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Brief Commentary: Cannabinoid Dosing for Chronic Pain Management

Kevin F. Boehnke, PhD, and Daniel J. Clauw, MD

Editors' Note: This commentary was selected for publication from among 100 submitted manuscripts in response to a call for readers' perspectives on prescribing or recommending marijuana.

As pain researchers, we are underwhelmed by systematic reviews of clinical trials of cannabinoids, which report modest effect sizes for chronic neuropathic pain but limited or insufficient efficacy in other pain conditions (1). These reviews also report substantial adverse events (1). Nevertheless, we cannot ignore the reality of cannabis's growing use as medicine, especially for chronic pain. As such, we believe that appropriately contextualizing cannabinoids is critical so that physicians and patients can navigate this uncertain territory.

Tetrahydrocannabinol (THC) causes most of the risks associated with cannabis, including intoxication, impairment, and addiction (2). By contrast, cannabidiol (CBD) is not intoxicating and is relatively benign (2). Indeed, the Drug Enforcement Administration recently classified the CBD-based product Epidiolex (GW Pharmaceuticals) as schedule V–the least restrictive schedule. The cannabinoid products most studied as therapies for chronic pain are THC-dominant and cause modest analgesia and somnolence (1). Preclinical evidence suggests that CBD has anti-inflammatory and analgesic properties in arthritic conditions (3). CBD also widens THC's therapeutic window when administered concomitantly, increasing the maximum tolerated dose and decreasing the risk for adverse events (2). Although CBD is becoming more available, the medical cannabis market is still skewed toward THC-dominant products (4). In response, we have developed the following framework, which we use when educating patients and physicians about cannabinoids for chronic pain management.

We do not regard cannabinoids as first-line treatments but as adjuvant therapies to be used before opioids if other options fail to control chronic noncancer pain. As with any pain medication, cannabinoids should be used as part of an integrated, patient-centric management program, with particular emphasis on appropriate nonpharmacologic treatment options (for example, exercise, cognitive behavioral therapy, and mindfulness). We recommend selecting products verified for safety and potency by third-party testing. We propose that patients use oral formulations (such as capsules) for long-term relief, with tinctures for breakthrough pain. We suggest vaping for patients who prefer to inhale cannabinoids, because this method probably has fewer adverse effects than smoking. We advocate a "start-low, go-slow" dosing philosophy, applied to both quantity and adverse effect profiles. We recommend starting with CBD extract, 5 to 10 mg twice daily, to be increased weekly over 1 to 2 months until pain relief is achieved. If CBD extract alone provides insufficient relief, we suggest adding THC, 1.0 to 2.5 mg, and slowly titrating up as needed.

We endorse this paradigm because conservative titration, delayed introduction to THC, and flexible administration allow patients to find their optimal personal dosing strategy without being prematurely pushed into using high-dose THC products–some of which contain more than 100 mg of THC per serving (4). Given the growing understanding of how long-term, high-dose opioid use dysregulates the endogenous opioid system (5), we are concerned that consistent, high doses of THC might do the same to the endogenous cannabinoid system. We are satisfied with how our paradigm mitigates such exposure.

Widespread use of medical cannabis is straining medicine's conventional boundaries, as patients venture without guidance into the unknown and return bearing strange medicines that seem strikingly nonmedical. As physicians and scientists, we must be willing to do our part by listening, showing compassion, and using the best available knowledge to support patients and keep them safe on their journey.

From University of Michigan Medical School, Ann Arbor, Michigan (K.F.B., D.J.C.).

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Corresponding Author: Kevin F. Boehnke, PhD, 24 Frank Lloyd Wright Drive, Ann Arbor, MI 48106; e-mail, kboehnke@med.umich.edu.

Current author addresses and author contributions are available at Annals.org.

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Current Author Addresses: Drs. Boehnke and Clauw: 24 Frank Lloyd Wright Drive, Ann Arbor, MI 48106.

Author Contributions: Conception and design: K.F. Boehnke, D.J. Clauw.
Analysis and interpretation of the data: K.F. Boehnke.
Drafting of the article: K.F. Boehnke.
Critical revision of the article for important intellectual content: K.F. Boehnke.
Final approval of the article: K.F. Boehnke, D.J. Clauw.
Administrative, technical, or logistic support: K.F. Boehnke, D.J. Clauw.
Collection and assembly of data: K.F. Boehnke.