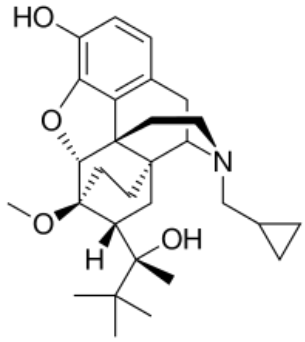
Buprenorphine

Buprenorphine is a semi-synthetic opioid derived from the opium alkaloid **thebaine**, it is classified among the **opioids**. It was patented in 1965 and in the early 1980s it began to be used in Europe and the USA as an **analgesic** with a high degree of safety and limited addictive potential. (Temgesic 0.2 mg tablets for sublingual use, Temgesic in the form of injections 0.3 mg for intramuscular and intravenous use). Although it is a strong analgesic and in weight-comparable doses it is 33 times (at **IV/IM administration**) to 100 times (**patch and sublingual administration**) more effective than morphine, it belongs to groups of partial agonists/antagonists, and with increasing doses, there is no further deepening of the effect, especially on the depression of respiratory and cardiac functions. This is the so-called ceiling effect. The smallest recommended dose of injectable buprenorphine of 0.3 mg is as effective as 10 mg of morphine in quality of analgesia and depression of the respiratory center. A double dose will deepen pain relief, but less Central nervous system depressant effects.



Buprenorphine

Acts **agonistically** on the **μ** (mu) **opiate receptor** (OP3), it is a partial agonist with high binding activity, but lower intrinsic activity. Its effect is submaximal. Compared to morphine, the effects are lower quantitatively, but not qualitatively. At higher doses, buprenorphine occupies most of the opiate receptors and it is almost impossible to overcome its effect with e.g. heroin, morphine. This can be a problem in the treatment of acute severe pain, postoperative pain, and wherever full agonists are indicated. However, there are enough free receptors in the analgesic doses and it is possible to combine patches with morphine, fentanyl, etc. opioids for breakthrough pain without weakening their analgesic effect. It acts as an antagonist at the **κ** (kappa) and **δ** (delta) **opioid receptors**.

Indication

For analgesic use, it is available in the Czech Republic in the form of transdermal patches with a strength of **35 μg/h, 52.5 μg/h and 70 μg/h**. (Under the company name Transtec, Bupretec, etc.) Patches are indicated in the **chronic treatment of moderate to severe pain**. The onset of action is slow, minimal analgesic plasma levels are reached within 24 hours. These continue to increase for another 60 hours, and the effectiveness lasts for 72-96 hours. With long-term use, steady-state plasma concentrations are achieved within two to three applications of the patch. According to the manufacturer, the **maximum recommended daily dose is 2 tablets of a strength of 70 μg/h**, which is equivalent to about 3.2 mg of buprenorphine per day. There are studies where the analgesically effective doses were much higher, eg 7 mg IV in postoperative pain.

For **substitution treatment** in addiction to opioids and opiates in the form of sublingual tablets with a strength of 0.4 mg to 8 mg. Tablets are usually taken once a day during long-term substitution therapy, when reducing doses in detoxes, administration in two doses is sometimes used (Subutex, Suboxone...). The usual dose is 8-12 mg. Doses above 16 mg are not used.

Pharmacokinetics

Buprenorphine is an unusually **long acting** opioid. It has a high affinity for opioid receptors and its **biological half-life is 36 hours in SL application**. With substitution, dosing is sometimes applied once every 48 hours or, exceptionally, even every third day. When either a double or triple daily dose is given. A patient stabilized on 8 mg per day could therefore take 16 mg on Monday and Wednesday and 24 mg on Friday. However, such a method of use is not common and the vast majority of patients take a dose every day. Due to its strong receptor binding, buprenorphine acts as an antagonist in patients dependent on full opioid agonists when administered concurrently and produces acute withdrawal syndrome. Therefore, when inducing substitution treatment, wait until the client experiences mild to moderate withdrawal symptoms. Then buprenorphine occupies the released receptors and relieves. The waiting time for morphine and heroin is usually 12 hours, for methadone 24-36, sometimes longer.

Effects

Buprenorphine produces the same or similar effects as other opioid analgesics. **The onset of effect is delayed** even with IV administration, so there is no "crash" like when using, for example, heroin. With tablet administration, the effect of the drug develops slowly within 4 hours and remains in full force for **12-24 hours**, even longer when suppressing withdrawal symptoms. When treating pain, we dose after 6-8 hours.

Suppresses the CNS, strongly suppresses pain, suppresses anxiety, often causes nausea and vomiting in intolerant users. **Constipation** is a constant adverse effect with long-term use. Unlike other opioids, buprenorphine has minimal sedative effects. It depresses the respiratory center, produces an elevated mood, suppresses the cough center and causes itching, occasionally urinary retention. Intoxication may not be noticeable to the user. Buprenorphine is a relatively safe drug. A dangerous combination is with other CNS depressantsing substances. It is mainly about the simultaneous use of benzodiazepines and alcohol. Intravenous administration (especially of crushed tablets) is also dangerous. In this case, there is a risk of overdose, endocarditis, abscess, devastation of the vascular system, etc..

Withdrawal symptoms

A **withdrawal state** develops slowly after stopping buprenorphine. It is usually objectively recognizable two or three days after withdrawal. It is milder than withdrawal from heroin, morphine or methadone, but lasts a long time. After two weeks, significant symptoms are observed, including **vomiting, diarrhea, insomnia, panic attacks and a severely depressed mood**. The user is tired, emotionally upset, has dilated pupils, sweats, goosebumps, sneezing, pain and feelings of bodily discomfort. Withdrawal subsides within a month, but anxiety and insomnia can persist long after withdrawal, and without supportive psychiatric treatment there is a high risk of relapse.

Links

Related Articles

- Opioid analgesics

Resources

- ROKYTA, Richard a kolektiv. *Léčba bolesti v primární péči.* - edition. Grada Publishing a.s., 2018. 188 pp. ISBN 9788027103126.
- MÁLEK, Jiří a kolektiv. *Praktická anesteziologie.* 2. edition. Grada Publishing a.s., 2016. 208 pp. ISBN 9788024756325.

References