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Letter to Editor

Auxiliary Pain Killer Drugs: Versatile Medications for Pain Management

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New concepts in our understanding of the mechanisms of pain nociception make it possible management of chronic pain and post operation pain by a variety of non opioid - non steroidal anti inflammatory drugs (NO-NSAIDs) medications. In addition to NO-NSAIDs, several new classes of drugs can be used to manage pain. These NO-NSAIDs include medications that block voltage sensitive sodium or calcium channels, facilitate opening of chloride channels, stimulate the gamma-aminobutyric acid (GABA) system, and modulate N-methyl-D-aspartate (NMDA) receptors [1-2].

Gabapentin was initially present as an antiepileptic agent and then approved for treatment of the pain. The probable Gabapentin's mechanism of action is voltage gated calcium channel blockage. Gabapentin is commonly prescribed for pain control in diabetic neuropathy, post-herpes neuralgia, triple neuralgia, and complex regional pain syndrome. Recently it used in cancer related pain, spinal cord injury and post operation pain in conjugation with NSAIDs and opioids. Prescribing 100 mg Gabapentin preoperatively has a significant effect on patient pain score, in post operation period [2-3].

Pergabaline is another voltage sensitive calcium channel inhibitor that knows as anticonvulsant medication. Pergabaline decrease excitatory neurotransmitters like glutamate and substance P. It has a rapid onset so in combination by other pain killer agents could be prescribed in management of acute sharp pain. Common adverse effects of Pergabaline are dizziness, drowsiness and peripheral oedema [3-4]. We prescribe 75 mg Pergabaline as premedication in our setting, in some cases.

Lidocaine known as a local anesthetic and Mexiletine is an oral Lidocaine congener. Intravenous injection of lidocaine has been used as a diagnostic method for intractable periodic sharp pain such as neuropathic pain. More than 75% of cases are associated with a positive response to it. When the appropriate response is obtained, mexiletine is prescribed orally to maintain the therapeutic effect. Lidocaine has a short-term effect and is not the drug of choice for pain management in our setting [1, 5].

Tri/ tetracyclic antidepressants (TCAs) are known as classic earliest antidepressants. Cyclic antidepressants work by preventing the re-absorption of neurotransmitters like serotonin, norepinephrine and dopamine. They act through NMDA antagonism, sodium, potassium and calcium channel blocking. TCAs also have a strong affinity as antagonists at the histamine, muscarinic and α1-adrenergic receptors. Cyclic antidepressants can be used to treat severe sharp pain

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caused by insulting neurons. TCAs including Imipramine, Amitriptyline, Nortriptyline, Clomipramine and, Desipramine have been shown to be effective in clinical practice on a variety of pain types like; neuropathic pain, cancer pain, migraine, phantom pain and, Fibromyalgia [1, 6].

Carbamazepine is used to prevent and control seizures. This medication is known as an anti-epileptic drug. The main mechanism of carbamazepine effects is sodium channel blockage, which reduce the spontaneous firing of nerve fibers involved in pain nociception. Carbamazepine is used to relieve sub-types of pain like facial nerve pain, trigeminal neuralgia specially. The major adverse effects of carbamazepine include aplastic anemia and agranulocytosis [1-7].

Ketamine is a phencyclidine derivative medication. An essential medicinal property of ketamine is the non-competitive NMDA receptor antagonist. Ketamine interacts with other receptors and channels, including opioid receptors, muscarinic and nicotinic acetylcholine receptors, monoaminergic receptors and, voltage-sensitive sodium channels. Ketamine is used for its sedative- hypnotic effects, analgesic properties and as an adjuvant drug in the perioperative setting. It is prescribed for opioid-resistant pain in palliative care and for untreated chronic noncancerous pain. It can potentially be prescribed to support end-of-life in cancer related pain besides, Ketamine was successfully administered for postoperative pain management. Ketamine reduced postoperative pain scores. In addition, it has significant analgesic benefits for major surgeries involving the upper abdomen and chest. Ketamine has been used to prevent chronic postoperative pain [7-8].

Magnesium sulfate is an inorganic salt with the formula $MgSO_4$. It plays an important role in a variety of physiological processes. Magnesium sulfate has been used in preeclampsia and for the treatment of cardiac arrhythmia and broncho-spasm in asthma. Its amplifying effects on postoperative analgesia have recently been considered. In terms of postoperative pain management, intraoperative magnesium infusion can reduce opioid consumption and pain score in the first 24 hours [8-9].

Dexmedetomidine is a new and highly selective central alpha-2-adrenoceptor agonist has sedative- hypnotic, analgesic, anti-sympathetic and anti inflammatory effects. It could reduce the levels of inflammatory cytokines including interleukin-1 and tumor necrosis factor. It has been shown that dexmedetomidine can reduce the inflammatory responses associated with ischemia and reperfusion injury [10-11].

Dexmedetomidine widely used in general anesthesia, neuroaxial anesthesia, nerve block and postoperative pain management. It has also been used to control chronic pain and drug resistance. Dexmedetomidine is used to treat chronic headaches, neuropathic pain, spastic pains, myofascial pain and, complex pain syndrome also; for multimodal analgesia approach [10, 12].

Lamotigine is used to prevent and control seizures. It categorized as anticonvulsant agents belong to the phenyltriazine class. Lamotigine has several action mechanism although, it known as central sodium and calcium channel blocker. Lamotigine prescribes for pain management in trigeminal neuralgia, neuropathic pain, spinal cord injuries and Complex Regional Pain Syndrome [13].

Topiramate is a drug used to treat epilepsy and prevent migraines and cluster headaches. Topiramate has a multiple mechanisms of action. It is a voltage sensitive sodium channel blocker besides it has GABA inhibitory action. Topiramate work as voltage sensitive calcium channel blocker and antagonist of NMDA receptors. It's used for lumbar radicular pain and neuropathic pain is controversial. Common adverse effects include fatigue, loss of appetite, abdominal pain, tingling and hair loss. [14-15].

Sodium valproate is a drug that is mainly used to treat epilepsy, bipolar disorder as mood regulator and to prevent migraine headaches. Proposed mechanisms of Sodium valproate include affecting Gamma-aminobutyric acid (GABA) levels and blocking voltage-gated sodium channels. Sodium valproate was used for refractory neuropathic pain and fibromyalgia. Neuropathic pain is caused by microscopic nerve damage that is often associated with changes in the central nervous system, and fibromyalgia is associated with complex pain syndrome. However, the efficacy of sodium valproate for neuropathic pain and fibromyalgia is under suspicious moreover, adverse events such as nausea, vomiting, drowsiness, vertigo, and hepatic insult are common with sodium valproate [15-16].

In summary, it can be concluded that there are different groups of drugs with different mechanisms of action that were not initially used to pain management but these drugs showed good analgesic effects in the clinic and some of them controlled acute and neuropathic pain well so; Chronic pain control and perioperation use were also added to prescribing indication of these drugs including Gabapentin, Carbamazepine, Lamotrigine, Mexiletine, Cyclic antidepressants and Magnesium sulfate. Pregabalin, ketamine and Dexmedetomedine are among top priority as an auxiliary pain killer drugs that used in the clinic.

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