

Clearing Away the Smoke: An Analysis of Current Affairs in Medicinal Marijuana

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Introduction

With regard to patients with Parkinson's, Alzheimer's, lupus, rheumatoid arthritis, and various cancers, a growing number of physicians have become in favor of the use of marijuana as an analgesic. Marijuana (cannabis) is a plant that is often used as a psychoactive drug that acts on the CNS; particularly the brain. Marijuana also gives the user a sense of bliss and relaxation.

In 1970, marijuana was categorized as a Schedule I drug under the Controlled Substances Act; such drugs have potential for abuse and have no accepted medical use in the USA. However, marijuana has been considered for medicinal usage as an analgesic for patients in excruciating, unavoidable chronic pain as well as for other medical purposes. Advocates of medicinal marijuana have targeted cancer patients as particular beneficiaries of the drug. As of 2016, 23 states and the District of Columbia have legalized medicinal marijuana (1). The states of Washington, Colorado, Oregon, and Alaska, as well as the District of Columbia, have gone as far as to legalize recreational usage of the drug. Under federal law, these state legislatures have defied the Controlled Substances Act, as marijuana is still considered a Schedule I drug. Even though a physician can prescribe marijuana to a patient under state law, he or she is violating a federal act. In this paper, the use of marijuana as medicine is analyzed and explored, as well as the challenges being faced with studying marijuana in research laboratories.

Synopsis of "Medicinal Use of Medicinal Marijuana"

In the New England Journal of Medicine (NEJM), Drs. Michael Bostwick, Gary Reisfield, and Robert



Micah Belzberg: *Rx*

Key Point: Antiemetic Medications

Ondansetron: a 5-HT₃ antagonist that targets a certain serotonin receptor found in the vagus nerve and the brain in order to treat nausea and vomiting mainly for cancer treatment and off-label for morning sickness in pregnancy

Prochlorperazine: a dopamine D₂ receptor antagonist used as an antiemetic for chemotherapy, radiation therapy and pre/post operative setting

Longstreth, G. F., & Hesketh, P. J. (2016). Characteristics of antiemetic drugs. Retrieved from: <https://www.uptodate.com/contents/characteristics-of-antiemetic-drugs>

DuPont provided an interactive article entitled "Medicinal Use of Marijuana" to objectively bring to light the ethical question of medicinal marijuana (2). In a selected case, a 68-year old patient named Marilyn suffers from breast cancer that has metastasized to

the lungs and spine. She is undergoing chemotherapy and complains of fatigue, minimal appetite, and spinal pain. To alleviate her symptoms, Marilyn is taking antiemetic medication (ondansetron and prochlorperazine) for nausea, along with acetaminophen and oxycodone for her pain. So far, her medications have had minimal success. Marilyn asks her primary care physician about the possibility of using marijuana to help alleviate the pain, nausea, and fatigue. This article presents two physicians' opinions: to use or disuse medicinal marijuana.

Psychiatrist Dr. J. Michael Bostwick recommends the use of medicinal marijuana. He argues that, despite limited research on cannabis, there is growing literature on its efficacy, though mostly anecdotal. A dearth of research is mainly attributed to the federal ban on the production, buying, and selling of marijuana. "Federal policy has failed to keep pace with recent scientific advances," he argues.

Dr. Bostwick sheds light on the most abundant cannabinoids in the marijuana plant: THC, or Δ^9 -tetrahydrocannabinol, and cannabidiol (CBD). These cannabinoids are structurally similar to the trace cannabinoids in our brains, called endocannabinoids. These endocannabinoids bind to these respective receptors on the presynaptic cell after neurotransmitters bind to the postsynaptic cell. Cannabinoids thus regulate the amount of neurotransmitter released and its duration. When THC is inhaled into the lungs, it quickly flows through the blood-brain barrier, where it binds to cannabinoid-1 (CB_1) receptors and prevents the neurons from resting in between action potentials. Neurotransmitters continuously flow from the presynaptic cell to the postsynaptic cell. This alters one's mood, cognition, and sense of reality.

