Cannabinoids and Low Back Pain

ABSTRACT

There is a great deal of interest in the use of cannabis-based products including medically authorized marijuana for the treatment of almost any pain condition including low back pain. There are many anecdotal reports of patients who found it an effective treatment for chronic low back pain, one that has allowed them in some cases to discontinue other treatments such as continuing opioid therapy. There is now easy legal access to cannabis-based preparations in Canada with or without medical authorization. However, with some notable exceptions, the evidence that would allow physicians to have a high degree of confidence in selecting this treatment modality is lacking.

KEYWORDS: Cannabis; Chronic Pain; Low Back Pain; Evidence

CME Pre-test Quiz

The following case studies help to understand the current level of evidence that we can use to better inform those patients who express an interest in this treatment option.

Case #1:

Susan is a 48-year-old schoolteacher, who has a long-standing history of chronic low back and left leg pain that has persisted following spinal surgery 8 years prior. She has diabetes. Her pain has been stable for many years on a combination of duloxetine 60 mg daily plus pregabalin 150 mg twice daily; she has not tolerated higher doses of either agent. In the past, when made aware of the potential for weight gain, she has declined trials of tri-cyclic medications. She is now reporting that, over the past 6 months, she has noticed the onset of right sided leg numbness and tingling in a stocking-like distribution, which is becoming more noticeable in both intensity and extent.

Investigations: Susan has been successful in maintaining her A1C at target levels below 7.0. A repeat lumbar spine MRI shows stable post-surgical changes at the level of her prior L4-L5 decompression and fusion without evidence of central or foraminal stenosis. Nerve conduction studies confirm a new diagnosis of diabetic peripheral neu-

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ropathy. Screening lab including thyroid function and Vitamin B12 levels are unremarkable.

Susan's teenage children have encouraged her to ask you for a medical authorization to approach a licensed cannabis producer for access to a high CBD:THC ratio marijuana product to assist with her pain complaints.

Discussion:

Cannabis based products date back to antiquity and have been used medically as well as recreationally for many years in North America.[1] For many patients recent legalization of marijuana in Canada has removed the stigma of searching for this therapeutic option and opened the doors for a new era of research, research that was not possible while marijuana products remained prohibited in Canada. And is still impossible in the United States. We are still at an early stage in having reliable evidence on which to base our therapeutic decisions for this class of product. What is generally accepted is that the body has an endocannabinoid system that appears to be important in regulating certain types of pain,[1,2] and that the various types of marijuana plants (indica and sativa) have widely varying concentrations and ratios of the two most studied cannabis extracts, delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD). The cannabis plant itself contains over 100 different cannabinoids,[3] most of which are unstudied. Some of the best research to date has included only 23 patients studied on a 9% THC potency used as an inhaled product for 5 days.[4] In contrast options available from approved suppliers now include potencies of over 30% THC as well as a range of THC:CBD ratios. Besides the available traditional dried leaf inhaled or vaporized products other delivery options including oils and drops are now legal in Canada with other formats such as infused beverages almost certain to enter the market as regulations further loosen in the coming months.

As is so often the case, Susan presents with a number of possible pain classifications. She has evidence of chronic low back pain that is likely mechanical in nature and an example of nociceptive pain. She also has evidence of diabetic peripheral neuropathy which is an example of neuropathic pain. Finally, she has persistent leg pain following surgery, referred to as failed back surgery syndrome, an example of what was recently termed nociplastic pain. Pain management guidelines recommend appropriately classification of a patient's pain complaints,[5] as the treatments for each classification can be very different. The recently published TOP guideline for Medical Cannabinoid prescribing is helpful in this regard, as it notes that the evidence for

the use of cannabis products in managing chronic pain is strongest only for neuropathic pain.[6] There is also support for its use in treating palliative pain, and spasticity associated with Multiple Sclerosis or Spinal Cord Injury. The guideline also notes other conditions for which there is some evidence of therapeutic value for cannabinoids such as chemotherapy induced nausea and vomiting (Table 1), that are outside of the scope of this article. In spite of anecdotal reports, the evidence is lacking that a higher CBD ratio product or pure CBD is more effective and produces fewer side effects than products with a higher THC balance.[6]

