

# MEDICAL CANNABIS today

*Perspectives, insights and real-world outcomes using medical cannabis*

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## **MEDICAL CANNABIS AND DE-PRESCRIBING**

Lydia Hatcher, MD, CCFP FCFP, CHE, D-CAPM

## **MEDICAL CANNABIS: CAN IT BE USED IN DEMENTIA PATIENTS?**

Celeste Thirlwell, MD, FRCPC

## **POLICY SCAN: THE USE OF MEDICAL CANNABIS IN PERSONAL CARE HOMES**

Todd Young, MD

## **TREATING CHRONIC PELVIC PAIN WITH CANNABINOIDS: A RETROSPECTIVE CHART REVIEW**

Sana-Ara Ahmed, MD

## **RESEARCH CORNER: CANNABIS IN THE TREATMENT OF HEADACHES, MIGRAINES, AND ANXIETY, AND IT'S IMPACT ON OPIOID AND PRESCRIPTION SUBSTANCE USE**

Philippe Lucas, MA, PhD(c)

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# WELCOME

## Greetings,

Welcome to our first issue of *Medical Cannabis Today* in 2019. You'll note that we've changed the name of our journal after 4 years. This was done to reflect the changing landscape and role that medical cannabis plays in Canadian healthcare and to reinforce that cannabis is a therapeutic option that is here today and that it's here to stay!

Research suggests that in Canada and other jurisdictions, more and more older patients are turning to medical cannabis to address the conditions associated with aging, including arthritis, poor sleep, and chronic pain. Therefore, we have focused this issue on important topics affecting the care of older populations. For example, the importance of medical cannabis and de-prescribing or the potential role for medical cannabis in the treatment of dementia. We also have a wonderful paper that scans the policy literature on the use of medical cannabis in personal care homes. And last but by no means least, one of our faculty contributes a synopsis of a case series that was recently presented as a poster at the 2019 American Academy of Pain Medicine meeting in Denver.

In closing, it's worth noting that Tilray is currently supporting a multi-site, prospective study titled Medical Cannabis in Older Populations (MCOP; please see Volume 3, Issue 5, 2018 for details) led by Dr. Blake Pearson MD. As we learn more about the impact of medical cannabis use on older populations, we look forward to providing updates that might inform treatment options in this population.



Sincerely,

A handwritten signature in black ink that reads "Philippe Lucas". The signature is written in a cursive, flowing style.

Philippe Lucas  
Vice President, Global Patient Research & Access  
Tilray

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### Lydia Hatcher, MD, CCFP FCFP, CHE, D-CAPM

Dr. Hatcher graduated with her MD in 1982 from Memorial University of Newfoundland. In 1984, she received certification with the College of Family Physicians of Canada (CFPC) and in 1994, was certified with the Canadian College of Health Service Executives. In 1998, she received the Canadian Psychiatric Association's annual Mental Health Awareness Award. In 2001, the College of Family Physicians of Canada awarded her a fellowship. She has been doing pain management for over 25 years. Her focus is on a bio-psycho-social

approach to pain management. She does a significant amount of teaching in chronic pain across the country and is a physician assessor for the College of Physicians and Surgeons of both Ontario and Newfoundland & Labrador. She chairs a subcommittee for the National Opioid Use Guideline Group. She is a member of the Canadian Academy of Pain Management and the Canadian Pain Society. She is a committee member of the CFPC community of practice in chronic pain. She is an Associate Clinical Professor of Family Medicine at McMaster University and former Chief of Family Medicine at St. Joseph's Healthcare in Hamilton, Ontario.

## MEDICAL CANNABIS AND DE-PRESCRIBING

We are all aware of the importance of limiting the number and quantity of medications a patient takes to minimize adverse effects. Many studies show significant risk of drug interaction when a patient is taking more than 5 medications, and this is compounded in the elderly. Recent research shows that more than 90% of patients are willing to stop a medication if their doctor says it is possible.<sup>1</sup>

We see many patients asking about the use of medical cannabis as a means of assisting them with stopping or decreasing doses of existing medications. Like most research with medical cannabis, much of the evidence is from observational studies, surveys of cannabis users, and small trials. Some of the more compelling evidence is still in the animal study stage and it will be years before we have high quality randomized controlled human trials completed.

Thus, the evidence and information in this article represent the current available evidence, opinion of experts and, perhaps most importantly, patient experience.

