

OPIJATNI I ALTERNATIVNI/ADJUVANTNI ANALGETICI

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Hroničan bol mogu izazvati, produžiti ili pogoršati različiti faktori: bolesti koje izazivaju bol ali koje se ne mogu izlečiti (artritis, kancer, migrena, fibromijalgija, dijabetična neuropatija); stanja izazvana bolešću, koja se održavaju i po prestanku bolesti (oštećenja senzornih nerava, simpatičke eferentne aktivnosti i bolne refleksne mišićne kontrakcije); i različita psihička stanja koja mogu pogoršati ili čak izazvati bol.

Osnovne grupe lekova koje se primenjuju u tretmanu hroničnog bola su: *opioidni analgetici; antidepresivi; antikonvulzivi i lokalni anestetici*. Dugotrajna oralna primena *opioidnih analgetika* se najčešće koristi u terapiji bola malignih oboljenja. U ove svrhe se preporučuje primena morfina sa produženim oslobađanjem, metadona ili dugodelujućih preparata levorfanola. Takođe se često primenjuje fentanil u formi transdermalnog flastera. Farmakokinetički profil ovih preparata omogućava produženo analgetičko dejstvo, i minimiziranje neželjenih efekata kao što su sedacija koja se javlja sa naglim povećanjem nivoa leka u plazmi, i ponovno javljanje bola, što je u vezi sa brzim smanjivanjem koncentracije opioda u plazmi. Konstipacija je čest neželjeni efekat, koji bi trebalo lečiti.

Triciklični antidepresivi (TCA) ostvaruju analgetički efekat u tretmanu hroničnog bola brže i pri manjoj dozi nego kada se primenjuju u terapiji depresije. Ovi lekovi potenciraju analgeziju izazvanu opijatima, te se koriste zajedno kod jakog upornog bola u malignim tumorima. Efikasnost TCA je zabeležena u lečenju postherpetičke neuralgije, dijabetičke neuropatije, tenzione glavobolje, i migrene. Najčešće se primenjuju amitriptilin, nortriptilin i dezipramin. Ali TCA mogu imati ozbiljne neželjene efekte kao što su ortostatska hipotenzija, EKG promene i aritmije, smetnje u pamćenju, konstipacija i retencija urina, koji mogu posebno kod starih pacijenata da budu problem, a neki od njih potenciraju istovrsne neželjene efekte opijata. Selektivni inhibitori preuzimanja serotoninu kao što su fluoksetin i venlafaksin imaju ređe i manje izražene neželjene efekte od TCA, ali i manju efikasnost u suprimiranju hroničnog bola.

Antikonvulzivi (karbamazepin, fenitoin, gabapentin) i *lokalni anestetici – i.v.* (lidokain i meksiletin) su posebno efikasni u lečenju neuropatskog bola.

U zaključku, opijatni analgetici ostaju osnovni lekovi u lečenju umerenog do jakog kancerskog bola. Uloga adjuvantnih analgetika u tretmanu kancerskog bola sve više raste, posebno u onih pacijenata kod kojih opijati ne mogu u potpunosti da antagonizuju bol. Sa druge strane, neki alternativni/adjuvantni analgetici imaju specifična analgetička svojstva u otklanjanju izvesnih tipova bola, posebno neuropatskog bola.

There are several diseases that are causing pain (arthritis, cancer, muscle spasm, secondary perpetuating factors) which has resolved (damaged tissue, muscle contraction); even cause pain.

The main class of drugs used in the treatment of chronic pain are *antidepressants; antidepressants; anticonvulsants; local anesthetics*; they are administered orally. For this purpose, it is desirable to use long-acting morphine compounds or levorphanol compounds. The pharmacokinetic profile of these drugs minimizes side effects by reducing the likelihood of side effects at low concentrations. Constipation is a common side effect that should be treated expectantly.

The analgesics used in the treatment of chronic pain have a more rapid onset and longer duration of action than depression. TCAs potentially relieve severe persistent pain. They are used in the management of tension headache and migraine. Amitriptyline and nortriptyline are used for hypotension, ECG changes, urinary retention, which are additive to the side effects of TCAs. Fluoxetine and venlafaxine are less effective for relief of pain.

Anticonvulsants (carbamazepine, phenytoin, gabapentin) and *local anesthetics* (lidocaine, mexiletine) are effective in the treatment of neuropathic pain.

In conclusion, opioid analgesics remain the mainstay in the treatment of cancer pain. The place of adjuvant analgesics in the treatment of cancer pain has grown, especially in patients who cannot tolerate opioids. Otherwise, they have specific properties in several types of pain.

OPIOIDS AND ALTERNATIVE/ADJUVANT ANALGESICS

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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 than 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: amitriptiline, 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.