Susan does present with a pain condition for which a cannabis trial might reasonably be considered, but is it the most appropriate next step? The guideline presents a very helpful illustrative table (Table 2) that compares the relative efficacy of various pharmaceutical agents in the management of neuropathic pain. Cannabis products appear at the bottom of the list compared to more commonly used medications such as tricyclic antidepressants, SNRI class antidepressants, and gabapentinoids. Cannabis products also have a high rate of adverse effects compared to placebo. The guideline recommends that patients have a trial of three or more first line neuropathic pain medications before considering a cannabis trial, and the use of a synthetic cannabinoid such as Nabilone prior to considering a medical marijuana trial (Table 3). Susan is already benefiting from two agents, duloxetine and pregabalin, and has valid reasons for declining the third option of a tricyclic antidepressant. After reviewing her options and being made aware of the potential side

Table 1: Percentage of People Experiencing Benefits

Benefits	Cannabinoids	Placebo
Chronic pain (≥30% reduction after 4 weeks)		
Neuropathic pain	38%	30%
Palliative pain	30%	23%
Chemotherapy-induced nausea/vomiting (in 1 day)		
Control of nausea & vomiting	47%	13%
Spasticity (≥30% improvement after 6 weeks)		
Spasticity	35%	25%

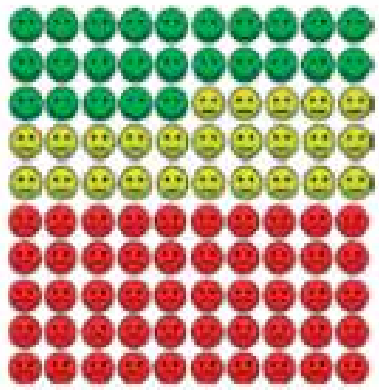
Table 1 (From the TOP Guideline)

