

Virtual Mentor

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OP-ED

Medicinal Cannabis and Painful Sensory Neuropathy

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Painful peripheral neuropathy comprises multiple symptoms that can severely erode quality of life. These include allodynia (pain evoked by light stimuli that are not normally pain-evoking) and various abnormal sensations termed dysesthesias (e.g., electric shock sensations, “pins and needles,” sensations of coldness or heat, numbness, and other types of uncomfortable and painful sensations). Common causes of peripheral neuropathy include diabetes, HIV/AIDS, spinal cord injuries, multiple sclerosis, and certain drugs and toxins. Commonly prescribed treatments come from drugs of the tricyclic and selective serotonin reuptake inhibitor (SSRI) antidepressant classes, anticonvulsants, opioids, and certain topical agents. Many patients receive only partial benefit from such treatments, and some either do not benefit or cannot tolerate these medications. The need for additional treatment modalities is evident.

Animal studies and anecdotal human evidence have for some time pointed to the possibility that cannabis may be effective in the treatment of painful peripheral neuropathy [1]. Recently, the Center for Medicinal Cannabis Research (CMCR) at the University of California [2] completed five placebo-controlled phase II clinical trials with smoked or inhaled cannabis [3-7]. Another study reported from Canada [8]. Patients included people with HIV neuropathy and other neuropathic conditions, and one study focused on a human model of neuropathic pain. Overall, the efficacy of cannabis was comparable to that of traditional agents, somewhat less than that of the tricyclics, but better than SSRIs and anticonvulsants, and comparable to gabapentin (see figure 1).

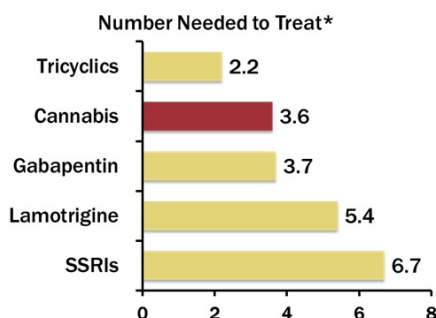


Figure 1. Common analgesics for neuropathic pain.

*to achieve a 30% reduction in pain.

Number needed to treat (NNT) = $1/(E-P)$, where E is the proportion improved in experimental condition and P is the proportion improved on placebo. Example: If 60% “improve” (according to a given definition) in the experimental condition, while 30% “improve” in the placebo condition, then $NNT = 1/(.6-.3) = 3.3$. Data adapted from Abrams et al. [3] and Ellis et al. [4].

The concentrations of tetrahydrocannabinol (THC) in these studies ranged from 2 to 9 percent, with a typical concentration of 4 percent resulting in good efficacy. Side effects were modest and included light-headedness, mild difficulties in concentration and memory, tachycardia, and fatigue. Serious side effects (e.g., severe anxiety, paranoia, psychotic symptoms) were not observed. Mild cognitive changes resolved within several hours of drug administration.

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While these were short-term trials with limited numbers of cases, the data suggest, on balance, that cannabis may represent a reasonable alternative or adjunct to treatment of patients with serious painful peripheral neuropathy for whom other remedies have not provided fully satisfactory results. Because oral administration of cannabinoids (e.g., as dronabinol, marketed as Marinol) can result in inconsistent blood levels due to variations in absorption and first-pass metabolism effects, inhalational (or potentially sublingual spray, e.g., nabiximols, marketed as Sativex) administration remains preferred to oral administration.

Cannabis as a smoked cigarette, while demonstrating efficacy, poses a number of challenges, inasmuch as it remains illegal under federal law, even though it is permitted in an increasing number of jurisdictions on physician recommendation. Figure 2 (see next page) provides a schematic approach for physician decision making in jurisdictions where medicinal cannabis is permitted [9].

This decision tree suggests key points that a physician should consider in making a determination. In the case of a patient assumed to have persistent neuropathic pain, the first determination to be made is that the patient's signs and symptoms are indeed consistent with a diagnosis of neuropathy. Assuming a patient does not respond favorably to or cannot tolerate more standard treatments (e.g., antidepressants, anticonvulsants) and is willing to consider medicinal cannabis, the physician proceeds to compare risk and benefit. Among these considerations is whether the patient has a history of substance abuse or a serious psychiatric disorder that might be exacerbated by medicinal cannabis. Even the presence of such a risk does not necessarily preclude the use of medicinal cannabis; rather, coordination with appropriate substance abuse and psychiatric resources is necessary, and, based on that consultation, a risk-benefit ratio can be formulated. In patients for whom the ratio appears favorable, the physician should discuss modes of cannabis administration including oral, smoked, or vaporized. Once risks and benefits are evaluated and discussed with the patient, cannabis treatment may commence as with other psychotropic medications, with attention being paid to side effects as well as

efficacy. Attention must also be paid to possible misuse and diversion, which can then trigger a decision to discontinue the treatment.

