



THE JOURNAL OF
GLOBAL DRUG POLICY AND PRACTICE

**Originally published in *Mayo Clinic Proceedings*, July 2016, Volume 91 Issue 7. Reprinted
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Medical Marijuana in Patients Prescribed Opioids: A Cloud of Uncertainty

William C. Becker, MD, and Jeanette M. Tetrault, MD

From the VA Connecticut Healthcare System, West Haven, CT (W.C.B.); and Yale University School of Medicine, New Haven, CT (W.C.B., J.M.T.).

With the widespread prevalence of long-term opioid therapy and rapidly expanding access to marijuana, combination therapy to treat chronic pain conditions has become commonplace. We use a brief case description to illustrate concerns and insights regarding this clinical conundrum.

Case

A 61-year-old man with a history of posttraumatic stress disorder, degenerative joint disease of the lumbar spine, and chronic low back pain presented for routine outpatient follow-up. He is seen in an integrated pain clinic that focuses on opioid safety and multimodal pain treatment; this clinic is prescribing opioids. In addition, the patient is certified by an outside provider to receive medical marijuana based on his diagnosis of posttraumatic stress disorder. As part of the routine safety monitoring at the pain clinic, the patient's name is queried in the state prescription monitoring program (PMP) database. Along with opioids, the results in the past 2 months include "Theraplant 19.62% loose flower, 3.5 g"; "Fioraden B 25.10% loose flower, 3.5 g"; "Nutella-flavored macaroon, 34.98 mg, edible, 0.04G"; and "Fioraleve B wax 1, 13.10% extract, 1 g." Although the patient displays no evidence of loss of control or other unsafe substance use, concerns are raised about the coadministration of opioids and medical marijuana. In addition, from a therapeutic perspective, he is sedentary and deconditioned and reports that pain is significantly interfering with daily functioning and quality of life.

Discussion

With the rapid increase in the number of states that allow medical marijuana (now nearly half), the fact that analgesics are the second most prescribed class of medications in the United States, and the urging of experts to

access PMPs in patients prescribed opioids and other controlled substances, the data contained in this PMP report raise a variety of questions increasingly likely to be faced by providers. The lack of dose standardization of medical marijuana, the unknown risk and benefit profile of combined opioids and medical marijuana, and multiple prescribers of controlled substances are all issues that deserve attention as we better understand the role of medical marijuana in the treatment of patients with chronic pain.

Prescribers of opioids are responsible for ongoing assessment of the medication's safety.¹ As such, we need to know not only a patient's opioid dose but also the doses of other centrally acting or psychoactive medications they are taking, including marijuana. Epidemiologic data show associations between prolonged marijuana exposure and important harms, such as cognitive impairment,² development of addiction, abnormal brain development, symptoms of mental health conditions, symptoms of chronic bronchitis, and measures of air flow obstruction.³ So, how much marijuana is the patient presented in this case receiving? What are the dose conversions for loose flowers, wax, and edible products such as macaroons? With respect to opioid analgesics, many state PMPs now include daily morphine equivalent dose estimates in their reports. We urge development of a similar standardization system to help providers interpret marijuana dose. Furthermore, we call for states to allow dispensing of only those marijuana formulations that have a reliable conversion based on clinical studies. A recent study demonstrating only a 17% accuracy rate in 75 different marijuana product labels from three cities suggests that some states have a long way to go in achieving satisfactory quantification of marijuana dose.⁴

The next important issue is the dearth of information on the safety and potential benefit of medical marijuana combined with opioids.

