Medical Marijuana for Chronic Pain

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In 1970, the Controlled Substances Act classified cannabis as a Schedule I drug; this category is reserved for drugs that are defined as having “a high potential for abuse,” “no currently accepted medical use in treatment in the United States,” and “a lack of accepted safety for use of the drug or other substance under medical supervision” [1]. Interest in the medicinal potential of cannabis has persisted, however, fueled by the isolation of the active compounds in marijuana, starting with tetrahydrocannabinol (THC) in 1964. This research continued in the 1990s with the discovery of the endocannabinoid system, a network of receptors that bind both compounds in marijuana and endogenous ligands produced by the human body. There are 2 types of cannabinoid receptors: CB1 receptors and CB2 receptors. CB1 receptors are present in areas of the brain that modulate pain, in the nociceptive pathways of the spinal cord, and on peripheral nerves; these receptors may help modulate pain signals in multiple areas. CB2 receptors are found primarily in the cells of the immune system and may help to down-regulate inflammation [2].

The prevalence of cannabinoid receptors in pain pathways suggests that marijuana or its components may have significant pharmaceutical potential for analgesia. There are currently 2 synthetic analogs of THC: dronabinol and nabilone, both of which have been approved by the US Food and Drug Administration for treatment of chemotherapy-induced nausea and vomiting and for AIDS-related anorexia and wasting. A third cannabinoid, nabiximols, is available in Canada for treatment of cancer pain and for treatment of neuropathic pain in multiple sclerosis. A recent systematic review and meta-analysis concluded that cannabinoids have moderate efficacy for the treatment of chronic pain but that side effects limit their use [3].

The term medical marijuana refers, not to the purified and regulated compounds described above, but to botanical cannabis, which contains at least 60 active compounds and is usually smoked. Eighteen states and the District of Columbia have now passed legislation permitting the use of marijuana for medical purposes [4]; North Carolina is not currently among these states. In October 2009, the US Department of Justice issued a directive stating that people who follow state laws that allow them to possess and use marijuana for medical purposes would not face federal prosecution. However, those who use, sell, and grow medical marijuana are still doing so in violation of federal law, and there continue to be federal raids on dispensaries and on marijuana growing operations in states that permit the use of marijuana for medical purposes. In the absence of federal oversight, the clinical conditions for which use of marijuana is permitted, the way in which permission for medical use is granted, and the amount of marijuana that a person may possess for medical use vary widely from state to state [5]. Chronic pain is an approved indication for use of medical marijuana in 15 states [4].

There are few studies of smoked marijuana because its Schedule I status means that strict limitations curtail research regarding its medical effects [1]. However, 5 randomized, placebo-controlled trials have evaluated the benefits of smoked marijuana for pain; the placebo in these studies was a marijuana cigarette that contained no cannabinoids (0% THC) [6-10]. One study of neuropathic pain [6] and 2 studies of HIV-associated sensory neuropathy [7, 8] found that use of marijuana led to significantly more individuals achieving a 30% reduction in pain. However, another study of neuropathic pain [9] showed a mean reduction of only 0.7 points on a 10-point pain scale in patients with refractory pain. Finally, a study of experimentally induced neuropathic pain [10] showed significant improvement in analgesia among individuals who smoked marijuana cigarettes containing 4% THC. Interestingly, there was no pain reduction when the marijuana in the cigarette contained only 2% THC, and there was an increase in pain when it contained 8% THC, suggesting that marijuana may have an optimal dosing window. These
studies are difficult to generalize to patients with chronic pain because of the short duration of these studies, the small numbers of subjects enrolled (between 15 and 50), the varying THC content of the plant material smoked, and the difficulty of blinding participants regarding which treatment they have been selected to receive [11].

Marijuana does not pose a risk of fatal overdose, and the public health burden of marijuana is estimated to be less than that of alcohol, tobacco, or other illicit substances [12]. However, use of marijuana has significant adverse effects. Acutely, marijuana increases the risk of motor vehicle accidents and can cause anxiety and panic; at high doses, it can even cause psychotic symptoms. Long-term users have a 9% risk of dependence and show signs of subtle cognitive impairment [13]. Adolescent users have decreased educational attainment and are more than twice as likely to develop schizophrenia. Finally, smoking marijuana has the advantage of delivering THC and other active components to the bloodstream much more efficiently than oral administration, but smoking carries with it an increased risk of chronic bronchitis, an increased risk of impaired respiratory function, and possibly an increased risk of lung cancer [12].

There are physiologic reasons to believe that marijuana may have analgesic properties, and trials of purified cannabinoids and of smoked marijuana furnish some preliminary support for this idea, particularly in the case of neuropathic pain. However, the current evidence is based on small trials whose results are difficult to generalize to widespread use of medical marijuana. We need more high-quality studies to determine whether the benefits of medical marijuana outweigh its risks. NCMJ

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References


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