Medical marijuana is the use of marijuana or “marijuana-like” compounds for medicinal purposes. It has remained essentially illegal in the United States since the Controlled Substances Act of 1970 classified marijuana as a Schedule 1 drug with no accepted medical use, a high potential for abuse, and lack of accepted safety evidence.

The debate as to whether marijuana truly has “no accepted medical use” has heated up dramatically in the past several years as more and more states pass legislation allowing its medicinal use. California’s landmark Compassionate Use Act of 1996 approved medical marijuana use for “seriously ill” individuals with a physician recommendation. As of February 2016, medicinal marijuana is now legalized in some form in 40 states, plus the District of Columbia and Guam. Twenty-three states have comprehensive public programs, while 17 allow low-content marijuana products for limited situations. This paper reviews the science behind the medical use of marijuana.

Pharmacology

The efficacy of medical marijuana is related to its active components, called cannabinoids, and their interaction with the receptors of the cannabinoid receptor system, which was discovered in 1990. The human body produces endocannabinoids, its own natural version of cannabinoids. Endocannabinoid receptors are found throughout the body, but are especially prevalent in the brain. There are two main receptors, aptly named cannabinoid receptor 1 (CB1) and cannabinoid receptor 2 (CB2).

CB1 receptors are primarily located in the brain and spinal cord in areas that affect pleasure, memory, pain, thinking, concentration and coordination. The main cannabinoid in marijuana, delta-9-tetrahydrocannabinol (THC), exerts its action on the CB1 receptors, hence the psychoactive effects commonly associated with marijuana usage.

The second most active cannabinoid in marijuana, cannabidiol (CBD), activates CB2 receptors which are located mainly on the cells of the immune system (e.g. spleen, white blood cells, tonsils). This activation produces no psychoactive effects and may actually mitigate some of the psychoactive effects associated with THC.

Clinical research evidence

Whiting et. al., recently conducted a systematic review of the medical effects of marijuana and concluded that the overall quality of scientific data is poor, and many studies have a high risk of bias and/or conclusions that are not statistically significant. Studies to date have also primarily considered oral cannabinoids and not other forms (e.g. inhaled or ingested).

WHAT YOU NEED TO KNOW

- Marijuana is not a first-line therapy for any medical condition
- Clinical research is lacking for most “approved” conditions
- Medical marijuana includes forms other than smoked herbal marijuana
- Potency and effects differ for smoked versus ingested marijuana
- Ongoing legalization of recreational marijuana complicates the picture
- This is a rapidly evolving landscape and more research is required
In the United States, there are currently two FDA-approved cannabinoid drugs (dronabinol and nabilone) for limited indications (nausea and vomiting due to chemotherapy and anorexia due to AIDS). Both are synthetic THC capsules taken orally, and it is important to emphasize that neither of them are designed to be smoked. An oromucosal spray containing a combination of THC and CBD extracts is currently undergoing phase three clinical trials, but this too is for limited indications (spasticity due to multiple sclerosis, neuropathic pain, and moderate to severe pain in advanced cancer).

Research targeting the various components of the cannabinoid receptor system with a focus on the individual cannabinoids in a more pure, non-smoked form is currently underway. Preliminary studies on a 99 percent cannabidiol (CBD) product with almost no THC have had very favorable initial results for intractable childhood epilepsy (as a syrup/oil) as well as for Parkinson’s disease (as a pill). These formulations provide two favorable therapeutic benefits: avoiding the harmful risk of smoking while also eliminating any adverse psychoactive effects. Researchers are actively investigating the pathways of the cannabinoid receptor system looking for possible enzyme inhibitors that might also produce therapeutic benefits. They are also investigating CBD’s potential role as an anti-inflammatory or anti-cancer drug.

Qualifying conditions
Surprisingly, treatment of many conditions that qualify for medical marijuana by state criteria is not supported by solid clinical research. It appears that approval is largely based on low-quality evidence, anecdotal reports, public opinion, or consensus opinion of an advisory board or council. Even more concerning is that there is no consistency as to how various medical conditions make the list. Some state’s criteria are very broad such that any “serious medical condition for which medical use of marijuana is deemed appropriate by a physician” can qualify.

The most common qualifying condition in Colorado, according to the Colorado Medical Marijuana Registry (as of January 31, 2016) is “severe pain.” The majority of Colorado’s pain patients are male with average age of 42.5 years. Chronic pain is reported more commonly in older-aged women. This has raised speculation that nearly all medical marijuana use in the United States is actually camouflaged access to recreational marijuana. Studies have shown most current users were already regularly marijuana users and 91 percent use for unspecified pain. There has also been a 33 percent increase in frequency of use in teens in states where medical marijuana is available (versus 6 percent increase for the rest of the country) and the adolescent population is well-known to be a high-risk group. One study did suggest lower mean annual opioid mortality rates in states with medical marijuana legislation, but a direct causal link could not be established. There have also been reports that medical marijuana helped people reduce their use of narcotic pain medication, but these are largely anecdotal.

Without clear supporting medical evidence, physicians who have been certifying patients for medical marijuana appear to be doing so with a trial and error approach. There are no clear best practices as to the amount, variety, or dosing regimen especially for smoked marijuana. “Start slow and titrate up” seems like the norm. Many physicians are hesitant to certify patients because they lack the knowledge and confidence to prescribe, worry about possible legal repercussions, and have the added ethical dilemma between providing compassionate care and contributing to adverse outcomes.

Concerns about edible varieties of marijuana
It is estimated that 16-26 percent of medical marijuana users consume edible products. While edibles lack the harmful effects of smoking, they introduce a new concern in delayed effects. THC concentration peaks later in ingested marijuana than when smoked (hours vs. minutes) and effects can last longer (12 hours vs. 2 hours when smoked). A compounding concern is that manufacturing of edible products is not standardized and there is evidence that the labeling of edible products is poor. A group of researchers concluded that only 17 percent of edible products are labeled correctly. Sixty percent contained at least 10 percent less than the labeled amount (some had negligible THC content), while 23 percent contained at least 10 percent higher amounts. Dosing regimens e.g. 1/6 cookie can make patient compliance difficult. These factors can increase the risk for unintentional overdose, intoxication, and, in a high-profile instance, even death.

Marijuana as medicine
Because there has been limited medical research on smoked marijuana, it is difficult to make any valid scientific conclusions regarding its efficacy for medical conditions. The ongoing legislation/decriminalization of recreational marijuana only complicates the picture.
There is a future value for the medicinal use of marijuana in our society, but it may well be found in further research delving into the various components of the cannabinoid receptor system and a focus on the individual cannabinoids in a non-smoked form. “Medical marijuana” does include forms other than the most familiar smoked herbal marijuana and studies are ongoing investigating THC capsules, THC oil, the combination THC/CBD oromucosal spray, and CBD only oils or pills. There is clear evidence that smoked marijuana is harmful and there are more efficacious ways to deliver a drug more consistently and with a better safety profile. Only time will tell the future role medical marijuana will play.

Selected references


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