



Radica Stepanović-Petrović

Department of Pharmacology, Faculty of Pharmacy, Belgrade

There are several factors that can cause, perpetuate, or exacerbate chronic pain: diseases that are characteristically painful for which there are presently no cure (arthritis, cancer, migraine headaches, fibromyalgia, and diabetic neuropathy); secondary perpetuating factors that are initiated by disease and persist after that disease has resolved (damaged sensory nerves, sympathetic efferent activity, and painful reflex muscle contraction); and a variety of psychological conditions that can exacerbate or even cause pain.

The main classes of analgesics administered in treating chronic pain are: *opioids; antidepressants; anticonvulsives and local anesthetics*. The long-term orally use of *opioids* is administered for patients with pain due to malignant diseases. For this purpose, it is desirable to use sustained-release morphine, methadone or long-acting levorphanol compounds. Transdermal fentanyl is another excellent option. The pharmacokinetic profile of these drug preparations enables prolonged pain relief, and minimizes side effects such as sedation that are associated with high peak plasma levels reducing the likelihood of rebound pain associated with a rapid fall in plasma opioid concentration. Constipation is a virtually universal side effect of opioid use and should be treated expectantly.

The analgesic effect of tricyclic *antidepressants (TCA)* in treating chronic pain has a more rapid onset and occurs at a lower dose that is typically required for the treatment of depression. TCAs potentiate opioid analgesia, so they are useful adjuncts for the treatment of severe persistent pain such as occurs with malignant tumors. TCAs are of particular value in the management of neuropathic pain such as postherpetic neuralgia, diabetic neuropathy, tension headache and migraine headache. The most frequently used drugs are: amitriptyline, nortriptyline and desipramine. But TCAs may have significant side effects such as orthostatic hypotension, ECG disturbances and arrhythmias, memory impairment, constipation, and urinary retention, which may be particularly problematic in elderly patients, and several are additive to the side effects of opioid analgesics. The serotonin-selective reuptake inhibitors such as fluoxetine and venlafaxine have fewer and less serious side effects than TCAs, but they are less effective for relieving pain.

*Anticonvulsives* (carbamazepine, phenytoin, gabapentin) and *i.v. local anesthetics* (lidocaine and mexiletine) are useful primarily for patients with neuropathic pain.

In conclusion, opioids remain the mainstay of treatment of moderate to severe cancer pain. The potential utility of adjuvant analgesics in the management of cancer pain has grown, especially for those patients whose pain is only partially responsive to opioids. Otherwise, some alternative/adjuvant analgesics possess specific analgesic properties in several types of pain especially neuropathic pain.