PARADIGM®

OUTCOMES

Medical and Rehabilitation Innovations

Medical Marijuana

BACKGROUND

The federal government designated marijuana as a Schedule 1 drug under the controlled substance act in 1970. This action classified it as a drug with high potential for abuse and lacking significant medical value. However, there is a growing movement toward legalizing marijuana in the United States with prescription marijuana being accepted in 23 states to date. Recent legalization of recreational marijuana in some states has sparked national and state level debates about cannabinoids from economic, social, political and public health perspectives.

Physicians are prescribing medical marijuana for a variety of symptoms and illnesses, including chemotherapy induced nausea and vomiting, HIV/AIDs related anorexia and cachexia, neuropathic pain, and muscle spasticity associated with Multiple Sclerosis. Although mostly anecdotal, literature suggests a number of unapproved marijuana therapies including but not limited to post-traumatic stress syndrome (PTSD), inflammation, epilepsy and glaucoma.

Marijuana or cannabis is the third most widely used recreational drug in the United States behind alcohol and tobacco, and it takes the top spot for being the most used illicit or illegal drug in the US and Western societies. The popularity of recreational cannabis has been due to its ability to produce euphoria and elation by altering sensory perception. Hence, growers of cannabis plants used selective breeding techniques over the many decades to identify cannabis varietals that had higher psychotropic potency through higher levels of THC or delta-9-hydrocannabinol. As a result, the THC potency in cannabis plants has steadily increased from 3% in the 1980s to 12% in 2012.[1]

The general term “cannabinoids” includes the naturally occurring human body’s endo-cannabinoids, phyto-cannabinoids from cannabis sativa/indica, and synthetic-cannabinoids that refer to pharmaceutically prepared cannabinoid compounds. In addition, research has confirmed the existence of an endocannabinoid system that modulates neurotransmitter networks throughout the human body through cannabinoid-1 (CB1) and cannabinoid-2 (CB2) receptors.[2] These cannabinoid receptors are preferentially distributed in the human body with CB1 receptors being more prominent in the brain and joints while CB2 are found mostly in the gut and immune related tissues.

Studies suggest there could be more undiscovered cannabinoid receptors involved in mediating the analgesic and anti-inflammatory neurobiological mechanism of action.[3] The existence of other potential cannabinoid receptors require more in-depth scientific research and analysis of the human body’s endocannabinoid system, as well as the range of physiologic responses modulated by chemical agonists and antagonists on these additional receptors.

From a medical therapeutic use perspective, there are two major phytocannabinoid chemical compounds identified and known to be abundantly present and biologically active in humans. The best studied and most abundant is delta-9-tetrahydrocannabinol or THC while the second most noted compound is cannabidiol or CBD. The Tetrahydrocannabinol or THC is the CB1

ligand that is primarily associated with psychoactive properties of euphoria and sensory alterations while cannabidiol appears to lack psychotropic activity but works synergistically with THC to maximize analgesic and anti-inflammatory effects. As a result, unlike previous growers of marijuana plants, suppliers with a medical therapeutic focus have fostered some interest in promulgating CBD-rich strains of cannabis plants. In fact, CBD is being considered to have a wider scope of medical applications than THC due to its pharmacodynamics.

It is important to acknowledge that there are at least 80 other cannabinoid related compounds associated with the cannabis plant that have yet to be fully characterized. This research must be completed in order to augment our understanding of cannabis related physiologic actions, efficacy, safety and bioavailability in the human body.

From a pharmaceutical front, synthetic cannabinoids currently available for therapeutic use include Marinol (Dronabinol), Cesamet (Nabilone) and Sativex (Nabiximols). Marinol is a synthesized THC while Cesamet is an analogue of THC currently available in the US. Although not yet approved in the United States, Nabiximols is an oral spray that contains a near 1:1 ratio of CBD and THC. The only other synthetic cannabinoid drug perhaps worthy of mentioning is rimonabant which is a selective antagonist of the cannabinoid type 1 (CB1) receptor. This drug can be considered an "anti-marijuana like agent" due to its effects being opposite of the appetite stimulating, anti-nausea and euphoric effects of THC. This drug is currently approved in Europe as an alternative therapy for obesity.

LITERATURE SUMMARY

Despite the seemingly growing consensus for medicalization of marijuana, there are very few evidence based scientific data and high quality clinical research studies traditionally required to validate and justify the promotion of a therapeutic medication in our medical industry. In addition, due to marijuana's Schedule I status, there has yet to be any FDA supported large clinical trials that compare medicinal marijuana with traditional analgesics. Furthermore, it is even more arduous and complicated to perform a high quality, double blinded, placebo controlled, efficacy study when dealing with smoked herbal cannabis with non-standardized and unknown quantities of potentially active chemical compounds (e.g. different strains of the cannabis plant have different percentages and ratios of the THC and cannabidiol).

Although limited, the following summarizes our understanding of medical literature to date.

