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PII: S0002-9343(19)30531-5
DOI: https://doi.org/10.1016/j.amjmed.2019.05.049
Reference: AJM 15234

To appear in: *The American Journal of Medicine*

Please cite this article as: C.B. Johnston and T. Vanderah, Lost in the Haze: The Physician's Role in Cannabinoid Prescribing and Advising, The American Journal of Medicine, https://doi.org/10.1016/j.amjmed.2019.05.049

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Neither author has conflict of interest to report. Both authors had a role in writing the manuscript.

Funding source(s) related to this manuscript: None
Article type: Commentary

Key Words: Cannabis, cannabinoids, marijuana, pharmacology,

Running Head: Physician's Role in Cannabinoid Prescribing

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Ten states and the District of Columbia have legalized cannabis for recreational use and 33 states have legalized cannabis for medicinal use.[1] Although the use of cannabis remains federally illegal, some of its derivative compounds have been approved by the Food and Drug Administration for prescription use (e.g., dronabinol, nabilone, Epidiolex®). According to a 2017 Gallup poll, 64% of Americans favored marijuana legalization.[2]

An increasing number of people are using cannabinoids to treat a variety of ailments. Extracts of cannabidiol (CBD) are proliferating in dispensaries and other outlets across the United States. Individuals and internet websites provide medical guidance - often based on minimal or no data - on what indications should warrant use of cannabinoids.

But where are physicians in this rapidly changing landscape? Increasingly, providers are left behind as dispensaries become the preferred experts on cannabis strains for specific conditions. Many institutions issue prohibitions or confusing policies on whether providers can recommend cannabis, leaving providers bewildered. Cannabis remains a Schedule 1 substance that is still illegal under federal law, and the science of cannabinoid effectiveness lags way behind anecdotal evidence, which understandably makes many providers uneasy in making recommendations regarding cannabinoids for their patients.

The best current evidence suggests that cannabinoids are effective for reduction of seizures in specific disorders, treatment of neuropathic pain, reduction of chemotherapy induced nausea and vomiting, and spasticity in multiple sclerosis.[3,4] The literature is more mixed on non-neuropathic pain, spasticity related to other disorders, weight gain in HIV infection, and sleep disorders. Research on many other medical conditions is largely inconclusive or negative.[3, 4] Which formulations are best for which conditions is still largely unexplored.

Ingestion of cannabinoids is associated with risks, including the anxiety and paranoia that can occur with acute ingestion, in addition to impairment in driving ability.[3,5,6] Cannabinoid ingestion is associated with an increased risk of psychosis and schizophrenia.[3,7] There is an association of cannabinoid use with low intellectual and occupational achievement that could be primarily or wholly due to confounders, but is still cause for concern.[3,8] Cannabinoid compounds may interact with other prescription medications to decrease efficacy or increase toxicity.[9]

One of the main components of marijuana is delta9-tetrahydrocannabinol (THC), the component that results in the euphoric, psychoactive effect that has characterized marijuana as a drug of abuse for many years. THC acts via the CB1 receptor, a receptor that is found widely within the human brain and body.[10] Besides CB1's ability to result in euphoria, a function known to occur in limited areas of the reward system in the human brain, there is little known of all the potential function of such receptor activation in other areas of the human CNS or organs of the body.

A second cannabinoid receptor, a receptor termed CB2, has been reported on immune cells in humans including macrophages, lymphocytes, microglia of the CNS, and osteoclasts.[11] Several studies shave also demonstrated that CB2 receptor expression can be induced on neurons in states of injury and inflammation.[12] Recent studies have also demonstrated their existence on neurons and glia cells of the reward pathway but, unlike CB1 receptors, do not result in euphoria or psychotropic effects and may play a role in reducing rewarding activities of substances of abuse like cocaine and opioids.[11,13]

The field of cannabinoid pharmacology has rapidly propelled toward understanding the endogenous system and how the body may generate its own cannabinoids. Several academic, and industry groups are making novel compounds that will regulate the endogenous cannabinoid system for a number of therapeutic indications. The idea here is to upregulate the endogenous system of cannabinoids that may reduce unwanted effects and act at receptors that may be upregulated during times of injury or disease. Uniquely synthesized cannabinoids are being developed that do not penetrate the CNS, sparing psychotropic effects while still acting on the peripheral nerves, organs, immune system and vasculature.[14]

The ingestion of cannabinoids is varied and complex, including smoking, "vaping", transdermal formulations, gums, and oral formulations. Orally ingested cannabinoids have a much slower onset of action than inhaled cannabinoids, which can increase the risk of inadvertent overdose if the desired effect isn't achieved rapidly enough, resulting in repeated ingestion.[5] Plant based cannabinoids can also contain an array of biologically active terpenoids and flavonoids, further increasing their complexity.

We believe that most providers are put in an impossible bind by the current crazy quilt of conflicting cannabinoid laws as well as the lagging scientific evidence base for the benefits and harms of cannabinoids. Providers need to advocate for a more rational national cannabis policy, beginning with reform of national cannabis laws and reclassification based on the currently available best scientific evidence. We agree wholeheartedly with the recommendations put forward by the National Academy's 2017 Report.[3]

At present, we recommend that providers discuss openly the current state of the evidence for the harms and benefits of cannabinoids. We think that physicians and pharmacists need to familiarize themselves with the basic differences between CBD, THC, and whole plant versus prescription cannabinoids, as well as the pharmacology of different modes of ingestion.

Providers need to know their state's laws and practices regarding regulation of cannabinoid products and what their role is, particularly in states where medicinal use is legal. Cannabinoid dosing labels may not be accurate,[15, 16] and states' policies vary widely in terms of how tightly they regulate cannabinoid production and sales. Health care providers need to caution patients on how they could be impacted by variations in THC or CBD content or possible adulterants, or both based on their own specific state policies. Providers should counsel patients that the use of cannabinoids may alter the pharmacokinetics and efficacy of other medications.[9]

Providers also need to advocate for a standard way of charting cannabinoid use in the medical record. Placing medicinally used cannabinoids under the recreational substances heading stigmatizes patients who are using cannabinoids for legitimate medical indications. Our belief is that cannabis products that are used for medicinal reasons should be included in the herbs and supplements component of the medical record, and that every attempt should be made to include the type of substance (CBD or THC), dosage, and route of administration in the record.

Cannabis use is growing. Legislation, regulation, research, and medical practice need to catch up with the times to protect both the public and well-intentioned health care providers.

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