ASRA STATEMENT ON CANNABIS

Approved by the ASRA Board of Directors, September 30, 2016

Background

The plant commonly known as marijuana, a general term for species of the genus cannabis, has a long-held reputation for its psychoactive and medicinal properties. For much of the 20th century, the plant has been criminalized worldwide. In recent years, there has been greater interest in the medicinal properties of marijuana given its potential benefits for various conditions that lack effective treatments, including pain.

Evidence for Pain Management

With respect to pain management, a small evidence base is available in the peer-reviewed literature and consists of clinical studies and systematic reviews/meta-analyses evaluating cannabis as an analgesic to alleviate pain associated with clinical conditions, including (but not limited to) neurological disorders, cancer, and rheumatic diseases.1

The American Academy of Neurology (AAN) published a systematic review and clinical guideline report regarding the safety and efficacy of medical marijuana in neurologic disorders, and provided support for the use of specific oral and oromucosal forms of cannabis to improve some symptoms in patients with multiple sclerosis (MS). They concluded that there is strong evidence that medical marijuana can help lessen central pain associated with MS and is “probably effective” for spasticity, painful spasms, and urinary dysfunction associated MS.2,3,4

Several systematic reviews have been published regarding chronic pain and spasticity,1 spasticity-associated pain from MS,4 pain associated with cancer,5 chronic neuropathic pain,6,7 and rheumatic diseases.8,9 The overall quality of available clinical studies regarding the safety and efficacy of marijuana for the treatment of pain is hampered by several limitations, including variability in the form and dosage of cannabis administered, the lack of generalizability of patient populations, and the lack of blinding of patients and assessors.1

Addiction and comorbidity

A recent study estimated that the 12-month prevalence (2012 to 2013) for cannabis abuse was nearly 3% among adults in the United States.10 The users most likely to become addicted are those who begin use at a young age and use heavy amounts of marijuana daily, as opposed to older adults using small amounts for symptom relief (this group is at higher risk for dependence).11 Individuals with pre-existing mood disorders are more susceptible to addiction and dependence. Approximately 61% of those who meet the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria for marijuana dependence and 31% of those who meet the criteria for marijuana abuse also have a mood disorder.
Of those who meet the DSM-IV criteria for cannabis dependence, 61% have a mood disorder and 46% have an anxiety disorder. For those who meet the criteria for marijuana abuse, these proportions are 36% and 25%, respectively.\textsuperscript{12}

Marijuana use has been shown to alter normal neural connectivity and brain structure. The adolescent brain may be particularly susceptible to the effects of marijuana use. The structural connectivity and grey matter volume of the orbitofrontal cortex (OFC), the primary reward center of the brain, is lowered in chronic users. One study concluded that chronic marijuana use can lead to neuroadaptive changes in the brain, which are modulated by age and duration of use.\textsuperscript{13} Adolescent use has been associated with lower IQ, even in adults who later stopped, suggesting that the changes to the brain may be permanent. Additionally, use in adolescence has been associated with adverse psychiatric outcomes. The innate endocannabinoid system in humans is believed to have an important role in normal development, thus, marijuana use among adolescents is suspected to disrupt the normal process at a crucial point in development.\textsuperscript{14} A recent study on adolescent rats found that chronic cannabis use did in fact lead to long-lasting changes in the prefrontal cortex. The study suggests that cannabis may impede the structural maturation of neuronal circuits in the prefrontal cortex.\textsuperscript{15}

When smoked, marijuana has been shown to affect lung function, which may be a special concern for immunocompromised patients, such as those living with HIV/AIDS or undergoing cancer treatment. Smoking marijuana can affect mucociliary clearance in the lungs by causing loss of cilia and increasing mucus secretion. In addition, some cannabinoids have been shown to exert an immunosuppressive effect by impairing alveolar macrophages and microbiocidal abilities of the lungs. This may increase the risk of lower respiratory infection.\textsuperscript{16} HIV positive patients have an increased rate of respiratory infections and chronic airway diseases, such as bronchitis. These respiratory issues are the results of an altered microbial profile in the airways, as well as suppressed mucociliary clearance. Smoking marijuana can compound the effects of HIV on the lungs.\textsuperscript{17} Another concern with smoking marijuana is that the leaves of the plant could be contaminated with microorganisms such as mold, which present as an additional risk for immunocompromised patients.\textsuperscript{18}

