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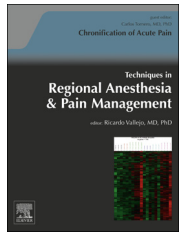

Drugs able to prevent chronic pain

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ABSTRACT

Using drugs that follow anatomical pathways and act on receptors to treat acute pain and prevent its transformation into chronic pain is an appealing idea. The challenge consists of providing personalized treatment based on risk factors, pain and surgery type, and the type of rehabilitation program to minimize complications and optimize the pain treatment to prevent chronic pain. Clinical practice has started to understand the pathophysiological mechanisms and various neurochemical receptors involved in the transformation of acute pain into chronic pain. Unfortunately, the clinical reality differs greatly from the theory and no studies based on medical evidence show that using drugs to prevent chronic pain is a real possibility, nor what kinds of pain can actually be prevented with the use of preventive drugs. This article examines what kinds of pain are most commonly referred to chronic pain centers, looks at which drugs can be used to prevent chronic pain, and aims to establish a preventive treatment algorithm based on the type of postoperative pain. There is growing interest in providing therapeutic patient education, which consists of health professionals transferring knowledge to patients. In the model proposed in this article, therapeutic patient education acts as a connecting thread to different factors and enables patients to become more responsible for and proactive in the healing process. Prevention should be comprehensive, and not just pharmacologic.

Introduction

Using drugs that follow anatomical pathways and act on receptors to treat acute pain and therefore prevent acute pain from becoming chronic pain is an idea that appeals to many physicians. The challenge is to not simply use a magic combination of drugs, but rather the right drugs to treat a specific type of pain and minimize complications. The ultimate goal is to optimize the pain treatment in the hope of preventing chronic pain.

Chronic pain prevention can be based on Hippocrates' dictum "*primum non nocere*." The first step in achieving this is realizing and accepting that acute pain exists. With this in mind, the topic of prevention must be considered.

In 1998, the World Health Organization[1,2] stated that prevention "covers measures not only to prevent the occurrence of disease, such as risk factor reduction, but also to arrest its progress and reduce its consequences once established." On the contrary, the World Organization of Family Doctors[3,4] defined quaternary prevention as "an action taken to identify a patient at risk of overmedicalization, to protect him from new medical invasion, and to suggest to him interventions which are ethically acceptable."

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Clinical practice has started to understand the pathophysiological mechanisms and various neurochemical receptors involved in the transformation of acute pain into chronic pain. Unfortunately, the clinical reality differs greatly from the theory explained in numerous published articles, basic research, and animal research. No studies based on medical evidence show that using drugs to prevent chronic pain is a real possibility, nor what kinds of pain can actually be prevented with the use of preventive drugs, in the way that certain infectious diseases can be prevented with the use of vaccines. The most important result to date is that the more intense and prolonged an acute pain episode, the more likely it would lead to chronic pain.

The scientific literature on drugs able to prevent chronic pain is numerous but often controversial. Some studies show positive results for certain drugs, others have no conclusive results, and several subtly suggest using the drugs that they tested. The first publication on this topic appeared in 1998 and was by Crombie et al.[5] Since then, thousands of articles have been published with the aim of preventing chronic pain.

This article has 2 parts. The first part examines what kinds of pain (potentially preventable) are most commonly referred to chronic pain centers. It then looks at which drugs can be used to prevent chronic pain. The second part aims to establish a preventive treatment algorithm based on the type of postoperative pain.

The pain pathologies in which chronic pain prevention has been more widely studied are complex regional pain syndrome (CRPS), postherpetic neuralgia (PHN), and acute postoperative pain.

Drugs and supplements able to prevent CRPS

CRPS, previously known as reflex sympathetic dystrophy, is one of the most challenging chronic pain conditions. In 1994, the International Association for the Study of Pain introduced the term CRPS to describe a wide variety of posttraumatic neuropathic pain conditions of the limbs.[6] Regarding preventive treatment, it is logical to believe that adequate pain treatment after a fracture can help prevent CRPS, but there is no published evidence to support this.

Vitamin C

Although supplements are not considered drugs, vitamin C reduces lipid peroxidation, scavenges hydroxyl radicals, protects the capillary endothelium, inhibits vascular permeability, and reduces injury to skeletal muscle caused by compartment syndrome.[7-9] Vitamin C also reduces the prevalence of CRPS in adults following trauma.[7-13] The Mayo Clinic recommendation after a wrist fracture is more than 1000 mg/d for 45 days.

The best preventive treatments for CRPS for subsequent broken limbs are therapeutic patient education (TPE) on the role of vitamin C, treatment with gabapentinoids, the use of regular analgesics when pain is mild to moderate, and early mobilization.

Drugs able to prevent PHN

PHN is a painful condition. In some patients, the pain does not resolve when the rash heals, but rather continues for months or years. The pain associated with herpes zoster (HZ) has 3 phases. The first phase is an acute herpetic neuralgia that accompanies the rash and lasts for approximately 30 days after the onset of the rash. The second is a subacute herpetic neuralgia that lasts for 30-120 days after the onset of the rash. The third is a chronic PHN, defined as pain that persists for 120 days after the onset of rash.[14]

There is high-quality evidence stating that oral acyclovir does not significantly reduce the incidence of PHN. In addition, there is insufficient evidence to determine the effects of other antiviral treatments.[15,16]

The Centers for Disease Control and Prevention recommends a dose of the HZ vaccine for people aged 60 years and older.[16] The HZ vaccine is safe and effective in reducing the incidence of HZ and PHN, as well as in attenuating the severity of HZ disease in older adults. The greatest benefit of the HZ vaccine is that it prevents chronic PHN, which can be extremely difficult to treat.[14,17] Nevertheless, evidence that the vaccine can prevent chronic pain has not been clearly established yet.

A better preventive treatment of chronic PHN could be to start in the acute phase with first-line treatments of gabapentinoids and topical lidocaine (patch 5%). Second-line treatments would then include weak opioid analgesics and tricyclic antidepressants (TCAs) if the pain is moderate to severe for the first 30 days after the rash. However, there is no published evidence to support this.

Drugs able to prevent postoperative pain

A publication by the International Association for the Study of Pain defines persistent postoperative pain as pain that develops after surgical intervention and lasts at least 2 months; other causes for the pain must be excluded, in particular pain from a condition preceding the surgery.[18,19]

The most frequent manifestation of neuropathic pain associated with postoperative pain is allodynia (pain due to a stimulus that does not usually provoke pain) and hyperalgesia (increased pain from a stimulus that usually provokes pain).[20]

Preemptive analgesia is defined as an antinociceptive treatment that prevents the establishment of altered central processing of afferent input, which amplifies postoperative pain.[21] The emphasis of preemptive analgesia is on the pathophysiological phenomenon that it should prevent altered sensory processing and its effectiveness has been demonstrated.[22]

To adequately treat chronic pain, we must know what type of pain is present and then start the appropriate treatment of each patient. Unfortunately, there are no epidemiologic studies that allow us to establish which kind of pain (nociceptive, neuropathic, or mixed) is the most frequent for different types of surgery.

The drugs most commonly used to prevent postoperative pain are described briefly in the following section.