Table 2: Neuropathic Pain: Pharmacotherapy Treatment

Outcome: Meaningful (~30%) Pain Improvement

Ordered by decreasing estimated efficacy

Amitriptyline

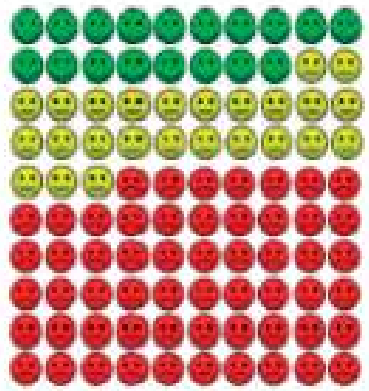


25 improve with treatment

25 improve with placebo or no treatment

50 No improvement

High Dose Opioids*

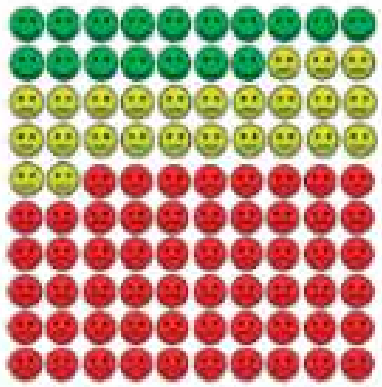


18 improve with treatment

25 improve with placebo or no treatment

57 No improvement

Venlafaxine

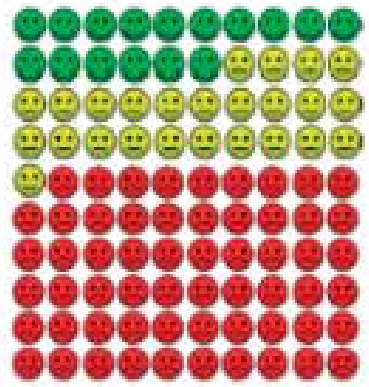


17 improve with treatment

25 improve with placebo or no treatment

58 No improvement

Pregabalin

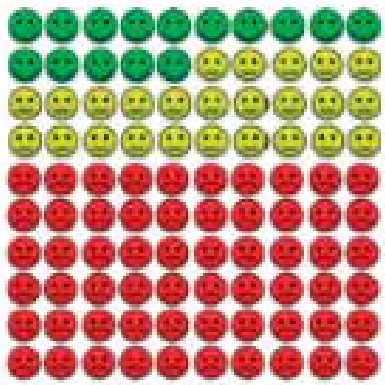


16 improve with treatment

25 improve with placebo or no treatment

59 No improvement

Gabapentin

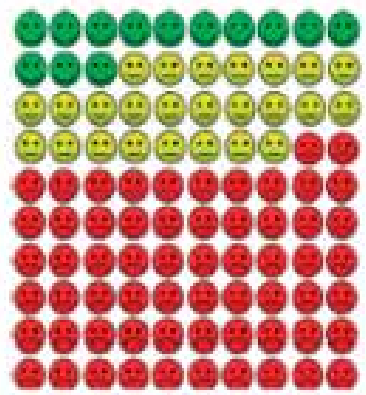


15 improve with treatment

25 improve with placebo or no treatment

60 No improvement

Duloxetine

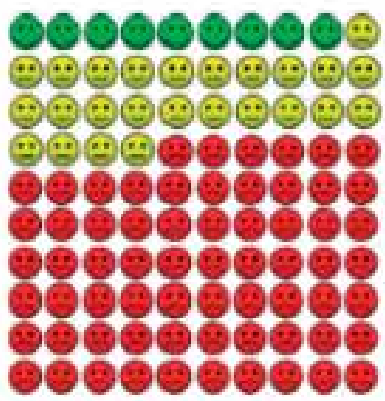


13 improve with treatment

25 improve with placebo or no treatment

62 No improvement

Cannabinoids



9 improve with treatment

25 improve with placebo or no treatment

66 No improvement

Limitations

1. Based on indirect comparisons.
2. Timeframe ~4 to 12 weeks.
3. Details on methods available in online supplement.

Table 2 (From the TOP Guideline)

effects of plant-sourced cannabis (Table 4) she accepts a trial of Nabilone.

Follow Up:

Susan returns to your office three months later reporting that she did try the Nabilone but was unable to tolerate side effects of nausea and fatigue. You have a discussion with her about the difference between a medical "authorization" versus prescription, and provide her with an authorization and a recommendation for a 1:1 ratio THC/CBD product to use at bedtime to help with pain and sleep initiation, and a 1:16 ratio THC/CBD product to use during the day. She prefers to use a concentrated oil rather than an inhaled product.

She returns three months later reporting that the evening THC/CBD product has little impact on her pain, but that it does provide her with a degree of "distraction" that she finds helpful in reducing anxiety and allowing sleep. Her daytime product is more helpful for her neuropathic symptoms but has had a disappointing lack of effect on her low back pain.

