January 21, 2016

Senate committee: Senate Heath and Public Welfare.

Consideration of SB 489 regarding medicinal hemp.

Chairman O'Donnell, committee members, this bill is built to disguise marijuana legalization for medical purposes by calling it "Hemp" which it clearly is not. This is another effort by the persistent and disingenuous marijuana lobby to put lipstick on a pig.

While the alleged intent of the hemp provisions of this bill were presented as narrow scope legislation to only supposedly allow cannabidiol to be available to help a limited number of patients with rare seizure disorders, the real intent appears to make true marijuana available to patients and thus broadly allow for "medicinal" purposes by disguising it as hemp. However, it allows for 3% THC rather than 0.3% THC which really means that it allows marijuana, and it IS psychoactive at that percentage.

If the intent is to allow this marijuana-like substance to be used for seizures, then the THC content should be 0.3% or less. There is no mention of CBD concentration requirements, which would be the actual substance that shows some promise for helping seizures despite uncertain dosing and safety concerns.

Making marijuana, hemp, or <u>any drug</u> available to the public by a legislative vote, bypasses the Food and Drug Administration requirements that demand careful research on the effectiveness of a drug as well as effective and toxic doses. The support for such a mistake is largely driven by anecdotes and unscientific individual observations- <u>not</u> borne out in research. Would you proceed this way for any drug other than marijuana?

Critical questions that you must ask as a governing body include:

1). Is there a clearly effective dose of the "hemp oil" that is safe and effective?

2). What toxic effects are present and how will they be monitored?

3). Who will standardize the available CBD or THC concentrations and certify them?

4). What sources and concentrations of CBD will be allowed?

5). What infrastructure is needed to safely monitor this and what is the cost to Kansas?

6). What is the requirement for medical follow-up and monitoring?

7). Would Kansans be better served by funding dedicated to these neurological disorders, and if so, why is the legislature singling out very rare disorders over others? Researchers at the KU Medical center have expressed willingness to research CBD use for seizures if funding were provided.

8) Since hemp is visually indistinguishable from marijuana, how will law enforcement be hindered?

9) While there is some medical evidence that Cannabidiol may be useful for certain seizure disorders, the dose concentration is not yet determined. There does not exist compelling solid data that marijuana is beneficial for any of the other conditions that it is being proposed for.

10) Provisions within this bill disallow tracking of the "prescribing" that we require with prescriptions drugs in the KTracs system.

To date, there is no evidence of any medical disorder or group of suffering patients for which marijuana or CBD is the only alternative or is superior to the available medicines. Bypassing the FDA opens doors to great difficulties such as those seen in Colorado where purity and dose consistency have been great problems. Most importantly, bypassing the FDA creates a dangerous environment of **Medicine by Popular vote,** such a move would jeopardize the public

Active pharmaceutical research is underway to find pure, safe, reliable, and effective doses of CBD. GW Pharmceuticals is conducting four randomized, placebo-controlled, double blind clinical trials, two in Dravet Syndrome (DS) and two in Lennox Gastaut Syndrome (LGS). The LGS and the first DS trials are fully recruited. The second DS trial is still accepting patients. Results from the fully enrolled studies are expected in H1 2016.

There are also a few state-initiated expanded access programs that are accepting patients. Patients or families who are interested in participating in the DS RCT or the state EAPs should send an email to: medicalinfo@gwpharm.com.

For background, in addition to practicing Internal Medicine, Addiction Medicine, and Pain medicine for thirty years, I serve as the Chairman of the Institute on Global Drug Policy. This international drug policy think-tank that contains some of the top world experts on marijuana. I have personally worked over thirty-five years for healthy drug

policy that, among other things, advocates against the legalization or normalization of marijuana. I have spent ten years as the medical director of a chemical dependence unit. I am attaching several important articles and medical research with my written testimony

Thank you for your consideration
Eric A. Voth, M.D., FACP

Supporting Attachments:

NBC News 3/23/15

This is not your father's weed.

Colorado marijuana is nearly twice as potent as illegal pot of past decades, and some modern cannabis packs triple the punch of vintage ganja, lab tests reveal for the first time.

In old-school dope, levels of THC — the psychoactive chemical that makes people high — were typically well below 10 percent. But in Colorado's legal bud, the average THC level is 18.7 percent, and some retail pot contains 30 percent THC or more, according to research released Monday.

