

Medical Marijuana: Answers to Your Burning Questions

Introduction

Marijuana, the leaves and buds of the plant *Cannabis sativa*, is a “drug” as defined by the U.S. Federal Food, Drug, and Cosmetic Act. It is classified as a schedule I controlled substance under the federal Controlled Substances Act. This scheduling makes the sale, possession, and use of marijuana illegal.¹ However, some states (Alaska, California, Colorado, Hawaii, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, and Washington) and the District of Columbia permit the medical use of marijuana.¹ Canada has a national program for medical marijuana use.¹ In these geographic areas, patients can get a recommendation from his or her physician to use marijuana, usually for a specific indication. The marijuana can then be bought or grown by the individual. This document reviews uses and side effects of medical marijuana, in addition to information on its legality.

Evidence for Medical Use of Marijuana

Medical marijuana is used primarily for the relief of various symptoms of disease, and not as a cure for disease.² States typically lay out acceptable indications for the medical use of marijuana, such as cachexia, chronic pain, multiple sclerosis, HIV/AIDS, etc. The main mechanism for the effects of marijuana involves partial agonist activity of tetrahydrocannabinol (THC), chemically classified as a “cannabinoid,” at CB1 receptors in the central nervous system.^{1,3} Experts point out that much of the evidence for the use of medical marijuana is not high quality, and is often anecdotal.^{1,3,4} The following is commentary on evidence for the use of marijuana for a number of indications.

Appetite loss. Smoking marijuana seems to stimulate the appetite of patients with AIDS. Marijuana cigarettes can increase caloric intake and weight gain in HIV positive patients also taking indinavir (*Crixivan*) or nelfinavir (*Viracept*) without affecting viral load.¹

Nausea and vomiting. An Institute of Medicine report points out that in recent years, considerable advancement has been made with regard to antiemetic therapy for chemotherapy-induced nausea and vomiting. In addition, cannabinoids are relatively modest antiemetics, and smoked marijuana may be poorly tolerated by cancer patients.²

Cannabinoids act through a different mechanism than other antiemetics, and for this reason might be useful as adjunctive therapy in patients whose nausea and vomiting is not controlled with other drug therapies.²

Multiple sclerosis. In animal models of multiple sclerosis, THC has been reported to reduce tremor and spasticity.¹ Marijuana seems to be effective when smoked, or when the cannabinoids are taken orally, for the treatment of spasticity and tremor associated with multiple sclerosis.¹ Oral cannabinoids may also reduce urge incontinence in individuals with multiple sclerosis.⁵

Pain. Based on data from animal studies, cannabinoids seem to be mild to moderate analgesics.² A systematic review and meta-analysis of clinical trials comparing various THC preparations to placebo for the treatment of chronic pain, including neuropathic pain, suggests it may be moderately effective. However, the risk for adverse events also appears to be relatively high, with a number needed to harm (NNH) of around five to eight subjects for side effects such as altered perception and altered cognitive function.⁶

Glaucoma. Smoking marijuana seems to reduce intraocular pressure in patients with glaucoma. There is some evidence marijuana can decrease intraocular pressure, but it also seems to decrease blood flow to the optic nerve. So far, it isn't known if marijuana can improve visual function.¹

There is insufficient reliable information available about the effectiveness of marijuana for other uses.¹

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Concerns About Medical Use of Marijuana

The risk for serious side effects with marijuana is relatively low in comparison with other prescription drugs, although evaluating safety data is complicated in light of the status of marijuana as an illicit substance under federal law. The true incidence and risks of side effects are difficult to ascertain.⁴

The use of marijuana can cause dry mouth, nausea, vomiting, and a characteristic reddening of the eyes.¹

Chronic use can cause apathy, psychic decline, sexual dysfunction, and abnormal menstruation, and has been associated with several cases of an unusual pattern of bullous emphysema. Regular use of marijuana in middle-aged persons has been associated with an increased risk of myocardial infarction. Unpublished evidence indicates that there is a nearly five-fold increase in relative risk of myocardial infarction within the first hour following smoking marijuana. Regular marijuana smoking was defined as smoking marijuana less than once a month to daily.¹

Intoxicating doses of marijuana impair reaction time, motor coordination, and visual perceptions, and can also produce panic reactions, hallucinations, flashbacks, depression, and other emotional disturbances. An individual's driving ability can be impaired for up to eight hours.¹ It should be noted that acute cognitive changes may be undesirable for individuals who are using marijuana for therapeutic purposes, and that these effects are dose related and can often be controlled by reducing the "dose."⁷

Long-term use of marijuana can cause cognitive impairment that lasts longer than the period of acute intoxication. These cognitive impairments develop slowly and worsen as the years of marijuana use increase, becoming clinically significant after about two decades of use.¹

Marijuana is said to have a high abuse potential.¹ However, its ability to produce dependence is less significant than that associated with either alcohol or nicotine, or some drugs such as diazepam, morphine, and phenobarbital.⁷ About 10% of regular marijuana users become addicted.⁷ Experts point out that the addiction potential may actually be even less when marijuana is used for medical purposes, as is the case with some other drugs that have addiction potential.⁷

Medical marijuana is typically smoked, inhaled, eaten, or applied topically.³ Marijuana smoke contains up to 70% more carcinogenic ingredients than cigarette smoke, and as such may increase the risk for lung cancer and head and neck cancer.³ Of course chronic smoking can increase the risk for symptoms of chronic bronchitis.³ Regular smoking of three to four marijuana cigarettes per day is reported to produce as many symptoms as an average of 22 tobacco cigarettes per day, and comparable airway histological effects as 20 tobacco cigarettes per day.¹ As such, vaporizing is considered the safest route for using medical marijuana.⁴ Vaporizers are different from water pipes (e.g., bongs). Vaporizers for "herbal mixtures or blends" heat the marijuana to produce vapor without causing combustion. They are available commercially in a variety of sizes, costs, etc.

