

Short Communication

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Cannabinoids in the management of chronic pain: a front line clinical perspective

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Abstract: Chronic pain is an escalating public health problem. Currently available treatments are inadequate to control chronic pain conditions, and there is a critical need for novel treatments. Over a half century of elegant pre-clinical research has identified the presence of a sophisticated endocannabinoid system that is part of our natural pain and immune defense network. Convergent work has supported the significant potential to exploit this system to decrease pain and inflammation. Although the clinical research remains in its infancy, recent systematic reviews have found that 25 of 30 randomized controlled trials have demonstrated a significant analgesic effect. The authors concluded that cannabinoids currently available for clinical use demonstrate a modest analgesic effect and are safe for the management of chronic pain. There is a critical need for more translational research so that the excellent work of Dr. Itai Bab and our basic science colleagues around the world can move forward in providing novel cannabinoid-based medicines. This should include more potent analgesics that are limited in side effects with several routes of delivery. Our patients deserve additional agents for pain control with a novel mechanism of action, and cannabinoids are the new frontier.

Keywords: cannabinoids; chronic pain; pharmacology.

Chronic pain is an escalating public health problem currently affecting approx. 1 in 5 people [1–5]. This is estimated to increase to 1 in 3 over the next decade owing to a combination of aging of the population and, ironically, the advancement of medical technology, which is

extending life beyond injury and illness that would previously have been fatal, leaving survivors coping with serious pain conditions [6]. There is an increasing cohort of survivors of cancer [7, 8] and HIV [9] who suffer from chronic neuropathic pain, and it is now well established that many of the increasingly performed surgical procedures are associated with a significant prevalence of persistent post surgical pain that can be severe in 2%–10% [10]. Currently available analgesics, even in combination, result in only partial relief, with 30%–40% obtaining only 50% relief. There is a critical need for novel agents for the treatment of pain.

A half-century of research has established that the body is equipped with an endocannabinoid system that is involved in the modulation of pain, inflammation, bone metabolism and neural repair, all of which are directly relevant to the management of pain [11]. Unfortunately, the current drug regulatory climate, which continues to categorize even non-psychotropic cannabinoids as equivalent to the most dangerous “narcotics”, has made it very difficult to move human cannabinoid research forward. Consequently, we do not have access to specific synthetic cannabinoid drugs for the treatment of pain like we do for drugs used in the treatment of other diseases such as hypertension or depression. In this climate, people living with chronic pain conditions have been requesting cannabis for pain control. This amounts to a significant number of people. Studies done a decade ago found that approx. 15% of patients presenting to a tertiary care-level chronic pain clinic [12] and to a multiple sclerosis clinic in Canada [13] reported using cannabis for the control of symptoms. Patients reported that pain, muscle spasm, sleep and mood were the main symptoms that decreased with the use of cannabis.

Since 1999, Health Canada has granted access to cannabis for medical purposes. In the first phase of the program, the process involved the patient applying to Health Canada for access to cannabis for medical purposes. This application had to be supported by a physician. As of December 2013, Health Canada reported that 37,884 people had been authorized to possess cannabis

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for medical use. In March of 2014, the program changed somewhat so that the patient now applies to a licensed producer, and with the support of a physician or nurse practitioner, the patient is registered with that producer and may order cannabis from the producer directly. There is no current update on the numbers of patients registered overall, but the numbers are expected to climb.

We have completed two systematic reviews of randomized controlled trials examining cannabinoids for the treatment of chronic pain: the first was published in 2011 [14], and the second was an updated systematic review of trials completed since then [15]. Combining these two reviews with one further randomized controlled trial published since that time [16], there are now 25 of 30 trials that have found a significant analgesic effect for the cannabinoid being investigated. Twenty-three of the trials examined oral or oromucosal cannabinoids, 18 of which were positive, and seven examined inhaled cannabis (either smoked or vaporized), all of which were positive. The majority of trials involved patients with neuropathic pain. The overall quality of the trials was excellent; several trials also reported significant improvements in secondary outcomes including sleep, muscle stiffness and spasticity. The most common adverse effects included fatigue, dizziness, dry mouth and nausea. The authors concluded that cannabinoids demonstrated a modest analgesic effect and were safe and reasonable to consider in the treatment of chronic pain.

The recently updated Canadian guidelines for the treatment of neuropathic pain have moved cannabinoids up to a third-line option [17]. In addition, the College of Family Physicians of Canada has recently published a preliminary guidance document regarding the authorization of medical cannabis [18]. The document states that family physicians are in a difficult position, explaining that “we are asked to authorize our patient’s access to a product with little evidence to support its use, and in the absence of regulatory oversight and approval.” It is “to address this predicament” that the preliminary guidance document was developed. There are 15 recommendations. I will summarize the key points. The guidelines state that use for neuropathic pain that has failed standard treatment is a reasonable indication to consider. It is recommended that pharmaceutical cannabinoids be tried first before cannabis. It is also indicated that cannabis is not appropriate for people younger than 25; for those with a history of psychosis, cannabis use disorder and cardiovascular disease such as angina or arrhythmia; or for patients who are pregnant or breastfeeding. Full assessment and follow-up of the patient with good documentation are advised. Suggested dosing is to “start low and go slow”,

and physicians are advised to specify the percentage of THC and CBD on the medical forms.

Physicians have called for more clinical research regarding cannabinoids. Fortunately, the National Institute of Health has just announced a new funding opportunity titled “Developing the Therapeutic Potential of the Endocannabinoid System for Pain Treatment” (<http://grants.nih.gov/grants/guide/pa-files/PA-15-188.html>). I am hopeful that this and other funding mechanisms will catalyze the much-needed translational research that will allow the excellent work of Dr. Itai Bab (in whose honor this article is written) and colleagues to move forward such that we will have a suite of cannabinoid agents to use in the treatment of human suffering.

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