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Medical Marijuana in HIV-Positive Patients: What Do We Know?

Sandro Cinti, MD

Abstract
On November 4, 2008, our state passed the Michigan Medical Marijuana Act (MMMA), which allows the medical use of marijuana for certain conditions and/or constellation of symptoms. This article will (1) review the current evidence that medical marijuana is useful for certain chronic conditions, particularly pain and wasting syndromes experienced by HIV-positive people; (2) discuss the adverse effects of marijuana; (3) summarize the new Michigan law and the challenges it poses for physicians, and (4) review the experience in California where medical marijuana has been legal since 1996.

Keywords
medical marijuana, wasting syndrome, neuropathy

Introduction
On November 4, 2008, our state passed the Michigan Medical Marijuana Act (MMMA), which allows the medical use of marijuana for certain conditions and/or constellation of symptoms. Twelve other states including Alaska, California, Colorado, Hawaii, Maine, Montana, Nevada, New Mexico, Oregon, Vermont, Rhode Island, and Washington already allow the use of medical marijuana. However, the US Supreme Court held in 2005 (Gonzalez v Raich) that patients prescribed marijuana in accordance with state law could be criminally prosecuted under federal statutes that prohibit use of the drug. In 2008, the American College of Physicians (ACP), the largest organization of internists, published a position paper supporting research into the medical use of marijuana and in 1999, the Institute of Medicine (IOM) published a report recommending, among other things, that “Research should continue into the physiological effects of synthetic and plant-derived cannabinoids and the natural function of cannabinoids found in the body.” Several countries, including The Netherlands and Canada, allow the use of medical marijuana and have been able to study its effects.

Marijuana’s medicinal effects have been demonstrated in several clinical settings. While marijuana derivatives such as dronabinol (synthetic tetrahydrocannabinol (THC)) and nabilone (dronabinol analogue) have been approved by the FDA, many patients prefer smoked or ingested marijuana because of a superior and more rapid effect. Marijuana has been used as an antiemetic and appetite stimulant in patients with cancer, as an antispasm and analgesic medication in patients with multiple sclerosis, as a treatment of glaucoma, and as an antiepileptic. Furthermore, medical marijuana has been proposed as a treatment of insomnia, mood disorders, and intractable hiccups. One recent study of the postsurgical analgesia demonstrated that patients getting 15 mg of oral cannabis extract (Cannador) after surgery were significantly less

The Benefits of Medical Marijuana
The use of medical marijuana is not new and as far back as 4000 years ago, healers used the plant when conventional therapies failed to relieve symptoms. Because of the US Food and Drug Administration’s (FDA) opposition to medical marijuana, very few controlled studies have been carried out in the United States. However, this has not prevented 13 states (including Michigan) from legalizing the use of medical marijuana and in 1999, the Institute of Medicine (IOM) published a report recommending, among other things, that “Research should continue into the physiological effects of synthetic and plant-derived cannabinoids and the natural function of cannabinoids found in the body.” Several countries, including The Netherlands and Canada, allow the use of medical marijuana and have been able to study its effects.

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likely to complain about breakthrough pain. Not all studies have shown a benefit. A large multicenter, 243-patient German study of oral cannabis extract as an anti-anorexia-cachexia drug in patients with cancer demonstrated no difference in appetite between patients on the oral cannabis extract and those on placebo.

Marijuana has long been used by HIV-infected patients as an appetite enhancer and pain-relieving medication. In a 2004 Canadian study, Furler et al found that 43% of people infected with HIV used marijuana and that 67% of these patients used it for medicinal purposes. Reasons for medicinal use included appetite stimulation (70%), sleep-relaxation (37%), nausea/vomiting (33%), pain (20%), anxiety/depression (20%), and stimulation/energy (10%). A multivariate analysis demonstrated that medicinal marijuana users had a significantly lower household incomes (< US $20 000), were more likely to be intravenous drug users, and were less likely to report “excellent” health than nonusers. A US study had slightly different responses, with only 23% of HIV-infected individuals admitting to marijuana use. The most common reason for smoking marijuana was for relief from depression and/or anxiety (57%) followed by appetite enhancement (53%) and pain relief (28%). More recently, marijuana has been shown to be effective in relieving the pain of both HIV-associated and antiretroviral (ARV) medication-associated neuropathies.

A recent study from the United Kingdom looked at the effect of cannabis on complaints of symptoms in 143 HIV-infected people. Participants were asked to fill out a questionnaire and rate (Much Better, Little Better, No Change, Little Worse, Much Worse) how certain symptoms responded to canna- note to the questionnaire may be biased by recreational use. A recent study by Haney attempted to address this issue by comparing smoked marijuana to oral THC for food intake.

Nine HIV-positive persons with active use of marijuana were enrolled and given, on 8 different occasions, THC with a placebo marijuana cigarette or a placebo “THC” tablet with an actual marijuana cigarette. After 3 to 4 weeks, even though marijuana cigarettes were rated as being “liked” better, more significantly increased food intake occurred when participants were taking oral THC versus smoked marijuana (45% vs 35%, respectively). Another reason for the use of marijuana in HIV-infected people is the side effects associated with the use of highly active antiretroviral therapy (HAART). Highly active antiretroviral therapy regimens can be difficult to take, and it is not unusual for HIV-positive patients to experience nausea and vomiting after taking certain ARV medications, particularly protease inhibitors. De Jong et al demonstrated that among HIV-positive patients on HAART who experienced moderate-to-severe nausea, those who smoked marijuana were 3.3 times more likely to be adherent to their HAART.

