second line weak opioid has continuously debated among the clinical practitioners and researchers due to its long lasting side effects. In Many cases the use of weak opioids lead to higher toxicity and low efficacy profile that may cause to switch over to the strong opioid treatment but sometimes, it is completely unacceptable [8]. Further after the pain relief the dosage of medicine has to be reduced in a revert order of the prescribed dose. Nevertheless, it has found that those patients who are on strong opioid face weak response for the first line of pain management medicine [9].

Results and Discussion

Based on pain ladder, the pain management medications are classified in a specific order. The segregation of these medicines depends on the severity of pain and course of a disease. However, there are many controversies associated with the guidelines of WHO as mentioned in pain ladder treatment [8]. Besides of this, it has been more acceptable for application of pain management and has been adopted by many medical practitioners. By following basic principles, pain medicines have divided into the following categories.

First line: the use of non-opioid analgesics

Acetaminophen (paracetamol): Acetaminophen is used for the mild and moderate pain. It is one of the oldest and highly used analgesics for the cure of controlled pain. This medicine was discovered in 1987, and it is significantly prescribed medicine to treat both the pain and fever [10]. According to the WHO, this medicine

has declared as the most needed medicine for the primary health system. Also, the combination of Paracetamol with the Non-Steroidal Anti-inflammatory drugs (NSAIDs) has proven to be more efficient for the pain relief.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): This class of drugs inhibits the activity of the Cyclooxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2) [11]. COX-1 and COX-2 are the essential enzymes, and these are responsible for the pain and inflammation. Aspirin, ibuprofen, and naproxen are most prominent drugs of this group. These drugs are easily available over the counter in all countries without any prescription. The term nonsteroidal make them separate from the steroids. These drugs are mostly used for pain which is associated with the central nervous system. Extensive developments for this class of compounds are in progress which permits lower the dose of the NSAIDs. The uses of the lower dosage of NSAIDs help to reduced adverse effect.

Second line: the use of opioid analgesics

In this class, there are two types of opioid in use, classified as a weak opioid and a strong opioid. The weak opioid analgesics are often used when the Non-Steroidal Anti-inflammatory drugs (NSAIDs) become inadequate to suppress the pain. The weak opioid consists of codeine and Dihydrocodeine. It has been proved that the weak opioid analgesics are more effective than the paracetamol and NSAIDs. A combination of weak opioid with paracetamol or with NSAIDs has more analgesic efficacy towards the pain [12]. However, due to their effectiveness and toxicity, the use of weak opioids are always a subject of debate in clinical research. The strong opioid includes morphine, hydromorphone, tramadol, buprenorphine, methadone, diamorphine, fentanyl, etc. The strong opioids are ten times more efficient than the weak opioids. The strong opioids are usually used for the relief of severe pain and long-term chronic pain [13]. Both classes of opioids binds with the specific opioid receptor located in central nervous system (brain and spinal cords). Also, they stop the feeling of pain and increase the capacity of tolerance for the pain.

Co-analgesics

The co-analgesics are those drugs which are not traditionally invented for the pain relief, but they have demonstrated high potential for acute and chronic pain. These drugs are highly active as they possess analgesic effect. There are several anticonvulsant drugs such as Gabapentin and Pregabalin which act as an effective pain reliever [14]. Mechanism of action of these drugs are well known, both of these drugs bind with the alpha-2-delta subunit of calcium channel of Central Nervous System (CNS). Additionally, by controlling the calcium influx in neurons, these drugs reduce feeling of pain. Many anti-depressant drugs are being used for the pain management therapies. The mechanism of action of these drugs includes the inhibitory effect on norepinephrine and serotonin pathway to control the pain. The anesthetic drug Ketamine [15] is well familiar with the pain management. The ketamine has shown antagonism towards the glutamate at NMDA receptor to manage the pain. A naturally occurring polypeptide hormone Calcitonin, secreted by the thyroid gland is used for the treatment of osteoporosis and Paget's disease. This hormone is now in the use of treatment for the chronic and acute pain [16]. Furthermore, the utilization of steroids and bisphosphonates are well introduced for the pain management [17,18].

Topical treatments

The pain relievers which can be applied to the skin come under the local pain management. Analgesic cream, rubs, and spray are very standard in this category. Lidocaine [19], called as Xylocaine is an amide local anesthetic. It is used to numb the tissue of a particular area. This is also used for the nerve blocks. The Lidocaine has shown good potential for the treatment of the neuropathic pain. It acts by the suppression of the sodium channels, and it has a better perspective for the treatment of neuropathic pain. However, the application of Lidocaine sometimes shows the systemic adverse effect. To reduce these adverse effects, the development of patches for this medicine has been done. This advancement minimizes the systemic adverse effect of the drug and acts actively to reduce the localized neuropathic pain. The Lidocaine patches are highly recommended for the first line treatment of the localized neuropathic pain. Due to the low side effect, it has recognized as a very safe medication for the elderly patients and patients having diseases like diabetes, postherpetic neuralgia, and allodynia. Similarly, capsaicin is another class of the topical pain reliever. Chemically, it is called as of 8-methyl-N-vanillyl-6-nonenamide and it is abundant naturally in chili peppers [20]. Exposure with capsaicin, generates a burning sensation in the human tissue. The active component of capsaicin binds with the Transient Receptor Potential Vanilloid (TRPV1) subunit located in the peripheral nociceptors which are receptive to heat and acidity. Research for the development of new active component to act as agonist and antagonist for the TRPV1 receptor are in progress for the management of the pain. While the application of capsaicin is painful, first it generates a burning sensation which finally leads to reduce the sensation of pain. The patches of capsaicin have shown high efficacy for the treatment of the postherpetic neuralgia and other chronic pains.

Conclusion

The published literature revealed that the past two decades had witnessed great awareness on the main issues of pain management. There are several reviews which explain the benefits of the guidelines for pain management. However, each pain management therapies involve its pros and cons that are overcome by the time. Cancer pain, the pain after surgery, and postherpetic neuralgia pain are an entire situation to treat. The acute and chronic pains severely affect the social life of patients and their families. The current understanding of the effects of pain on human lifestyle, it is clearly evident that the management of pain has become a fundamental human right. Though significant achievements have been made for adequate pain management of the patients, still, a great need for research and development is required.

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