

### Chronic Pain

As many as one in five Americans lives with chronic pain.[1] Many of these people suffer from neuropathic pain (nerve-related pain) -- a condition that is associated with numerous diseases, including diabetes, cancer, multiple sclerosis, and HIV. In most cases, the use of standard analgesic medications such as opiates and NSAIDs (non-steroidal anti-inflammatory drugs) is ineffective at relieving neuropathic pain. Further, long-term use of most conventional pain relievers, including acetaminophen, opioids, and NSAIDs, is associated with a host of potential adverse side effects, including stroke, erectile dysfunction, heart-attack, hepatotoxicity, and accidental overdose death.

Survey data indicates that the use of cannabis is common in chronic pain populations[2] and several recent FDA-designed clinical trials indicate that inhaled marijuana can significantly alleviate neuropathic pain. These include a pair of randomized, placebo-controlled clinical trials demonstrating that smoking cannabis reduces neuropathy in patients with HIV by more than 30 percent compared to placebo.[3-4] (Additional details on these studies appear in the HIV section of this book.) In addition, a 2007 University of California at San Diego double-blind, placebo-controlled trial reported that inhaled cannabis significantly reduced capsaicin-induced pain in healthy volunteers.[5] A 2008 University of California at Davis double-blind, randomized clinical trial reported both high and low doses of inhaled cannabis reduced neuropathic pain of diverse causes in subjects unresponsive to standard pain therapies.[6] A 2010 McGill University study reported that smoked cannabis significantly improved measures of pain, sleep quality and anxiety in participants with refractory pain for which conventional therapies had failed.[7] A 2013 clinical trial reported that both inhaled cannabis and oral THC significantly decreased pain sensitivity and increased pain tolerance in healthy subjects exposed to experimental painful stimuli.[8]

A review of these and other trials in 2011 in the *British Journal of Clinical Pharmacology* concluded, "[I]t is reasonable to consider cannabinoids as a treatment option for the management of chronic neuropathic pain with evidence of efficacy in other types of chronic pain such as fibromyalgia and rheumatoid arthritis as well." [9] A separate review published in 2012 in *The Clinical Journal of Pain* further concluded, "Overall, based on the existing clinical trials database, cannabinergic pain medicines have been shown to be modestly effective and safe treatments in patients with a variety of chronic pain conditions. ... Incorporating cannabinergic medicine topics into pain medicine education seems warranted and continuing clinical research and empiric treatment trials are appropriate." [10]

# NORML

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Preclinical data indicates that cannabinoids, when administered in concert with one another, are more effective at ameliorating neuropathic pain than the use of a single agent. Investigators at the University of Milan reported in 2008 that the administration of single cannabinoids such as THC or CBD produce limited relief compared to the administration of plant extracts containing multiple cannabinoids, terpenes (oils), and flavonoids (pigments).

Researchers concluded: "[T]he use of a standardized extract of *Cannabis sativa* ... evoked a total relief of thermal hyperalgesia, in an experimental model of neuropathic pain, ... ameliorating the effect of single cannabinoids," investigators concluded. ... "Collectively, these findings strongly support the idea that the combination of cannabinoid and non-cannabinoid compounds, as present in [plant-derived] extracts, provide significant advantages in the relief of neuropathic pain compared with pure cannabinoids alone." [11]

In 2009, an international team of investigators from the United Kingdom, Belgium and Romania affirmed these preclinical findings in a clinical study of intractable cancer pain patients. They concluded: "[I]n this study, the THC/CBD extract showed a more promising efficacy profile than the THC extract alone. This finding is supported by evidence of additional synergy between THC and CBD. CBD may enhance the analgesic potential of THC by means of potent inverse agonism at CB2 receptors, which may produce anti-inflammatory effects, along with its ability to inhibit immune cell migration. ... These results are very encouraging and merit further study." [12]

A 2011 clinical trial assessing the administration of vaporized plant cannabis in chronic pain patients on a daily regimen of morphine or oxycodone reported that inhaled "cannabis augments the analgesic effect of opioids." Authors concluded, "The combination (of opioids and cannabinoids) may allow for opioid treatment at lower doses with fewer side effects." [13] A separate 2013 FDA-approved trial assessing the impact of vaporized cannabis on neuropathic pain reported that even low doses of THC (1.29 percent) "provided statistically significant 30% reductions in pain intensity when compared to placebo." [14]

Based on these findings, some pain experts are now advising that physicians recommend cannabis therapy in addition to or in lieu of opiate medications to "reduce the morbidity and mortality rates associated with prescription pain medications." [15]

## REFERENCES

[1] *New York Times*. October 21, 1994. "Study says 1 in 5 Americans suffers from chronic pain."

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- [2] Cone et al. 2008. Urine drug testing of chronic pain patients: licit and illicit drug patterns. *Journal of Analytical Toxicology* 32: 532-543.
- [3] Abrams et al. 2007. Cannabis in painful HIV-associated sensory neuropathy: a randomized placebo-controlled trial. *Neurology* 68: 515-521.
- [4] Ellis et al. 2008. Smoked medicinal cannabis for neuropathic pain in HIV: a randomized, crossover clinical trial. *Neuropsychopharmacology* 34: 672-80.
- [5] Wallace et al. 2007. Dose-dependent effects of smoked cannabis on Capsaicin-induced pain and hyperalgesia in healthy volunteers *Anesthesiology* 107: 785-796.
- [6] Wilsey et al. 2008. A randomized, placebo-controlled, crossover trial of cannabis cigarettes in neuropathic pain. *Journal of Pain* 9: 506-521.
- [7] Ware et al. 2010. Smoked cannabis for chronic neuropathic pain: a randomized controlled trial. *CMAJ* 182: 694-701.
- [8] Cooper et al. 2013. Comparison of the analgesic effects of dronabinol and smoked marijuana in daily marijuana smokers. *Neuropsychopharmacology* 38: 1984-1992.
- [9] Lynch and Campbell. 2011. Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials. *British Journal of Clinical Pharmacology* 72: 735-744.
- [10] Sunil Aggerwal. 2012. Cannabinergic pain medicine: a concise clinical primer and survey of randomized-controlled trial results. *The Clinical Journal of Pain* [E-pub ahead of print].
- [11] Comelli et al. 2008. Antihyperalgesic effect of a Cannabis sativa extract in a rat model of neuropathic pain. *Phytotherapy Research* 22: 1017-1024.
- [12] Johnson et al. 2009. Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of the efficacy, safety and tolerability of THC: CBD extract in patients with intractable cancer-related pain. *Journal of Symptom Management* 39: 167-179.
- [13] Abrams et al. 2011. Cannabinoid-opioid interaction in chronic pain. *Clinical Pharmacology & Therapeutics* 90: 844-851.
- [14] Wilsey et al. 2013. Low-dose vaporized cannabis significantly improves neuropathic pain. *The Journal of Pain* 14: 136-148.
- [15] Mark Collen. 2012. Prescribing cannabis for harm reduction. *Harm Reduction Journal* 9: 1.