"That was higher than expected," said Andy LaFrate, president of Charas Scientific. His Denver lab is licensed by the state and paid by marijuana businesses to measure the THC strength in their products before they go to market. "It's common to see samples in the high 20s."

How the pros make legal marijuana

CNBC

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What's really in — and not in — Colorado's retail weed surprised LaFrate. After analyzing more than 600 samples of bud provided by certified growers and sellers, LaFrate said he detected little medical value and lots of contamination. He presents those findings Monday to a national meeting of the American Chemical Society, a nonprofit scientific group chartered by Congress.

"We don't want to be alarmists and freak people out, but at the same time we have been finding some really dirty marijuana," LaFrate told NBC News.

Some green buds he viewed were covered in funghi — and he estimated that several marijuana flowers were "crawling" with up to 1 million fungal spores.

"It's a natural product. There's going to be microbial growth on it no matter what you do," LaFrate said. "So the questions become: What's a safe threshold? And which contaminants do we need to be concerned about?"

For example, he also examined more than 200 pot extracts or "concentrates" and found some contained solvents like butane. All the tests were done with high-performance liquid chromatography, a method to separate, classify and measure individual compounds.

What LaFrate didn't see, however, also astonished him. The 600-plus weed samples generally carried little or no cannabidiol, or CBD — the compound that makes medical marijuana "medical." The average CBD amount: 0.1 percent, his study reports.

CBD is anecdotally known to control depression, anxiety, and pain. About 200 families with ill children also moved to Colorado to access a strain called Charlotte's Web, which appears to control seizures in some kids.

"It's disturbing to me because there are people out there who think they're giving their kids Charlotte's Web. And you could be giving them no CBD — or even worse, you could be giving them a THC-rich product which might actually increase seizures," LaFrate said. "So, it's pretty scary on the medical side."

The majority of samples tested came from recreational-pot merchants. Under Colorado law, recreational weed must be tested for potency. Some medical-pot sellers voluntarily provided samples to LaFrate. Colorado does not require pre-sale testing of medical marijuana. LaFrate did not analyze any edibles.

"Really, there is very little difference between recreational and medical in terms of the THC-to-CBD ratio, at least at the aggregate level," LaFrate said.

What does that mean for buyers? There may be little difference in how various strains make users feel, even though some people claim one type induces relaxation and another hikes alertness, LaFrate said.

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"These samples are representational, I think, of what's happening here in the state and, probably, across the country," LaFrate said. "Because most of the new states coming online with medical or retail marijuana have people from Colorado coming in to set up those markets.

"We found there's a tremendous amount of homogeneity within the genetics, at least as far as potency."

But some legal weed producers have launched new breeding projects, using different genetic combinations to boost CBD content, said Sean Azzariti, a cannabis advocate in Denver.

Azzariti also champions contamination testing as "an integral part of our industry."

"I personally am very excited to see technology in testing continue to advance. You would be very hard pressed to find a garden that hasn't at one point had some sort of issue, whether it's an infestation, microbial problems," said Azzariti, an Iraq War veteran. He uses cannabis to help treat post-traumatic stress disorder.

On Jan. 1, 2014, he became Colorado's first buyer of legal weed.

Meanwhile, pot-legalization opponents are using LaFrate's findings to compare retail weed to food raised or grown with genetically modified organisms or GMOs. And pot foes continue to link the rise of the marijuana industry to the long-ago advance of Big Tobacco.

"This study is further evidence that Colorado legalization is not working. It proves that even under government control, there's no way to ensure marijuana is free of bacteria and chemicals," said Kevin Sabet, president of Smart Approaches to Marijuana (SAM). "This shows that marijuana is a GMO product just like other products sold by big business. And just like other industries, now you have a big marijuana industry determined to hide these findings from the public. Where is their outcry? Where are the promises to change the way they do business?" Sabet said. "I won't hold my breath. For years, the tobacco industry did the same thing. Welcome, America, to Big Tobacco 2.0 — Big Pot."

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June 23, 2015

ATLANTA (WXIA) –

It's been one week since the State of Georgia began providing a legal way for Georgians who have certain medical conditions to possess and use medical marijuana, in the form of cannabis oil; the patient must submit a doctor's written permission to the state, and then receive a state registration card.

But some physicians are raising some serious red flags. They are uneasy or unwilling to give their patients that written permission.