Despite the fact that there is an obvious lack of standardization for dosing of medical marijuana, it should be noted that smoking in and of itself is a highly unpredictable route of administration, highly dependent on the user, the method used to inhale, the time to exhale, etc.⁴

Drug-drug Interactions with Marijuana

Marijuana is believed to be a cytochrome P450 3A4 (CYP3A4) inhibitor and possibly a CYP1A2 inducer.⁴ It may potentiate the effects of opioids and CNS depressants. It may increase INR and bleeding risk for patients on warfarin.^{1,4}

Legal Use of Medical Marijuana

Federal and state laws on the use of marijuana don't always match up.³ The fact that marijuana is a schedule I substance under the federal Controlled Substances Act (CSA) means that it is considered to have no accepted medical use, a high potential for abuse, and a lack of accepted safety.³ This is in conflict with some state laws, where marijuana has been legalized for medical use.³ Normally, federal law, being stricter, would preempt these state laws. In the case of medical marijuana specifically, this preemption has been upheld by the Supreme Court.^{3,7}

However, the vast majority of drug convictions in the U.S. are made on a state level. Medical use of marijuana is allowed on a state level, and prescribers and other healthcare professionals are licensed on a state level. For these reasons,

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experts point out that criminal conviction and professional discipline in states that allow the medical use of marijuana is unlikely. However, it also must be said that the DEA does have the right to enforce the Controlled Substances Act.³

Accessing Marijuana for Medical Use

In 1996, California was the first of the current 14 states (and the District of Columbia) to legalize the medical use of marijuana. In these states, there are possession limits for both usable marijuana and for plants. An application which has been completed by the patient and/or caregiver and his or her physician must be submitted to the state agency that administers the program, along with a small fee, usually less than \$100, for a registry identification card. State specific information can be found at <http://medicalmarijuana.procon.org/view.resource.php?resourceID=000881>.

In Canada, the Marijuana Medical Access Regulations went into effect on July 30, 2001. These regulations establish a framework for allowing individuals to access marijuana for relief of symptoms associated with diseases and conditions such as multiple sclerosis, spinal cord injury, cancer, HIV/AIDS, etc., when conventional treatments are not adequate. Individuals can access marijuana through Health Canada, obtain a license to grow their own supply, or designate a person to grow it for them. There are possession limits, for both users and growers.⁸ Health Canada's supplies of marijuana are produced and distributed directly to the patient by Prairie Plant Systems, Inc. This is the only business legally permitted to produce/provide medical marijuana in Canada.¹⁵ A guide and application form can be accessed online (<http://www.hc-sc.gc.ca/dhp-mps/marihuana/how-comment/index-eng.php>) for use by patients, but which requires documentation from a physician.

Alternatives to Medical Marijuana

The DEA points out that there is legal medical marijuana, in the form of dronabinol. Dronabinol (*Marinol*), or synthetic THC, is a schedule III controlled substance in the U.S. and a schedule II controlled substance in Canada. It's indicated in both the U.S. and Canada for the treatment of anorexia associated with weight loss in patients with AIDS, and for nausea and vomiting

associated with chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.^{9,10}

Nabilone (*Cesamet*), which is another synthetic cannabinoid, has the same indication for use in patients with nausea associated with chemotherapy that is refractory to other antiemetics.^{11,12} *Cesamet* is a schedule II controlled substance in both the U.S. and Canada.^{11,12}

Sativex buccal spray, made from *Cannabis sativa* extracts, is approved in Canada, and is being studied for various indications in the U.S. In Canada, it's indicated for the relief of neuropathic pain with multiple sclerosis in adults, and as an adjunctive treatment for pain in patients with advanced cancer.¹³

Conclusion

Avoid recommending the use of medical marijuana as a first-line agent for conditions which have therapies that are better supported and possibly better tolerated [Evidence level C; expert opinion].¹⁴ Advise patients who are using medical marijuana to abide by possession limits. Recommend avoiding public use of marijuana, driving under the influence of marijuana, etc.^{3,4} (A number of states have laws against operating a motor vehicle if there is any detectable level of a prohibited drug or its metabolites in the blood.) Advise individuals that testing positive for marijuana may put them at risk for job termination.⁴

Screen patients who are using medical marijuana for drug-drug interactions, and counsel them about the potential risks.

Users of this document are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and Internet links in this article were current as of the date of publication.

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Levels of Evidence

In accordance with the trend towards Evidence-Based Medicine, we are citing the **LEVEL OF EVIDENCE** for the statements we publish.

Level	Definition
A	High-quality randomized controlled trial (RCT) High-quality meta-analysis (quantitative systematic review)
B	Nonrandomized clinical trial Nonquantitative systematic review Lower quality RCT Clinical cohort study Case-control study Historical control Epidemiologic study
C	Consensus Expert opinion
D	Anecdotal evidence In vitro or animal study

Adapted from Siwek J, et al. How to write an evidence-based clinical review article. *Am Fam Physician* 2002;65:251-8.

Cite this Detail-Document as follows: Medical marijuana: answers to your burning questions. Pharmacist's Letter/Prescriber's Letter 2010;26(9):260906.



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