Letters to the Editor

Marijuana for Pain Relief: Don’t Jump to Conclusions

To the Editor:
The title of Wilsey et al’s recent study “Low-Dose Vaporized Cannabis Significantly Improves Neuropathic Pain” piqued our interest, as did the abstract that compared the calculated numbers-needed-to-treat of 2.9 to 3.2 favorably to “traditional neuropathic pain medications.” The abstract describes minimal psychoactive effects and deems the overall results as “a clinically significant outcome.” Unfortunately, these conclusions are not borne out by careful examination of this study and contrasting it with other available treatments.

The study involves inhaling cannabis vapor (2 concentrations) or placebo vapor under a hood (4 puffs) and then a second treatment 120 minutes later of 4 to 8 puffs. Outcomes are assessed up to 300 minutes after baseline measurements, which is 240 minutes after initial treatment. The subjects were exposed to all 3 treatments separated by a minimum of 3 days to allow adequate recovery. There was significant reduction in pain following the inhalation of both concentrations of cannabis vapor. All subjects had neuropathic pain (including complex regional pain syndrome) with a median duration of 9 years of symptoms.

This study accurately represents pilot, preliminary data suggestive of a potential beneficial effect. However, it is clear that vaporized cannabis lacks sufficient data to be compared in any way to “traditional neuropathic medications.” When the authors make such a comparison to standard treatments, they must provide evidence that they are comparing apples to apples. Without even looking at the literature, many problems with the authors’ overreaching conclusions are evident.

First, many treatments have initial effects that are not sustained. For subjects with 9 years of pain, how meaningful is pain relief 240 minutes after administering a treatment? Does the effect persist for a day, a week, a month, or 9 years? Does it provide around-the-clock relief? How many times a day must a person administer the cannabis to provide consistent relief? If cognitive effects reportedly diminish with chronic use, does a tolerance to the analgesic effects also develop over time? Are there any other salutary effects that appear or disappear over time? Are there any placebo controlled data of comparable duration to the typical pharmaceutical trial (4–12 weeks)?

Second, how does this laboratory experiment translate to real-life treatment? For a pill or capsule, patients can store the medication in a secure medicine cabinet and take it in essentially any setting. How does use under a hood of a carefully prepared vapor translate to home, work, or public use?

Third, function is becoming an increasingly important outcome measure for pain treatment studies. The subjects in this study were preselected to have had previous cannabis exposure to “reduce the risk of adverse psychoactive effects in naive individuals,” a requirement that is typically not required in other pain treatment efficacy studies and degrades the quality of the reported adverse effects. Additionally, all participants were “accompanied home by a responsible adult,” experienced a significant dose effect for “bad drug effect,” and cannabis produced a “general cognitive decline as indicated by the difference of scores between treatment groups on all tests over time.” Would these effects lessen, worsen, or remain the same over time? Would repeated dosing lead to more impact on function and cognition? It would appear that cognition and the ability to drive are important functional correlates of a favorable clinical outcome. The authors’ conclusion is that the effect sizes seen with learning and memory are “unlikely to have significant impact on daily functioning,” but is this supported by research? The reassurances that nonprospective data for recreational and “medical” users of marijuana reveals fewer negative effects with chronic use falls short of answering these questions. The U.S. Food and Drug Administration wouldn’t allow such data to fill in for prospective data. For the noncontrolled studies, how aware are the patients of the cognitive impairment? Is the patient the best judge of any impairment?

Fourth, for most medications, there is an established therapeutic window, meaning a dose range that is associated with a clinically meaningful response with minimal or controlled adverse effects. What is that window for cannabis? How easy is it for a person to exceed the minimum analgesic dose and end up with more cognitive effects? The researchers were not even able to report on the actual amount of cannabis each patient consumed in the study, aside from numbers of puffs.
Finally, a quick review of the literature reveals many areas of controversy: mental illness correlates with cannabis use,1,3,4,10,18,20 impairment of driving ability,1,2,6,8,9,13,22,23 cannabis use associated with drugs of abuse,16,19,21 impacts on work,12 and other health issues associated with cannabis.3,5,7,11,17,20 Cannabis isn’t just another experimental medication or treatment.3 It has a cultural and scientific context that is unique in our society, and new data are needed to move beyond emotional-based discussions. The burden on researchers to publish valid conclusions is high and was not met in this study.

Sincerely,

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References