They want patients, at least, to understand that there are risks, despite all the success stories that have dominated the news about Georgia children who suffer from severe, untreatable seizures getting better after their parents administer treatments of cannabis oil.

http://www.11alive.com/story/news/health/2015/06/16/medical-marijuana-registry-unveiled/28796627/

"We've seen children that have had rather severe reactions while on medical marijuana products," said Amy Brooks-Kayal, M.D., a Colorado pediatrician who is president of the American Epilepsy Society. "We don't know if that's from the medical marijuana product or something else, because it wasn't done in a controlled setting."

Dr. Brooks-Kayal supports the clinical trials underway now across the country, and advises parents not to treat their sick children with cannabis oil until clinicial trials are complete.

"Just because a single child or person or even a few may respond well to a treatment, that doesn't mean that the majority of them will," she said.

In Colorado, "the success stories are very heartening," yet she said that only one-third of parents who administer medical marijuana to their children report seeing any benefits from it. She said that in 20 percent of the cases that a team from Children's Hospital in Colorado reviewed, seizures worsened with the use of cannabis oil.

She warned that some manufacturers and dealers in the unregulated market place could be selling parents "who knows what" disguised as cannabis oil, which may or may not

have the correct ratios of THC and CBD appropriate for varous groups of patients, and may contain contaminants.

"They can't be guaranteed of the quality of the product that they are using," she said. That's what Augusta physician Yong Park said at the Georgia State Capitol last week to the state commission that's drawing up regulations for medical marijuana in Georgia. Dr. Park is helping run the clinical trials in Georgia.

"You've got to have scientific evidence, and know what the drug interactions are, what the side effects are," Dr. Park said. "We don't have those data yet. That's the biggest [issue] that's very concerning. So this is the patient's own risk," since it is difficult to know whether the supplier is delivering the right mix of THC and CBD. "How do you know that that's the correct one? How much pesticides are in it? We don't know the long term effect to the brain development."

"Physicians are concerned," said Atlanta pediatrician Cynthia Wetmore, M.D., Ph.D. Under the new state law, when doctors sign a letter approving patients for the state registry that allows them to possess medical cannabis oil, "they are required to keep track of the patients. But how do we know what dose to recommend? The oil patients have access to is not standardized. Each batch can be different. There's a lot of variability in each batch. What side effects is it causing, if any? We have to report to the state on each patient, quarterly. It will be hard to know if it's helping or hurting."

Dr. Wetmore is working with Dr. Park on the clinical trials in Georgia. She is a physician with the Department of Pediatrics, Division of Hematology/Oncology, at Emory University School of Medicine and Children's Health Care of Atlanta.
She has, in other states, worked with patients who were using forms of medical marijuana as part of their treatments. "I would tell them, 'Please stay in touch on how it is helping or not,' just as I would with patients who chose to take any other sort of herbal supplement. And a number of my patients saw reduced numbers of seizures, they were better able to talk. I do believe the oil helped. I'm excited about the trials here in Georgia."

As of now, would Dr. Brooks-Kayal recommend to the parents of her young patients that they treat their children with medical marijuana?
"I would, only if they were doing it as part of a clinical trial. I would not if I could not guarantee the family the quality and safety of the product that they were using, and if they weren't being carefully observed as part of a clinical trial," she said. "There's no question that this treatment is not without risks. There's no question that it does not work for every child. And what we really need to do is complete the good clinical research studies that will get us the answers -- about which children are going to benefit from this, how should we give it, what do we need to be concerned about, and to make sure that we know that the product that we are giving to people with epilepsy is the highest quality and consistent product that they can get. I don't think we have those answers at this point."

Rep. Allen Peake, (R) Macon, said Monday that parents in Georgia who have registered with the state under the new law are able to buy safe, lab-tested cannabis oil from two, trusted, out-of-state manufacturers. And he said he knows of 17 Georgia families, so far, who have been administering it to their children, and all 17 report that the children experienced reduced seizures and improved cognative ability.
As long as doctors inform their patients of all the risks, he said, they can make their own decisions about it.

And Rep. Peake said that, even though statistics in Georgia are not yet available, "significant numbers of Georgia doctors have signed the permissions to let their patients make their own decisions," based on medical advice.
Peake has repeatedly urged Congress to repeal Federal laws that hinder the use of medical marijuana; he wants Congress to make it legal for people to transport it across state lines, and he wants Congress to establish uniform standards that would asssure that the medical marijuana products are safe and effective.