Table 3: Medical Cannabinoids Prescribing Algorithm

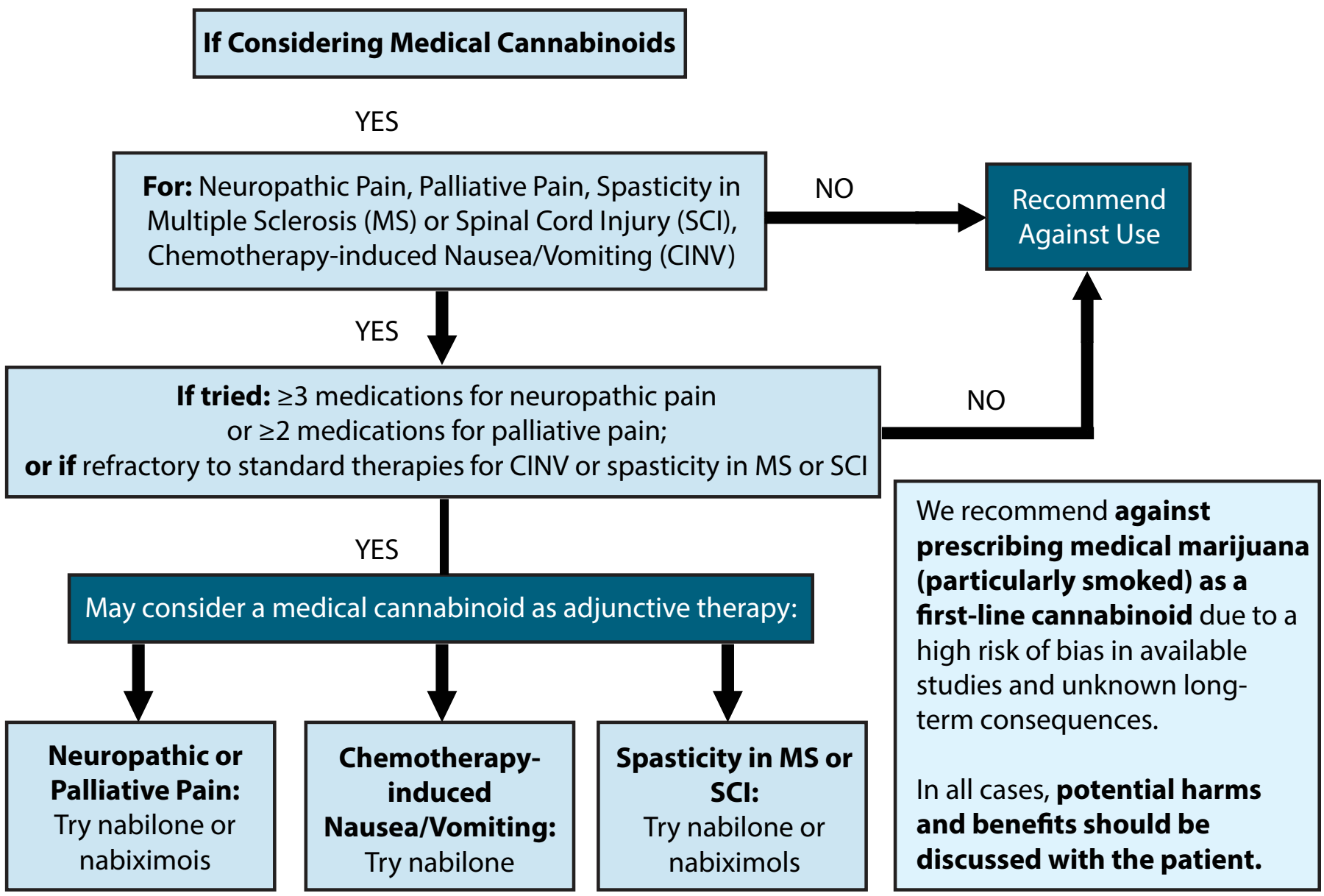


Table 3 (From the TOP Guideline)

Case #2:

Joshua is a 28-year-old male labourer who presents on chronic opioid therapy for low back pain. He has recently quit taking what had been a substantial daily amount of alcohol and he would like your help in getting his "life back in order" by helping him to reduce or even eliminate his current use of controlled release oxycodone 80 mg twice daily. He has friends who have overdosed after obtaining street sourced oxycodone contaminated with fentanyl. He is frightened of his own dependency on the medication and what he might do if he was ever cut off from his medical supply. He has plans to return to school to complete his high school degree and pursue an eventual career as an artist. He is a pack-per-day smoker, and he has been stabilized on a daily prescription of divalproex plus fluoxetine for the management of bipolar disorder. He has an older sister also a member of your practice who has psychiatric support for psychosis. He reports current consumption of approximately 2 grams/day of street sourced cannabis for recreational reasons but no other street drugs. A random urine drug screen is appropriately positive for oxycodone and cannabis and negative for other opioids or street drugs.

Table 4: Percentage of People Experiencing Harms

Type of harm	Cannabinoids	Placebo
Sedation	50%	30%
"Feeling high"	35%	3%
Dizziness	32%	11%
Speech disorders	32%	7%
Ataxia/Muscle twitching	30%	11%
Hypotension	25%	11%
Numbness	21%	4%
Psychiatric	17%	5%
Euphoria	15%	2%
Dysphoria	13%	0.3%
Impaired memory	11%	2%
Withdraw due to harms	11%	-3%
Dissociation/Acute psychosis	5%	0%

Table 4 (From the TOP Guideline)

Discussion:

There has been a lot of interest in the use of cannabinoids as an alternative to opioids for chronic pain, perhaps with an opioid sparing effect. However, recent articles have raised cautions about the enthusiasm resulting from earlier anecdotal reports. These studies found that cannabis users had experienced more pain and demonstrated lower self-efficacy in managing pain, and that cannabis use appears to increase rather than decrease the risk of non-prescription opioid use and opioid use disorder.[7,8]

On reviewing the 2015 College of Family Physicians of Canada "Initial Guidance for the use of Marijuana",[9] you find that one of the specific contra-indications for the use of this product is a personal or family history of psychosis or active substance use disorder. There are potentially dangerous interactions combining cannabis with high dose opioids, alcohol, or other sedating agents. It must also be used with caution in the presence of concurrent mood or anxiety disorders, and with tobacco smokers. Further, the rate of side effects for cannabinoids compared to placebo is not insignificant (Table 4). After learning about these cautions, Joshua wonders if you could suggest something else to assist him with getting off his opioids and more effectively treating his back pain.