Under the auspices of the FDA, no trials "have compared medicinal marijuana with traditional analgesics." The federal law limits research on marijuana and its components. Studies are seldom done on its psychiatric and neurological side effects due to its national ban. While some say that marijuana has no business being used in a clinical setting, many Schedule I drugs, such as heroin, morphine, codeine and ecstasy have legal medicinal derivatives. The structures of THC and CBD, for instance, differ only

by an esterification of a hydroxyl group. Furthermore, no vaporized inhalants are currently available in the United States as an alternative to marijuana, and oral cannabinoids are "ill suited to relieving Marilyn's acute distress." It is with this in mind that Dr. Bostwick would recommend the medicinal use of marijuana only after conservative options have failed and the patients are fully informed.

In opposition to medicinal use of marijuana are anesthesiologist Dr. Gary M. Reisfield and psychiatrist Dr. Robert L. DuPont. It is interesting to note these two doctors' areas of expertise: Dr. Reisfield has had fellowships in pain medicine and addiction medicine; Dr. DuPont served as the second White House Drug Czar (1973-1977) and has been on the forefront of marijuana prohibition. In their segment of the article, Drs. Reisfield and DuPont argue two main points. Firstly, there is not enough evidence to support the use of smoked marijuana for nociceptive pain. There has not been a meaningful amount of research done on the analgesic effects of smoked marijuana, as opposed to the high-quality research supporting medicinal use of specific cannabinoids. Additionally, the cannabis plant contains hundreds of pharmacologically active compounds, most of which have not been properly examined. Perhaps the use of smoked marijuana following chemotherapy would cause more harm than good to the patient. Could these unknown active compounds destroy the already weak brain cells, immune cells, or lymphatic cells? Too much is left uncertain with regard to the use of smoked marijuana.

Secondly, prescriptions of specific cannabinoids are available, including dronabinol and nabilone. Both of these compounds are quite similar to THC and are FDA-approved for the treatment of chemotherapy-related nausea. These drugs have shown to be effective, but are orally administered and demonstrate slower onset. Nonetheless, dronabinol and nabilone are chemically pure and have precise dosages.

After the article was published, 1,446 readers participated in a poll about recommending the use of medicinal marijuana. Interestingly, this prompted a subsequent article explaining the results with 76% in favor of the use of marijuana for medicinal purpose and that most of the votes came from countries in

which this use is illegal. However, this poll was concluded as skewed; over 1,000 (73.5%) of the votes polled were from North America. Given that North America represents a minority of the NEJM readers, the surveyors concluded that the topic (namely, use of medicinal marijuana) “stirs more passion among readers from North America than among those residing elsewhere” (3).

Discussion

After reading these two positions, it seems the most crucial factor to this ethical question is the lack of research. Because of the federal ban on marijuana, there is minimal literature and study on the topic. Drs. Reisfield and DuPont express a fear of the unknown. There is tremendous uncertainty regarding the hundreds of compounds in the cannabis plant. Yet, scientists cannot determine these compounds, their effects when smoked, and their impact on cancer patients. Furthermore, physicians in states that have legalized prescription marijuana face, as Dr. Bostwick puts it, a catch-22: “Although 18 states have legalized medicinal marijuana, physicians in those states who write prescriptions violate the law of the land.” If prosecuted enough times, these doctors could face significant time in prison. Although US government is preventing further abuse of marijuana, it is also causing distress to medical patients.

Then again, the enforcement of marijuana laws has not been especially successful. While marijuana law enforcement costs hover over the billion-dollar mark, the drug is still the most consumed illicit substance in the United States, with about 6% of the population having tried marijuana in their lifetime (4). Indeed people can abuse marijuana and become addicted to it. However, this abuse should not result in a total outlaw of the drug. Many drugs are addictive that are still legal, including alcohol, nicotine, and oxycodone. Legalization and regulation would allow for further research on the cannabis plant. This would solve many of Drs. Reisfield and DuPont’s concerns.