**Legal Status**

As of May 2016, a total of 24 states, including the District of Columbia, have enacted laws to legalize medical marijuana with varying possession limits. Four of these states have also legalized marijuana for recreational use. However, these state laws are in conflict with federal laws. At the federal level, the United States Drug Enforcement Administration (DEA) has classified marijuana as a Schedule 1 controlled substance as a part of the Controlled Substances Act (CSA). Schedule 1 substances are illegal and considered to be the most dangerous, meaning they have “no currently accepted medical use and a high potential for abuse.”\textsuperscript{19} Consequently, health care providers are caught in the crosshairs of this legal contradiction since dispensing marijuana for any reason is a felony under federal regulation.

The classification of marijuana as a Schedule 1 drug has hindered the generation of scientific evidence to evaluate the risks and benefits of marijuana use for medical purposes. Limitations imposed by federal agencies involved in approving clinical trials create challenges for investigators to conduct rigorous clinical research. Researchers must collaborate with three federal agencies in order to obtain study approval. Per the CSA, investigators are required to register with the DEA to obtain a site license, and submit an investigational new drug application (NDA) with the FDA. If a study is approved, the marijuana preparation must be obtained from the National Institute on Drug Abuse (NIDA).\textsuperscript{20} As a result of these barriers, there remains a dearth of high quality evidence available in the peer-reviewed literature regarding both the safety and efficacy of marijuana treatment.
State law reform for medical marijuana is also hindered by its classification as a Schedule 1 drug. In 17 states that had enacted a medical marijuana law by 2013, cost saving benefits to Medicare Part D have been observed. Prescriptions for FDA-approved drugs decreased substantially, and cost savings amounted to $165.2 million in the year 2013 because marijuana can serve as an alternative treatment for a range of conditions. Medical marijuana is a possible way to alleviate budgetary constraints for Medicare programs, however, the conflict between federal and state law makes this reform more difficult.\(^2\)

Furthermore, as more states enact laws legalizing marijuana use, in conflict with federal regulation, many health care providers face difficult legal and ethical questions regarding providing their patients access to medical marijuana.\(^2\) More importantly, the gaps in clinical knowledge and unanswered questions regarding the safety and efficacy, dosing, potency, interactions, and side effects place the increasing numbers of patients who seek marijuana treatment in states that have legalized its use at unnecessary risk. Although anecdotal evidence and observational clinical studies may increase public support for medical marijuana, such evidence must be further confirmed by rigorous, well-designed clinical trials.\(^2\)

**ASRA calls for rescheduling marijuana**

ASRA strongly encourages the federal government to remove research barriers by downgrading marijuana from a Schedule 1 to a Schedule II substance, a classification under which cannabis could be studied in clinical trials, similar to other pharmaceutical agents with a high potential for abuse, but still possessing medical benefits.

**ASRA calls for more clinical outcome research**

Expanded research, which is only feasible if marijuana is rescheduled to a Schedule II classification, will bolster the emerging evidence base to better inform healthcare providers about those patients most likely to realize the greatest treatment benefit from marijuana. In addition, further research will aid in the development marijuana-based agents that have minimal psychoactive properties and minimal association side effects, while retaining its beneficial therapeutic effects.

ASRA pleads to the National Institutes of Health (NIH) to implement special guidelines to encourage grant applications and the conduct of well-designed clinical research on the medical utility of various Cannabis preparations.

Further clinical research is also needed to determine and better understand the long-term safety profile for the utilization of marijuana for pain management purposes. In addition, comparative studies are needed to examine the clinical efficacy and safety of marijuana in comparison to other analgesic classes.