Peripheral neuropathies have been associated with didanosine (ddI), zidovudine (ZDV), and stavudine (d4T), and they can sometimes be irreversible. Several studies have demonstrated a beneficial effect of smoked marijuana on neuropathic pain in HIV-positive patients.

Abrams et al studied 50 patients who were randomly and blindly assigned to receive either real marijuana cigarettes or placebo cigarettes for peripheral neuropathy. Each patient used the randomized drug for 5 days in an outpatient setting and then was followed up for 7 days in the outpatient setting. Participants who received marijuana cigarette reported a significant 34% (P = .03) decrease in daily pain compared to the placebo group.

Adverse Events Associated With Marijuana Use

Physicians must be aware that chronic marijuana use can cause other health problems. Chronic use of marijuana has been associated with both dependence and withdrawal. Withdrawal presents as irritability, depression, insomnia, nausea, anorexia, and tremor. Pulmonary diseases including chronic obstructive pulmonary disease (COPD) and lung cancer have been attributed to marijuana smoking and the fact that marijuana contains 4 times more tar and 50% more carcinogens than tobacco. The use of hot air vaporizers (Volcano) may decrease the level of the more toxic components in marijuana but that remains to be seen. Men who smoke marijuana have decreased serum testosterone levels, sperm counts, and sperm motility, which may lead to decreased libido, impotence, and decreased fertility. Cognitive dysfunction or “chronic cannabinoid syndrome” manifests as deficits in memory, attention, and retrieval function as well as loss of executive function, psychomotor speed, and manual dexterity in long-term and heavy marijuana users. These effects can last for hours to days after marijuana use. Several studies have demonstrated an increased risk of psychosis or psychotic symptoms with marijuana use. Depression and anxiety also seem to occur more frequently in marijuana users. Patton et al studied a cohort of 1601 14- and 15-year-old subjects and found a dose-related effect between marijuana use and anxiety. Finally, marijuana use has been associated with impaired immunity, an increase in risk-taking behavior, and it may increase the risk of myocardial dysfunction. While there is some concern that marijuana may be a “gateway drug” that leads to the use of harder drugs like cocaine and heroin, the 1999 IOM report stated that “there was no evidence that giving the drug to sick people would increase illicit drug use in the general population. Nor is marijuana a ‘gateway drug’ that prompts patients to use harder drugs like cocaine and heroin.”

There is currently no evidence that the use of marijuana has any adverse effect on an HIV-positive patient’s CD4 count and/or viral load. Abrams et al studied this question in 62 HIV-positive patients on stable HAART, who were randomized to get smoked marijuana, dronabinol capsules, or placebo. The authors demonstrated that after 21 days of treatment, there was
The California Medical Marijuana Law—Proposition 215

California, which has allowed the use of medical marijuana since 1996 (Proposition 215), provides some insight into how medical marijuana might be managed. Since the passage of Proposition 215 more than 200,000 people in California have been approved to use medical marijuana under a system similar to the MMMP. Furthermore, in 2003, California passed Senate Bill 420, which allowed patients who could not cultivate their own marijuana to obtain the drug from a “patients’ collective or cooperative.” While not explicitly allowing the sale of marijuana, this tacit approval resulted in the creation of a network of marijuana growers and dispensaries throughout California. Growers, who are mostly located upstate, sell to dispensaries, which provide medical marijuana to patients with a physician’s note. Patients give a “donation” to the dispensary based on the amount and type of marijuana. If dispensary owners avoid advertising in newspapers, on billboards, or flyers and avoid selling to minors, they are rarely bothered by local police or the federal Drug Enforcement Agency (DEA). Periodically dispensaries are shut down by the DEA and the agency has been known to pressure landlords to evict dispensaries.

Developing a Protocol for HIV-Positive Clinic Patients

Starting on April 6, 2009, Michigan physicians began getting requests for signatures of the Physician Certification form from MDCH. Although this is not a prescription, a signature almost guarantees that a patient will be permitted to use medical marijuana. We struggled with this in our HIV clinic at the University of Michigan because, essentially, any patient in the clinic qualifies under the MMMA. After much discussion, we settled on a protocol that was true to the attestation at the bottom of the Physician Certification form: “The medical use of marijuana is likely to be palliative or provide therapeutic benefits for the symptoms or effects of the applicant’s condition.” This protocol allows us to support the use of medical marijuana by people living with HIV/AIDS who might derive benefit. It will not always be easy to determine which patients qualify and furthermore, it is likely that some recreational marijuana users may see the MMMA as a way to legitimize the use of the drug. However, physicians already juggle the risks and benefits of giving a wide variety of medications to their patients. At least medical marijuana offers us yet another way to alleviate the genuine pain and suffering that some of our HIV-positive patients experience.

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