ARE CANNABINOIDS REALLY ANALGESICS?

B. Kraft
Dept. of Special Anesthesia and Pain Therapy, Medical University of Vienna, Vienna, Austria

Numerous animal models have demonstrated anti-nociceptive and anti-hyperalgesic properties of plant-derived (Δ9-tetrahydrocannabinol, Dronabinol) and synthetic cannabinoid compounds.
But despite the increasing number of clinical studies, their potential role as analgesics remains still unclear.

Acute pain conditions:
Only inconsistent data exist from controlled clinical trials with cannabinoids on acute pain. In the 80ies, two small-sized studies investigated the parenterally applied synthetic cannabinoid levonandradol in postoperative pain. Two other, more recent trials were performed with oral cannabinoids. Whereas in the smaller trial by Buggy et al. no significant analgesia was produced by a single oral dose of 5mg THC, a well-designed multicenter dose-escalation trial using oral cannabis extract showed a small, but significant dose-related reduction of postoperative patient-controlled analgesia requirements. But the dose-escalation was associated with an increased severity and incidence of side effects.
In trials using human pain models of acute nociceptive or inflammatory pain and hyperalgesia, 20mg of oral THC or cannabis extract failed to produce significant analgesic effects, moreover, hyperalgesia and decreased pain thresholds were found.
Interestingly enough, similar results were seen in postoperative pain after 2mg nabilone. Significantly higher pain scores were reported compared to placebo, ketoprofen or only 1mg nabilone. As recently shown by Wallace et al., not only oral cannabinoids, but also a high-dose smoked cannabis produced hyperalgesia, whereas an analgesic effect on capsaicin-evoked spontaneous pain was reported after the medium dose, demonstrating an complex and not well understood dose dependency.
To conclude, in most of the studies, cannabinoids proved more or less ineffective and side effects occurred frequently. Therefore they cannot be recommended for the treatment of acute pain.

Chronic pain conditions:
In chronic pain, data from trials with patients suffering from chronic neuropathic, inflammatory and spasticity-associated pain with orally and sublingually administered cannabinoids showed inconsistent results. There is some evidence that cannabinoids are effective in Multiple Sclerosis (MS)-associated pain. Besides numerous case reports, a relatively small study with oral THC in 24 patients suffering from central neuropathic pain due to MS showed a number-needed-to-treat of 3.5 for a 50% pain relief. The results were confirmed by Rog et al. with an oromucosal spray and by a large multicenter study with oral THC and cannabis extract. But in chronic neuropathic pain caused by other diseases, the data are still less convincing. Besides few other studies, one trial with oromucosal spray in 48 patients with neuropathic pain after brachial plexus avulsion showed a statistical significant, but clinically not relevant pain reduction. In a recent cross-over study, oral nabilone was even less potent than dihydrocodeine in 96 patients with neuropathic pain. Nevertheless, although cannabinoids proved only a weak analgesic potency, all studies in chronic pain patients reported consistently an improvement of sleep, mood, coping behaviour and Quality-of-Life Scores, indicating that cannabinoids are rather psychoactive than potent analgesic drugs. It is still unclear, which diagnoses, pain characteristics, and clinical variables are most amenable to treatment. There are no data available concerning the long-term effectiveness of cannabinoids; optimal drug selection and dosages; the risk-benefit ratio of combining cannabinoids with other drugs; and how adverse effects can be minimized.