Drs. Reisfield and DuPont mention that cannabinoid medications already exist that have been studied and purified. These medications are orally administered, not inhaled. They argue that the option of cannabis inhalants is not necessary. It is only fair that a fully

informed patient should decide if he or she wants to administer a fast-acting inhalant to relieve pain.

The literature regarding adverse effects of marijuana use is quite fuzzy. Some research has shown associations between marijuana use and negative consequences. A 2014 publication from NEJM titled “Adverse Health Effects of Marijuana Use” states that long-term marijuana use can lead to addiction, especially when starting in adolescence when the developing brain is still vulnerable to environmental insults (5). One particular finding shows that frequent use of marijuana can lead to IQ decline (6). However, the 2014 article explains that causality has not been established. The associations of marijuana as a gateway drug have not been confirmed, as there are numerous factors as to how further drug addictions may occur. Furthermore, the relationship “between cannabis use by young people and psychosocial harm is likely to be multifaceted, which may explain the inconsistencies among studies” (5).

Other studies, including a 2009 publication from *The Lancet*, suggest the importance of other factors to the potential issues with frequent marijuana use. This publication refers to data pertaining to the THC content in cannabis in the United States, which has greatly increased from less than 2% in 1980 to 4.5% in 1997 and 8.5% in 2006 (7). This *Lancet* paper, in particular, also presents potential, but mild, adverse effects on neonates when cannabis is given to pregnant mothers, including decreased birth weight and developmental abnormalities in the first couple months of life. However, “no effects were seen at 1 month, or on ability tests at 6 and 12 months.” At 12 years of age, children who were exposed to cannabis prenatally did not differ on full-scale IQ scores from children who were not exposed (8). Additionally, drivers intoxicated with THC have shown impaired reaction time, information processing, attention, and motor performance (9). Many other studies, as presented in a 2004 publication from *Multiple Sclerosis*, have shown favorable results when cannabis is administered to patients with glaucoma, nausea, AIDS-associated anorexia, chronic pain, epilepsy, and multiple sclerosis (10). These are among many other factors that must be taken into account when assessing the usefulness and possible dangers of cannabis use.

Implementation of medicinal marijuana laws may also show economic benefits, especially with regard to federal spending. In a 2016 study from Health Affairs, it is suggested that increased prescription of medicinal marijuana in states that have executed its legality have decreased prescriptions of more traditional FDA-approved drugs for various conditions (i.e., pain, depression, anxiety, seizures). Overall, this led to a reduction of \$165.2 million in federal spending in 2013 for Medicare Part D (11).

Although federal law in the United States of America restricts cannabis research, it is more liberally studied in other countries such as Israel, where THC was first isolated in 1964 (12). A recent study at Sheba Medical Center evaluated the use of cannabis for cancer patients of which the cannabis treatment was defined by referring physicians mainly for palliative care (13). Overall, the results to this study shows that 70% of patients reported pain control improvement, improved appetite by 60%, and reduced nausea by fifty percent. Eighty-three percent of those surveyed reported high overall efficacy.

Conclusion

Patients should have the option to administer medicinal marijuana only if traditional alternatives for pain or other related symptoms have failed and the patient is fully informed. With the policies recently implemented by the Obama administration to study the marijuana in research laboratories, more research in this field is definitely warranted in order to understand the utilization of marijuana for clinical use. Lastly, patients should not become victims of bureaucratic dictums during their time of struggle and pain and the recent actions to study marijuana as medicine indicate that progress is being made.

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Key Point: What is Medicare?

Medicare: a public health insurance program available to patients ≥ 65 years old, < 65 with certain disabilities, and with four distinct parts:

- Part A (hospital insurance)
- Part B (basic medical bills; diagnostic tests)
- Part C (additional care from HMOs/PPOs)
- Part D (prescription drug coverage)

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