An Overview of Pharmacologic Management of Chronic Pain

Benjamin R. Beal, MD, Mark S. Wallace, MD*

KEYWORDS

• Chronic pain • Pharmacologic management • Neuropathic pain
• Intrathecal drug delivery • Nonopiate pain medication • Evidence based

KEY POINTS

- The need to adequately treat chronic pain is widely accepted.
- Proper patient selection is essential for initiation of long-term opiate therapy.
- Multiple alternatives to opioids for treating chronic pain are effective and widely available.
- Intrathecal drug delivery systems can be used both for cancer-related and non–cancer-related pain.

OVERVIEW OF THE PHARMACOLOGIC MANAGEMENT OF CHRONIC PAIN

The treatment of patients with chronic painful conditions can at times be difficult at best. Historically, the opiates were the primary class of medications used to treat patients with both acute and chronic pain. More recently, multiple studies have been published revealing the adverse consequences of chronic opiate therapy in the noncancer population and questioning its safety.[1] This has resulted in an increased interest in nonopiate pain medications currently available for the management of chronic pain.

Pain can be broadly categorized in several ways. However, for the purpose of this article, pain will be broadly categorized into 2 major subtypes: nociceptive pain and neuropathic pain. Nociceptive pain is due to normal activity in neural pathways resulting from actual tissue damage or potential tissue damage as seen with postoperative pain, osteoarthritis-related pain, or mechanical low back pain.[2] Neuropathic pain is pain that results from damage to the nervous system itself, as is seen, for example, in painful diabetic peripheral neuropathy, central poststroke pain, and postherpetic neuralgia.[3] Although many of the therapies mentioned in this article have been shown

Division of Pain Medicine, Department of Anesthesiology, University of California, San Diego, San Diego, CA, USA
* Corresponding author. 9300 Campus Point Drive, MC 7651, La Jolla, CA 92037-1300.
E-mail address: mswallace@ucsd.edu

Med Clin N Am 100 (2016) 65–79
http://dx.doi.org/10.1016/j.mcna.2015.08.006 **medical.theclinics.com**
0025-7125/16/$ – see front matter

to have some degree of efficacy in treating nociceptive pain, the primary focus of this article is on medications used for the treatment of chronic neuropathic pain.

The types of medications used to manage both chronic and acute pain can be broadly classified into 8 major categories: opiates, nonopioid analgesics (primarily nonsteroidal anti-inflammatories), antidepressants, anticonvulsants, cannabinoids, botulinum toxin, topical agents, and intrathecal drugs. The focus of this review is on the more common oral preparations used in the treatment of chronic pain.

CLASSES OF MEDICATIONS

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) affect varying degrees of pain modulation through the inhibition of prostaglandin (PG) synthesis. Prostaglandins are synthesized from arachidonic acid via cyclooxygenase (COX) and have both proinflammatory effects as well as homeostatic effects, which are necessary for the proper maintenance of kidney, gut mucosa, and smooth muscle function.[4] The COX-2 isoform is responsible for synthesizing the proinflammatory prostaglandins and is the target of the newer NSAIDs known collectively as COX-2 inhibitors.[5] The remainder of the NSAIDs nonselectively inhibit both COX-1 and COX-2 to varying degrees.

NSAIDs have been shown to be effective in the treatment of chronic low back pain as well as chronic pain due to osteoarthritis.[5,6] There is also some evidence that NSAIDs are modestly effective in treating lumbar radiculopathy; however, in general, NSAIDs are considered minimally effective in treating other types of neuropathic pain states.[7] Additionally, multiple studies as well as a recent meta-analysis have consistently shown that the addition of an NSAID to a pain management regimen can have an opioid-sparing effect of between 20% and 35%.[8,9]

OPIOIDS

The opioids as a class are medications whose clinical effects are similar in that they cause analgesia, respiratory depression, sedation, and constipation primarily through their action as agonists of the mu opioid receptor. In addition to the mu receptor, the kappa and delta opioid receptors also contribute to the clinical effects, such as respiratory depression and sedation to lesser degrees.[10] The opioid receptors are located centrally throughout the brain and spinal cord, more specifically on primary afferent dorsal horn neurons. High densities of mu receptors are found throughout the periaqueductal gray (PAG) of the midbrain. Agonism of the mu receptor in the PAG is thought to remove a tonic inhibitory gamma aminobutyric acid (GABA)-ergic tone, allowing the PAG to exert its inhibitory effect at the level of the spinal cord.[11] Opioids acting on the dorsal horn neurons inhibit glutamine release, thereby decreasing the transmission of nociceptive information from A-delta and C nerve fibers.[10]

Over the past decade, an increased awareness of the undertreatment of chronic pain has paralleled a significant increase in opioid prescribing.[12] Between 1991 and 2011, opioid prescriptions dispensed by retail pharmacies increased from 76 million to 219 million. With this increase in opioid use by people experiencing chronic pain, the number of drug overdose deaths involving opiate analgesics increased fourfold and the number of admissions for the treatment of opioid dependence has increased to an almost identical degree.[12]

Recent studies have called into question both the efficacy and safety of chronic opiate therapy in the non–cancer-related pain population. Although there is a rather large volume of strong evidence supporting the short-term use of opiates in managing pain, the evidence supporting the long-term use of non-cancer pain is not as