On further questioning you find that he has never been offered a program of goal oriented active physiotherapy for his back pain, and that becomes your treatment recommendation.[10] You also review with him the recent guidelines on the treatment of opioid use disorder with buprenorphine/naltrexone (Suboxone).[11] While he currently does not meet all the clinical criteria for an opioid use disorder he does recognize that he may be at risk and agrees to your suggestions as an alternative to cannabis authorization.

Follow-up:

Joshua visits your office on a frequent basis over a month for stabilization on Suboxone, and six months later, he remains off his chronic opioid therapy. He has achieved significant improvement in pain control. Engagement first with the physiotherapy exercise and lifestyle modification and subsequently with a community-based yoga program has greatly increased his functional ability. He is now asking for your help with a smoking cessation plan.

Summary:

Cannabis is a plant-based product that traces back to the ancient world, with evidence of medicinal use since AD 400. It was widely used in the United States as a patent medicine in the 19th and early 20th centuries, until federal restriction of sale and use occurred in 1937 with the passage of the Marihuana Tax Act. It was dropped from the United States Pharmacopoeia in 1942, and prohibited under federal law with the Controlled Substances Act of 1970.[1] By restricting the procurement of cannabis for academic purposes this legislation along with similar Canadian restrictions, has led to severe limitations on research.

Endocannabinoid receptors are found throughout the human body including in the nervous system, internal organs, connective tissues, and immune cells. The endocan-

SUMMARY OF KEY POINTS

1. Compared to medically authorized cannabis, street sourced products are at high risk of contamination including insect remains, fungi, chemical fertilizers and herbicides.
2. Unlike most plant-sourced medications, the active ingredients are located on the cannabis leaf, which raises the risk of contaminant exposure.
3. Cannabis leaves by themselves are inert until heated in a process known as decarboxylation.
4. While inhaled cannabis has a rapid onset of action, ingested products have a delayed onset producing a risk of overdose if continuing to consume while waiting for an expected effect.
5. Little is yet known about potential drug interactions with cannabis use.

nabinoid system has a homeostatic role sometimes characterized as "eat, sleep, relax, forget and protect".[1] Cannabinoid receptor type 1 (CB1) is widely distributed in the central nervous system, with a particularly dense expression in the substantia nigra, globus pallidus, hippocampus and cerebral cortex. CB2 is principally associated with cells governing immune function.[1] Non-cannabinoid targets include the mu and delta opioid receptors as well as norepinephrine, dopamine and serotonin receptors.[1] With such a target rich environ-

CLINICAL PEARLS

Cannabis authorizing physicians will often recommend a higher THC:CBD ratio product for evening or bedtime use, and a higher CBD:THC ratio or pure CBD for daytime use.

As is true for any potential intoxicant, patients need to be cautioned about the risks of operating a motor vehicle or any machinery while under the influence of cannabinoids, especially higher THC ratio products.

Because it is a lipid soluble chemical, urine, blood, or hair tests can detect THC for many days after use.

Physicians in Canada provide medical "authorization" for cannabis use, verifying that the patient has a medical condition for which cannabis could be a valid therapeutic option. This authorization then allows the patient to purchase from a licensed producer up to a recommended quantity in grams per day. Although the basic patient demographics and birthday are required, unlike a prescription, the exact component percentage and potency, method of ingestion, and frequency are not components of the authorization.

CME

Post-test Quiz

Members of the College of Family Physicians of Canada may claim MAINPRO-M2 Credits for this unaccredited educational program.

ment that widely overlaps so much of the pain neurophysiology, it is no wonder that the potential role of cannabis products in chronic pain management has generated such interest.

However, this enthusiasm must be tempered with the lack of research and current evidence. Further, while it is appreciated there are substantial differences between neuropathic, nociceptive and nociplastic pain, there has been a tendency to conflate study results in summaries of the research. The effects on nociceptive pain is, in fact largely unstudied.[12] Increased use of cannabis is not without its risks including mental health and addictions concerns particularly among vulnerable groups particularly adolescents and young adults.[9] While it is not a perfect comparison, lessons can be learned from the opioid crisis. We do not yet know how cannabis affects the long-term experience of chronic pain. As pointed out in a recent commentary discussing the use of cannabis for treating chronic pain: "We simply do not know the answer."[12] It is important to maintain an open mind about the role of cannabis and to continue non-judgemental conversations with our patients, upholding our role as a trusted source of unbiased information.

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