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Medical Marijuana May Worsen PTSD Symptoms, Increase Violence

Deborah Brauser | December 15, 2014

AVENTURA, Florida — Although a growing number of states have approved posttraumatic stress disorder (PTSD) as a qualifying condition for medical marijuana use, new research shows that the drug may actually worsen symptoms and increase violent behavior.

A large observational study of more 2000 participants who were admitted to specialized Veterans Administration treatment programs for PTSD showed that those who never used marijuana had significantly lower symptom severity 4 months later than those who continued or started use after treatment. Veterans who were using marijuana at treatment admission but quit after discharge ("stoppers") also had significantly lower levels of PTSD symptoms at follow-up.

On the other hand, the highest levels of violent behavior were found in the so-called "starters," those who were not using the substance at admission but who started use after discharge.

At the American Academy of Addiction Psychiatry (AAAP) 25th Annual Meeting, lead author Samuel T. Wilkinson, MD, from the Yale University School of Medicine, in New Haven, Connecticut, told conference delegates that the findings suggest marijuana nullifies the benefits of intensive PTSD treatment.

"This wasn't a randomized controlled trial. But at least in this study, we found that marijuana is not associated with improvement in PTSD and that initiating marijuana was associated with worsening outcomes in a number of measures," said Dr Wilkinson.

Little Substantive Evidence

Despite the fact that a number of states have approved the use of medical marijuana for PTSD, there's little evidence to support its use for treatment of the disorder.

"There have been a few longitudinal assessments, but no randomized controlled trials showing efficacy and safety," added Dr Wilkinson.

The investigators evaluated data from the Northeast Program Evaluation Center for veterans who were admitted across the United States between 1991 and 2011 into specialized intensive PTSD treatment programs lasting a mean of 42.5 days.

A total of 2276 representative veterans were included in this analysis. They were split into four groups: in addition to the marijuana starters (n = 831), those with no use at treatment admission or after discharge were placed in the "never used" group (n = 850); those using at admission and after discharge were placed in the "continuing use" group (n = 296); and those who quit using after treatment were in the "stoppers" group (n = 299).

All were evaluated at admission and at a follow-up 4 months after discharge. Measures used included the short version of the Mississippi Scale (MISS) to assess PTSD symptom severity, the drug and alcohol subscales of the Addiction Severity Index (ASI), and reports of violent behavior.

Results showed that use of marijuana was significantly associated with higher PTSD symptom severity, as well as higher levels of violent behavior and alcohol and drug use.

Scores on the MISS showed that all groups except the starters had at least some improvement. However, the lowest levels of PTSD symptoms at the 4-month follow-up were in the marijuana stoppers, with a score decrease of 7.9% ($P < .0001$ vs the continuing users and the starters), and in the never users, with a score decrease of 5.5% ($P < .0001$ vs the starters).

Surprise Finding

Although there were changes in violence scores in all three groups, improvement was significantly less in the starters than in the other 3 groups ($P < .0001$ for all three comparisons). "This was a surprise because generally, marijuana is not thought to be associated with violence. There's been a little bit of literature investigating this, but this was interesting," said Dr Wilkinson.

The starters also had greater severity in scores on both the ASI drug use and alcohol use subscales vs the other three groups ($P < .0001$ for all).

On the other hand, the stoppers had significantly lower severity scores on the drug use subscale ($P < .0001$ vs the other 3 groups) and lower alcohol subscale scores ($P < .0001$ vs continuing users; $P < .001$ vs never users).

"This showed that those who started marijuana did turn to other drugs to cope with residual PTSD symptoms, which is to be expected," Dr Wilkinson said. "However, there was no evidence that those who stop cannabis use turn to other drugs or alcohol."

During the Q&A session after his presentation, an audience member pointed out that there was no implication that cannabis drove PTSD severity and asked whether it could just be that the patients with more severe symptoms use more cannabis.

"There wasn't a sense of that from these data," replied Dr Wilkinson. However, he added that they found only an association and not causation, because the study was not prospective or randomized.

"When we looked at a different analysis, there was a dose response. Those who used more marijuana or who had greater change in marijuana use had worse PTSD symptoms," he said.

When another attendee mentioned that she had seen violent behavior in some veterans who use marijuana and have traumatic brain injuries (TBIs), Dr Wilkinson noted that the investigators did not evaluate whether any of the study participants specifically had a TBI.

A Band-Aid Solution?

Session moderator Carla Marienfeld, MD, told *Medscape Medical News* that public perception has been that marijuana soothes those with PTSD.

