In chronic pain patients currently prescribed opioids, does adjunctive therapy with medical marijuana result in reduced opioid dosages?

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INTEGRIS

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Answer:

Inconclusive. There are some theoretical pathways, but ongoing research is required for a definitive answer.

Level of Evidence: 2B

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SUMMARY

Clinical Question: In chronic pain patients currently prescribed opioids, does adjunctive therapy with medical marijuana result in reduced opioid dosages?

Answer: Inconclusive. There are some theoretical pathways, but ongoing research is required for a definitive answer.

Level of Evidence: 2B

INTRODUCTION

Marijuana has been used for medicinal purposes dating back over 5000 years. It was prescribed in the US until 1937 when it was banned by Congress despite testimony from the AMA strongly opposing the ban. Medical marijuana was first legalized in California in 1996. Currently, 33 states have legalized medical marijuana including our nation's capital as well as 25 other countries. Oklahoma legalized medical marijuana on June 26, 2018 (1). There have been 314,900 medical marijuana applications received and 295,132 licenses approved in the state of Oklahoma as of May 1st, 2020 (2).

The Oklahoma Bureau of Narcotics states they have no objection to physicians prescribing opioids to marijuana card holders. Physicians are constitutionally protected when they issue recommendations for medical marijuana (3). The current state law requires pain management physicians to actively search for and try strategies to reduce opioid doses in chronic pain patents. This provides physicians with the opportunity for allowing patients to use medical marijuana to reduce opioid dosages.

Currently, the biggest issue regarding medical marijuana is the limited guidance and recommendations for prescribing. Most of the research revolves around the analgesic properties displayed by marijuana. The term "opioid sparing" has been used to describe the mechanism by which marijuana could reduce opioid usage (4). However, there are no current recommendations or guidelines regarding type of medical marijuana, route of administration, dosage, or frequency. This is challenging for prescribers when discussing medical marijuana with patients. Without clear prescribing guidelines, physicians are essentially prescribing a drug without control of how that drug is taken, the dosage of drug, and frequency of drug.

PHARMACODYNAMICS AND NEUROBIOLOGICAL PATHWAYS

The activities of the endocannabinoid system revolve around cannabinoid 1 (CB1) and 2 (CB2) receptors which are scattered throughout the body. CB1 receptors mediate the behavioral and psychotropic effects of cannabinoids while CB2 receptors are concentrated primarily in the peripheral tissues and immune cells where they influence the release of cytokines, chemokines, and cell migration including neutrophils and macrophages and impact the body's inflammatory response. CB2 receptors may also likely affect CYP450 isoenzymes in the liver potentially affecting the metabolism of various medications which may contribute to significantly altered serum levels of drugs (5).

A synergistic effect on analgesia between opioids and cannabinoids has been documented in animal models. These results are based upon the suggested ability of delta-9-tetrahydrocannabinol (THC) to enhance the effects of morphine's interaction with mu opioid receptors by activation of both kappa and delta opiate receptors (6). There have also been reports that cannabinoids increase the synthesis and/or release of endogenous opioids.

SUMMARY OF EVIDENCE

While there is some evidence of medical cannabis use reducing opiate medication use and/or reducing pain in opioid users, these studies are generally small and do not have reliable data to recommend use of medical cannabis. One small retrospective cross-sectional survey of patients with chronic pain showed a 64% decrease in opioid use (7). Another small study with only 21 individuals showed that pain was significantly decreased after the addition of vaporized cannabis to opioid regimen with morphine or oxycodone and concluded that vaporized cannabis augments the analgesic effects of opioids without significantly altering plasma opioid levels (8). Most of the studies we found related to medical cannabis with opioid use were small, survey based, retrospective studies.

Although there is some literature that seemingly supports the use of cannabis with opioids the larger studies are less conclusive about the positive effect of concomitant cannabis use with opioids for chronic non-cancer pain. One large 4-year prospective cohort study that included 1514 participants in Australia looked at the associations between amount of cannabis use and pain, mental health, and opioid use, the effect of cannabis use on pain severity and interference over time, and potential opioid-sparing effects of cannabis

CONTINUED

One large 4-year prospective cohort study that included 1514 participants in. This study concluded that while cannabis use was common in the sample, the patients who had used cannabis had greater pain severity and interference with lower pain self-efficacy and with increased and worse generalized anxiety. There was no evidence that adjunctive therapy with cannabis reduced opioid prescriptions or assisted patients with opioid discontinuation (9).

CONCLUSION

More studies with large, representative samples are needed to make any firm conclusion about cannabis as an adjunctive therapy to opioid analgesics or cannabis to replace opioids for chronic non-cancer pain patients. However, it is important to remember the pharmacodynamics and neurobiological pathways of cannabinoids that suggest synergistic effects with opioids as evidence to suggest their ability to reduce opioid dosages. Given the lack of statistically significant data, we cannot say, at this time, that medicinal marijuana reduces opioid dosages. Currently, there are no standardized guidelines for the introduction or monitoring of adjunct medical marijuana in clinical practice. As an increasing number of states legalizes medical marijuana, further studies should be conducted to develop such standards of practice. It is reasonable to engage in a shared decision-making discussion with appropriate chronic pain patients regarding the possible benefits, risks, and alternatives of adjunct medical marijuana in managing their chronic pain.

Citations

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