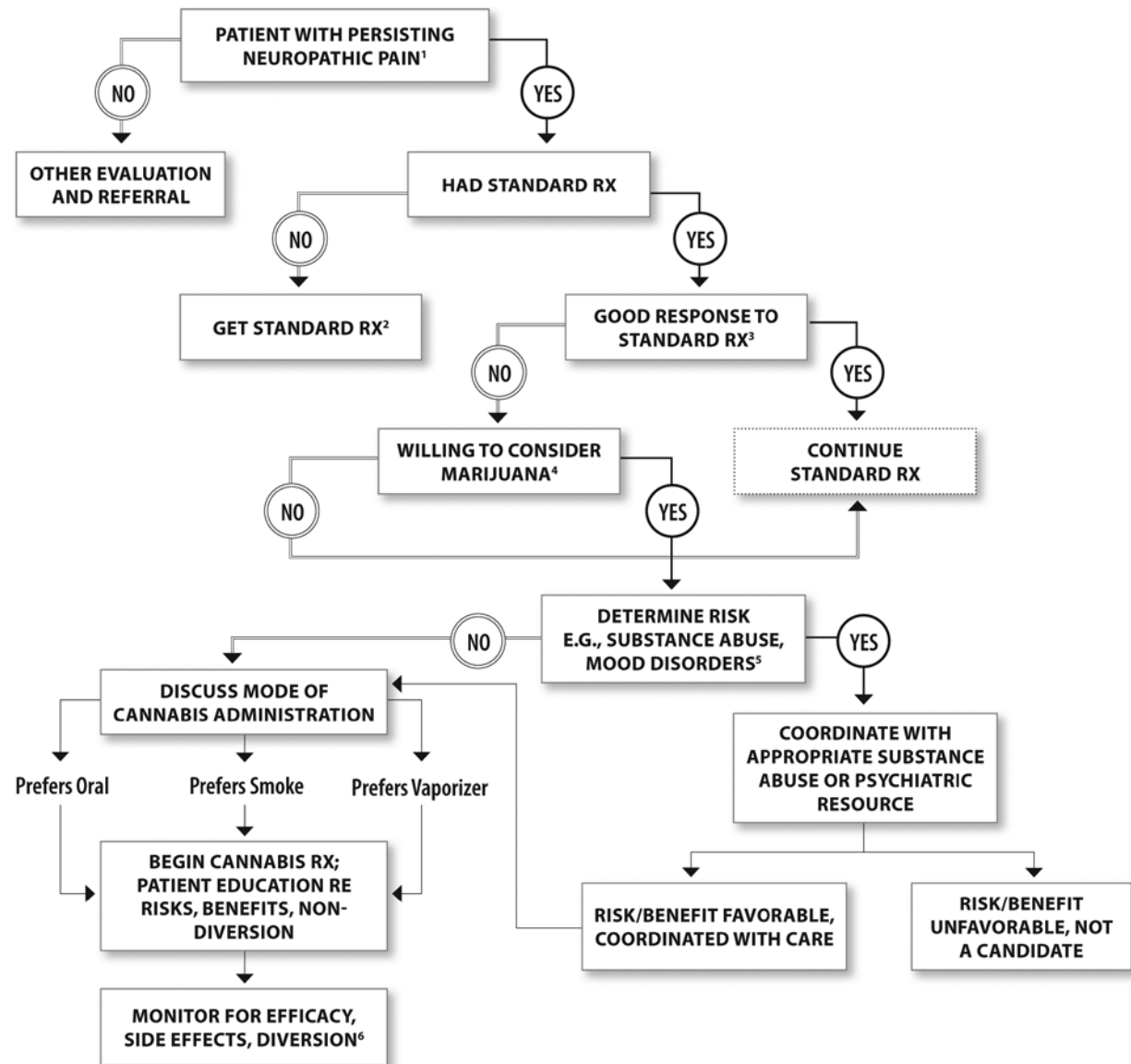


Figure 2. A decision tree approach for physicians who may be considering recommending medicinal cannabis to a patient (from Grant et al. [9]).

Key

1. Daily or almost daily pain with typical neuropathic characteristics for at least 3 months; affects life quality.
2. Standard Rx = e.g., antidepressants, anticonvulsants; opioids; nonsteroidal anti-inflammatory drugs.
3. For example, at least 30% reduction in pain intensity.
4. Consider past experience, possible past history of side effects; willingness to smoke.
5. Determine history of substance abuse. If yes, or at “high risk” of aberrant drug behavior; proceed with close observation; possibly coordinate with substance abuse treatment program.
6. Efficacy = at least 30% reduction in pain intensity.

In summary, there is increasing evidence that cannabis may represent a useful alternative or adjunct in the management of painful peripheral neuropathy, a condition that can markedly affect life quality. Our society should be able to find ways to separate the medical benefits of making a treatment available to improve lives when indicated from broader social policy on recreational use, marijuana legalization, and unsubstantiated fears that medicinal cannabis will lead to widespread cannabis addiction [10-12].

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