"Addiction psychiatrists struggle a lot with how to communicate with our patients about this. People assume that there aren't a lot of risks, but there are some papers starting to show that there really are," she said.

"Most people assume things based on their own experience. So when you talk to patients, they often say, 'it's the only thing that helps me sleep' or 'it's the only thing that calms me down.' But when you actually start looking into the symptoms of whether or not they get better with marijuana use, I don't think studies, at least with these initial data, are going to bear that out."

Although Dr Marienfeld, like Dr Wilkinson, is from the Yale University School of Medicine, she was not involved with this research. She noted that it could be that cannabis is acting as a Band-Aid instead of being a long-term solution.

"Marijuana use may make patients feel better for the short term, and we need to look at that. Does it make things better for a few hours and then it gets worse the next day? That would be an important study to understand," she said.

She added that because Dr Wilkinson presented an association study, "there's not really a take-away for clinicians yet. But I think it's important for them to bear this in mind and watch for this kind of data."

Dr Wilkinson reports having received a past grant from the American Psychiatric Foundation/Janssen through Yale University for a project involving electroconvulsive and cognitive-behavioral therapies.

American Academy of Addiction Psychiatry (AAAP) 25th Annual Meeting: Paper presentation 5, presented December 6, 2014.

Send comments and news tips to news@medscape.net.

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EDITORIAL

Medical Marijuana
Is the Cart Before the Horse?

Deepak Cyril D'Souza, MBBS, MD; Mohini Ranganathan, MD

There is a pressing need to develop new medications for many debilitating conditions. Novel approaches based on marijuana or its constituent cannabinoids, if proven, could be added to the armamentarium of available treatments. In this issue of *JAMA*, reviews by Whiting et al[1] and Hill[2] provide detailed assessment of the pharmacology, indications, benefits, adverse effects, and laws related to medical marijuana and the cannabinoids, and the results and conclusions are consistent. There is some evidence to support the use of marijuana for nausea and vomiting related to chemotherapy, specific pain syndromes, and spasticity from multiple sclerosis. However, for most other indications that qualify by state law for use of medical marijuana, such as hepatitis C, Crohn disease, Parkinson disease, or Tourette syndrome, the evidence supporting its use is of poor quality. State laws vary widely regarding conditions for which marijuana is approved and the dispensable legal limit. Both reviews raise important issues worthy of further discussion.

Author Audio Interview at jama.com

Related articles pages 2456 and 2474

First, for most qualifying conditions, approval has relied on low-quality scientific evidence, anecdotal reports, individual testimonials, legislative initiatives, and public opinion. Imagine if other drugs were approved through a similar approach. The US Food and Drug Administration (FDA) requires evidence from at least 2 adequately powered randomized clinical trials before approving a drug for any specific indication. For most of the conditions that qualify for medical marijuana use, the evidence fails to meet FDA standards. It has been argued that the lack of high-quality evidence reflects the difficulty in conducting marijuana research in the United States. If so, the federal and state governments should support and encourage such research so that high-quality evidence can be generated to guide decisions about medical marijuana use for the conditions for which the existing evidence is either insufficient or of poor quality.

Second, there are inconsistencies in how medical conditions are qualified for medical marijuana use within a state and between states. For example, in Connecticut, psoriasis and sickle cell disease but not Tourette syndrome qualify, even though the supporting evidence for all 3 conditions is uniformly of very low quality. Similarly, posttraumatic stress disorder (PTSD) is approved as a qualifying condition in some but not all US states. These differences reflect inconsistencies in evaluating and applying current evidence toward decision making about qualifying indications for medical marijuana use.

Third, unlike most FDA-approved drugs that typically have 1 or 2 active constituents, marijuana is a complex of more than 400 compounds including flavonoids and terpenoids and approximately 70 cannabinoids other than Δ^9-tetrahydrocannabinol (THC)[3]. These cannabinoids have individual, interactive, and even entourage effects (effects of a compound that are only appreciable in the presence of other compounds) that are not fully understood and that contribute to the net effect of marijuana. Although clinical trials for some of the qualifying conditions and studies in animal models of those conditions have been conducted with individual cannabinoids (eg, THC or cannabidiol [CBD]), given that marijuana has so many constituents, the results of studies with individual cannabinoids (eg, THC or CBD) cannot be extrapolated to marijuana and vice versa. In addition, unlike FDA-approved medications that have a relatively uniform composition, the composition of cannabis preparations can vary substantially in its content of THC and CBD, such that precise dosing may be difficult. Given the variable composition, patients will have to experiment with different strains and doses to achieve the desired effects, without much input or oversight by physicians.