1. Oral THC 10 mg was found to be equipotent to codeine 60 mg; while oral THC 20 mg was equally effective as codeine 120 mg in managing pain. The higher dose of oral cannabis or THC is associated with greater a likelihood for adverse effects involving mental clouding, ataxia, dizziness, disorientation, memory impairment, visual difficulties, dry mouth, paranoia and acute psychosis. These adverse side effects of psychomotor, physiologic and cognitive impairment were dose dependent, and the severity and frequency of these adverse effects were higher than those associated with codeine 60 mg and 120 mg.[4]

2. The risk of addiction is clearly present with long-term marijuana use where 9% of those who experiment will become addicted by DSM IV criteria. For those who start during teenage years, the addiction rate is 1 out of 6 (approximately 17%) and 25-50% among those who smoke marijuana daily. There also exists cannabis withdrawal syndrome, with symptoms of irritability, sleep disturbances, dysphoria, cravings and anxiety, that makes cessation difficult.[1]
3. Marijuana related adverse effects include near-term impairment of memory, learning, judgment and decision making. THC may also have a more lasting negative impact on brain development where its interference with cytoskeletal dynamics critical for the establishment of axonal connections between neurons leads to impaired neural connectivity in specific brain regions involved in alertness and awareness, learning and memory, and executive decision making. This raises a significant detrimental implication for a younger aged population of users. In addition, there is an increased risk of chronic psychosis disorders, including paranoia and schizophrenia, in people with a predisposition to psychiatric conditions. Lastly, heavy marijuana use is associated with lower income, a greater need for socioeconomic assistance, unemployment, criminal behavior and a general state of attenuated motivation level.[1]
4. Marijuana definitely impairs motor coordination and driving. Driving performance and fatal accidents are directly related to blood THC concentrations. The overall risk of motor vehicle accidents doubles when a person drives soon after its use. The study reported a significant shift toward impairment for THC serum concentrations between 2 to 5 ng/ml. At concentrations between 5 to 10 ng/ml, approximately 75-90% of the observations were consistent with significant impairment in every performance test. At THC concentration greater than 30 ng/ml, the significant impairment rate was 100%. Hence, THC concentration between 2 to 5 ng/ml established the lower and upper range of THC limit for impairment.[5]
5. So far, the risk of lung cancer and increase in vascular disease such as MI, TIA and CVA with marijuana use is unclear.[1]
6. The pharmacokinetics of smoked or inhaled marijuana result in rapid maximum blood levels of THC with the psychoactive effects peaking at 30 to 60 minutes. Oral or ingested marijuana is more slowly absorbed with THC concentration in the blood rising over 1 to 3 hours with delayed onset of somatic and psychoactive symptoms but with longer duration of effects. In addition, the oral marijuana will be subject to the body's first pass hepatic metabolism which can further vary the actual amount of THC reaching target tissues.
7. There is currently no clear optimal dose of marijuana or any of its chemical components for its various approved conditions.[6]
8. A synthetic CBD analog of tetrahydrocannabinol CT-3 has been found to be a potent anti-inflammatory, analgesic and antiallodynic agent without the psychotropic effects in a study involving 21 patients.[3]
9. Medical marijuana growers have developed a strain of cannabis plant called Avidekel that is high in CBD but very low in THC. In fact, unlike the other cannabis plants, Avidekel has 15.8% CBD and less than 1% of THC which has the highest CBD to THC ratio of any other variants developed to date.[7]

10. A randomized, placebo-controlled trial with cannabis cigarettes to treat neuropathic pain showed a mixed linear model demonstrating some analgesic response to smoking cannabis and neuropathic pain. However, there were no effects noted with evoked pain, and psychoactive effects were dose dependent with acute cognitive effects, particularly with memory related functions. The study's authors concluded there may be some evidence that cannabis is effective in ameliorating neuropathic pain if the patient does not respond to or was unable to tolerate other traditional drugs. The use can be limited by method of administration and acute cognitive effects at higher doses.[8]

PARADIGM OUTCOMES' POSITION

The topic of medical marijuana is very complex with a gamut of allegations and implications that vary from social, political and economic perspectives. It is beyond the scope of this position paper to address the overall merits of medical marijuana for our society. Our objective is specific to identifying the efficacy and safety of medical marijuana based upon evidence based medicine for the restoration of functional abilities to enable return-to-work or recover productivity of injured workers.

Despite the current public sentiments driving the medical marijuana and legalization movement, there is currently inadequate and insufficient amount of scientific data or scientific evidence to support or validate the current use of medical marijuana in the form of herbal plants or FDA approved pharmaceutical synthetic cannabinoids in the treatment of workers' compensation related injuries and health conditions. The overwhelming conclusion is the need for more high-quality research and clinical trials to better understand the actual health-modulating active chemical compounds of cannabinoids, as well as their respective degrees of beneficial and deleterious health effects. In addition, there is an explicit need for more research into therapeutic potential of synthetic or pharmaceutically pure cannabidiol compounds (CBDs) that is noted to have more targeted health effects and fewer psychoactive and negative symptoms in defining the utility of cannabinoids in medicine.

Summary

There is currently insufficient evidence based medicine data to explicitly support the use of medical marijuana in facilitating the functional restoration and recovery of injured workers' medical conditions and injuries.

Help: Therapeutic uses of medical marijuana include treatment of chemotherapy induced nausea and vomiting refractory to traditional anti-emetics, and treatment of anorexia/cachexia and wasting syndrome noted in HIV/AIDs conditions.

Hope: The drug is potentially beneficial in the treatment of muscle spasticity associated with Multiple Sclerosis; managing neuropathic pain refractory to conventional therapy options; treatment of glaucoma; epileptic seizures; and obesity.

Hype: The growing list of therapeutic uses for a wide range of medical conditions including ulcerative colitis, Crohn's disease, rheumatoid arthritis, fibromyalgia, migraine, diabetic neuropathy, PTSD, sleep apnea, adrenal disorders and psoriasis.

ENDNOTES

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