Recent data concerning the combination of opioids and benzodiazepines is instructive: in a large case-cohort study of individuals prescribed opioids for pain, those prescribed concurrent high-dose opioids and benzodiazepines had a 0.7% annual overdose mortality rate,⁵ which approaches the estimated overdose mortality rate in individuals using heroin (1%).⁶ However, although the potential dangerous interaction between opioids and benzodiazepines is relatively well-established, the interaction between opioids and marijuana is much less well-understood. There are studies suggesting that marijuana augments the analgesia produced by opioids,⁷ potentially allowing opioid dose lowering, thus possibly enhancing safety.⁸ However, if the opioid dose is not lowered and marijuana is added to the regimen, it seems likely that the synergistic effects on psychomotor slowing, depressed sensorium, and delirium would lead to an increased risk of motor vehicle crashes, falls, trauma, and overdose mortality. Furthermore, observational data suggest that marijuana use is associated with opioid misuse in patients receiving long-term opioid therapy⁹ and that recreational prescription opioid misuse is associated with previous use of marijuana among adolescents and young adults.¹⁰ Given this potential complication and the substantial risk of progression from opioid misuse to opioid use disorder,¹¹ screening patients for opioid misuse before considering marijuana certification and throughout cotreatment is strongly advised.

Regarding potential benefit of long-term use of marijuana for chronic pain in the setting of long-term opioid therapy, there are no data on which to make credible recommendations. However, given the decidedly unsuccessful experience in the United States with widespread expansion of long-term opioid therapy, we are not optimistic that the addition of another potentially addictive substance to which individuals become tolerant will achieve real chronic pain treatment success: helping patients achieve functional goals. The growing understanding of chronic pain pathophysiology—neuronal plasticity leading to central sensitization¹²—argues more for durable, low-risk, lifestyle-modifying nonpharmacologic approaches, such as exercise and cognitive behavioral therapy, over loading the brain's reward centers with more

psychoactive substances. The bottom line is that speculation on these issues is not enough; frontline clinicians need clinical science to catch up with decisions they are already being forced to make in everyday practice. Without these data, the primary responsibility of the individual prescribing controlled substances—making an informed assessment that benefit outweighs risk—is impossible.

The final issue that this case illustrates is the conundrum of states legalizing what the federal government still considers illegal. Safety-minded guidelines for opioid therapy strongly recommend a single prescriber (or team) who makes treatment decisions with the patient. This prescriber ideally has full knowledge of the patient's medical history with which to make a thoughtful assessment of risks and potential benefits. Having a single prescriber is not possible in patients using both marijuana and opioids because one cannot legally "prescribe" marijuana. Furthermore, in practice, the medical marijuana certifier may often be someone other than the patient's usual provider. To make a decision about the appropriateness of marijuana therapy in someone already prescribed opioids, there would need to be provider-to-provider communication, a nontrivial task. More importantly, potential conflicts in treatment philosophies among providers may arise. One provider's assessment of potential benefit and risk may be quite different than another's, and guidance on how such a discrepancy should be adjudicated is nonexistent. Finally, issues of provider liability may become complex; in the tragic instance of a patient overdosing who has an opioid prescriber and a medical marijuana certifier, will both be vulnerable to litigation? On balance, we advise prescribers of opioids to maintain the standards they follow with other controlled substances (or illicit ones for that matter, including marijuana). If a prescriber does not support the decision for concomitant use of marijuana, she or he should feel empowered to make ongoing receipt of opioids contingent on cessation of marijuana use.

Conclusion

To improve our ability to guide patients in informed decisions about the use of medical

marijuana in conjunction with opioids, we outlined several suggestions aimed at improving the quality of care. Without dose conversion data, better science on the interaction between marijuana and opioids, and improved tools and data to assess the risk-to-benefit ratio, we recommend avoiding medical marijuana certification in a patient prescribed high-dose opioids. Given the dearth of evidence for long-term opioid therapy for chronic pain, adding more uncertainty with marijuana seems unwise. Until evidence is forthcoming, we recommend that if opioid prescribers do not support patients' concomitant use of marijuana, be it medically certified or illicit, they should make continued opioid receipt contingent on marijuana use cessation.

ACKNOWLEDGMENTS

The authors' views expressed herein do not necessarily represent those of the Veterans Health Administration.

Grant Support: Dr Becker was supported by a Veterans Health Administration Health Services Research & Development Career Development Award (08-276).

Correspondence: Address to William C. Becker, MD, VA Connecticut Healthcare System, Mail Stop 151B, 950 Campbell Ave, West Haven, CT 06516 (william.becker@yale.edu).

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