Fourth, some individual cannabinoids are already commercially available in the form of dronabinol and nabilone. These drugs are administered orally, and some published data are available to guide dosing. In contrast, there are few data on dosing smoked medical marijuana for many of the qualifying medical conditions for which it is used.

Fifth, while the acute adverse effects of marijuana are quite well known, the effects of repeated exposure, as would occur with medical marijuana, need further study. Approximately 1 in 10 adult users of marijuana develops addiction, and this number is even higher among adolescents.[4] Tolerance and dependence with accompanying down-regulation and desensitization of type 1 cannabinoid receptors occur with repeated exposure.[5] Based on this profile, marijuana dosing will have to be increased over time to achieve the same effect. A distinct withdrawal syndrome is also well recognized.

There is also a small but definite risk of psychotic disorder associated with marijuana use, as well as a significant risk of symptom exacerbations and relapse in patients with an established psychotic disorder.[6] Thus, explicit contraindications such as schizophrenia, bipolar disorder, or substance dependence need to be identified along with measures to minimize the likelihood that persons with contraindications would be able to obtain medical marijuana. Perhaps US states should establish clinical follow-up programs to monitor long-term outcomes prospectively, especially negative outcomes (eg, new cases of psychosis) in patients with contraindications.

Sixth, the interactions of marijuana with other drugs that may be concurrently prescribed for qualifying conditions need further study. There are claims that medical marijuana may allow patients to lower their opioid analgesic doses. However, the existing evidence does not support this contention.[7,8] Furthermore, there is some evidence of cross-tolerance between cannabinoids and opioids[9] that should be considered in attempting to partially or fully substitute opioids with marijuana in the treatment of pain syndromes. Perhaps medical marijuana should also be included in monitoring databases as has been done for opioids and benzodiazepines, so physicians could have a more complete understanding of the medication profile of their patients.

Seventh, emerging evidence suggests that the endocannabinoid system is critical in brain development and maturational processes, especially during adolescence and early adulthood. The endocannabinoid system is involved in axon elongation, neurogenesis, neural maturation and specification, glia formation, neuronal migration, and synaptic pruning.[10,11] Furthermore, the endocannabinoid system evolves during adolescence.[12] Unlike endocannabinoids, which have short durations of action, exposure to exocannabinoids (present in marijuana [eg, THC]) activates the endocannabinoid system in a prolonged nonphysiological manner. In preclinical studies, adolescent exposure to cannabinoids has been linked to long-lasting alterations in the endocannabinoid system, as well as other neurotransmitter systems.[13] Collectively, these changes in the endocannabinoid system have been linked to affective, behavioral, cognitive, and neurochemical consequences that last into adulthood. Data on the effects of repeated exposure to marijuana among youth must necessarily rely on epidemiological studies, which thus far support the animal data in demonstrating long-term consequences including cognitive deficits and increased risk for psychosis. Careful consideration is needed to determine at what age exposure to medical marijuana is justifiable because of the following factors: (1) brain development continues until age 25 years; (2) the endocannabinoid system is involved in brain development; and (3) cannabinoid exposure during critical periods of brain development is associated with long-lasting changes in behavior and cognition.

Eighth, it is important to understand the mechanism(s) underlying the potential beneficial effects of marijuana or its constituent cannabinoids. Specifically, it is uncertain how or why marijuana could be effective in treating epilepsy, sickle cell disease, PTSD, Crohn disease, psoriasis, or amyotrophic lateral sclerosis—conditions with no obvious common pathophysiology. Perhaps marijuana provides nonspecific subjective relief, similar to the effects of benzodiazepines.

For physicians, the legal implications of certifying patients for medical marijuana remain unclear given the differences between the views of state vs federal government. Marijuana is classified as a Schedule I substance by the FDA, meaning it has no currently accepted medical use and a high potential for abuse from a federal perspective. The prescription, supply, or sale of marijuana is illegal by federal law. Furthermore, it is not known to what extent, if any, a physician who certifies a patient for medical marijuana may be liable for negative outcomes (eg, motor vehicle crashes). It is not known if malpractice insurance will cover liability attributable to physicians certifying medical marijuana use.

In conclusion, if the states' initiative to legalize medical marijuana is merely a veiled step toward allowing access to recreational marijuana, then the medical community should be left out of the process, and instead marijuana should be decriminalized. Conversely, if the goal is to make marijuana available for medical purposes, then it is unclear why the approval process should be different from that used for other medications. Evidence justifying marijuana use for various medical conditions will require the conduct of adequately powered, double-blind, randomized, placebo/active controlled clinical trials to test its short- and long-term efficacy and safety. The federal government and states should support medical marijuana research. Since medical marijuana is not a life-saving intervention, it may be prudent to wait before widely adopting its use until high-quality evidence is available to guide the development of a rational approval process. Perhaps it is time to place the horse back in front of the cart.

ARTICLE INFORMATION

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Medical Marihuana Involved in CA Fatal Crashes

Al Crancer, M.A. Phillip Drum, Pharm.D.

Abstract

In the Medical Marihuana state of CA, marihuana was found in drivers which resulted in 1,551 fatalities in the last 5 years. Nationally, in the 23 states and D.C. with state-approved Medical Marihuana, there were more than 1,000 fatalities in the single year of 2014. In the 27 states with no legal marihuana of any kind there were 1,619 marihuana related fatalities.

If CA marihuana use increases from the 2014 level of 18.8% to the level of WA and AK (two recreational marihuana states) at 31%, we could expect an additional 223 CA fatalities each year, for about 565 fatalities a year.

Alcohol is also heavily involved in the marihuana fatalities with 46% of the marihuana drivers were also impaired by alcohol at 0.05% and 38% legally DUI at 0.08+ BAC.

Despite the heavy use of alcohol by marihuana drivers, alcohol involvement in fatal crashes has increased less than 1% in the last 5 years.

Drivers with marihuana in Medical Marihuana states had a 29% higher involvement in fatal crashes than No Medical Marihuana states. Every percent increase in CA driver marihuana involvement in crashes will results in 19 more fatalities.

The growing legalization of marihuana for recreational use, along with the present Medical Marihuana use will cause a tidal wave of motor vehicle fatalities and injuries. This has already happened in Washington State where the level of drivers with marihuana is almost equal to the level of drivers DUI, the No.1 preventable traffic safety problem.

Table of Contents

Multiple sclerosis and cannabis

A cognitive and psychiatric study

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ABSTRACT

Background: A significant minority of patients with multiple sclerosis (MS) use cannabis, yet no study has examined the possible effects on mentation. Here, we report the emotional and cognitive correlates of street cannabis use in patients with MS.

Methods: A sample of 140 consecutive patients with MS were interviewed with the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) Axis I disorders (SCID-IV) from which details of cannabis use were recorded. Cognition was assessed using the Neuropsychological Battery for MS supplemented with the Symbol Digit Modalities Test (SDMT), an index of information processing speed, working memory, and sustained attention.

Results: Ten subjects (7.7%) were defined as current cannabis users based on use within the last month. Compared to non-cannabis users (n = 130), they were younger ($p = 0.001$). Each of the 10 current cannabis users was matched on demographic and disease variables to four subjects with MS who did not use cannabis (total control sample n = 40). Group comparisons revealed that the proportion of patients meeting DSM-IV criteria for a psychiatric diagnosis was higher in cannabis users ($p = 0.04$). In addition, on the SDMT, cannabis users had a slower mean performance time ($p = 0.006$) and a different pattern of response compared to matched controls (group × time interaction; $p = 0.001$).

Conclusions: Inhaled cannabis is associated with impaired mentation in patients with multiple sclerosis, particularly with respect to cognition. Future studies are required to clarify the direction of this relationship. ***Neurology***® ▪▪▪

GLOSSARY

7/24 = 7/24 Spatial Learning Test; **BSS** = Beck Suicide Scale; **COWAT** = Controlled Oral Word Association Test; **DSM-IV** = Diagnostic and Statistical Manual of Mental Disorders; **EDSS** = Expanded Disability Status Scale; **HADS** = Hospital Anxiety and Depression Scale; **MS** = multiple sclerosis; **NPBMS** = Neuropsychological Battery for MS; **PASAT** = Paced Auditory Serial Addition Task; **SCID-IV** = Structured Clinical Interview for DSM-IV Axis I disorders; **SDMT** = Symbol Digit Modalities Test; **SRT** = Selective Reminding Test; **SSSI** = Social Stress and Support Inventory.

The use of cannabis as a therapeutic agent in multiple sclerosis (MS) is controversial.[1] Unequivocal, objective evidence of efficacy in MS symptom control is lacking, as exemplified by a large scale clinical trial of cannabinoids that failed to find improvement in spasticity as noted on the primary outcome measure, the modified Ashworth score of spasticity.[2] Nonetheless, other data suggest benefits for lower urinary tract symptoms[3] and pain.[4] Furthermore, a significant minority of patients with MS in Europe[5] and North America[6,7] endorse smoking cannabis as an alternative treatment for symptom control, notwithstanding the availability of conventional medications including cannabinoid-based therapeutic agents.

Although cannabis is a well-recognized psychoactive substance known to induce delirium, psychosis, and anxiety in healthy individuals,[8] no study has specifically examined the potentially deleterious effects of cannabis (be it prescribed or smoked illicitly) on

Editorial, page XXX

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SPECIAL ARTICLE

AMERICAN ACADEMY OF NEUROLOGY

Summary of evidence-based guideline: Complementary and alternative medicine in multiple sclerosis

Report of the Guideline Development Subcommittee of the American Academy of Neurology

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ABSTRACT

Objective: To develop evidence-based recommendations for complementary and alternative medicine (CAM) in multiple sclerosis (MS).

Methods: We searched the literature (1970–March 2011; March 2011–September 2013 MEDLINE search), classified articles, and linked recommendations to evidence.

Results and recommendations: Clinicians might offer oral cannabis extract for spasticity symptoms and pain (excluding central neuropathic pain) (Level A). Clinicians might offer tetrahydrocannabinol for spasticity symptoms and pain (excluding central neuropathic pain) (Level B). Clinicians should counsel patients that these agents are probably ineffective for objective spasticity (short-term)/tremor (Level B) and possibly effective for spasticity and pain (long-term) (Level C). Clinicians might offer Sativex oromucosal cannabinoid spray (nabiximols) for spasticity symptoms, pain, and urinary frequency (Level B). Clinicians should counsel patients that these agents are probably ineffective for objective spasticity/urinary incontinence (Level B). Clinicians might choose not to offer these agents for tremor (Level C). Clinicians might counsel patients that magnetic therapy is probably effective for fatigue and probably ineffective for depression (Level B); fish oil is probably ineffective for relapses, disability, fatigue, MRI lesions, and quality of life (QOL) (Level B); ginkgo biloba is ineffective for cognition (Level A) and possibly effective for fatigue (Level C); reflexology is possibly effective for paresthesia (Level C); Cari Loder regimen is possibly ineffective for disability, symptoms, depression, and fatigue (Level C); and bee sting therapy is possibly ineffective for relapses, disability, fatigue, lesion burden/volume, and health-related QOL (Level C). Cannabinoids may cause adverse effects. Clinicians should exercise caution regarding standardized vs nonstandardized cannabis extracts and overall CAM quality control/nonregulation. Safety/efficacy of other CAM/CAM interaction with MS disease-modifying therapies is unknown.

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GLOSSARY

AAN = American Academy of Neurology; **AE** = adverse effect; **CAM** = complementary and alternative medicine; **CBD** = cannabidiol; **CI** = confidence interval; ***DSM-IV*** = *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition; **EDSS** = Expanded Disability Status Scale; **FDA** = US Food and Drug Administration; **FSS** = Fatigue Severity Scale; **GB** = ginkgo biloba; **GNDS** = Guy's Neurological Disability Scale; **HRQOL** = health-related QOL; **MFIS** = Modified Fatigue Impact Scale; ***MS*** = multiple sclerosis; ***MSIS*** = *Multiple Sclerosis Impact Scale*; ***OCE*** = oral cannabis extract; ***PPMS*** = primary progressive MS; **QOL** = quality of life; **RCT** = randomized controlled trial; **RRMS** = relapsing-remitting MS; **SAE** = serious adverse effect; **SPMS** = secondary progressive MS; **THC** = tetrahydrocannabinol; **VAS** = visual analog scale.

Complementary and alternative medicine (CAM) therapies are nonconventional therapies used in addition to or instead of physician-recommended therapies. CAM use is prevalent in 33%–80% of patients with MS,[1-10] particularly among those who are female, have higher education levels, and report poorer health.[1-4,11] This document summarizes extensive information provided in the complete

Supplemental data at Neurology.org

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