**THE BODY OF EVIDENCE IS GROWING THAT SHOWS THAT MEDICAL CANNABIS MAY DECREASE THE AMOUNT IN MORPHINE EQUIVALENT DOSES OF OPIOIDS NEEDED TO CONTROL PAIN**

### CHRONIC PAIN

Preclinical animal trials certainly show a sparing effect of less opioid use with cannabis use.<sup>2</sup> Other factors from preclinical studies include colocalization of opioid and endocannabinoid receptors in the septum striatum, periaqueductal area, and amygdaloid nucleus. These studies show that tetrahydrocannabinol (THC)-based cannabinoids prevent development of tolerance to and withdrawal from opiates.<sup>3,4</sup> Cannabinoid receptors might also interrupt signalling in the opioid receptor systems, thus affecting both cravings for opiates and withdrawal severity.<sup>5</sup> Studies are underway in addiction centres looking at cannabis as a tool to potentially help opioid addiction.

*Expert opinion:* Patients can often significantly decrease or stop their opioid dose. Try weaning patients to the lowest possible level either in conjunction with starting cannabis or once the effective cannabis dose is reached. Patients will typically be able to self-regulate how quickly they do this, which is likely based on genetic differences (as yet not well defined), personal preferences, and their comfort levels.

*Patient experience:* Some patients using medical cannabis are able to discontinue or decrease not only opioids but gabapentinoids, muscle relaxers, sleep medications, and benzodiazepines, and maintain good control of their pain.

### ANXIETY AND STRESS

The most common self-reported reasons for cannabis use are chronic pain, anxiety, stress, and insomnia.<sup>6</sup>

*Expert opinion:* Experienced users commonly report multiple benefits from their cannabis use. We are in the very early stages of recruitment for large-scale human studies with legal source cannabis strains, but patients currently using ingested oils report calming effects without euphoria with low-dose use of cannabidiol (CBD) and/or balanced CBD to THC strains.

*Patient experience:* Experienced cannabis users (those using long term and prior to legalization), tell us that they did not use cannabis to get high but rather to calm themselves down, and to help them cope with anxiety and stress, which often helped them sleep better. Many of them failed or were unable to tolerate traditional medications. These users typically report that 1 joint would often last them 2 or 3 days. These are patients who have now chosen to go with safer options and have moved to legal source ingested oils or vaping. Additionally, many of them use smaller doses and report fewer euphoric or dysphoric effects.

## INSOMNIA

As cannabis is multimodal in its actions, patients using it for pain, post-traumatic stress disorder (PTSD), and mood disorders often report improved sleep. The Health Canada 2018 systematic review looked at the evidence for the use of cannabinoids for the management of insomnia.<sup>7</sup> The review states, “Human experimental data suggests cannabis and THC have a dose-dependent effect on sleep—low doses appear to decrease sleep onset latency and increase slow-wave sleep and total sleep time, while high doses appear to cause sleep disturbances. Limited evidence from clinical studies also suggests that certain cannabinoids (cannabis, nabilone, dronabinol, nabiximols) may improve sleep in patients with disturbances in sleep associated with certain chronic disease states.”<sup>7</sup>

The National Academies of Sciences, Engineering, and Medicine’s 2017 systematic review also provides some evidence for the role of cannabis in insomnia.<sup>8</sup> “There is moderate evidence that cannabinoids, primarily nabiximols, are an effective treatment to improve short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis.”<sup>8</sup>

*Expert Opinion:* Many patients are using benzodiazepines and “Z” drugs for insomnia, both of which affect the

sleep centres of the brain and potentiate the risk of central sleep apnea. Being able to stop or decrease dosing of these medications is safer and allows for deprescribing. Anecdotally, many patients report improvement in sleep disturbances when they start nabilone or medical cannabis for other medical reasons. Patients will often report best effect with low-dose THC, with or without CBD, taken in the evening. For the older patient, CBD alone may be enough to improve sleep.

*Patient experience:* Surprisingly, many patients on long-term benzodiazepines and “Z” drugs are able to stop them with the use of low-dose THC or even CBD-based products. As already mentioned, the multimodal benefit of cannabis helps their pain, sleep, and mood allowing for fewer prescription medications.

## POST-TRAUMATIC STRESS DISORDER (PTSD)

Many of the most commonly used PTSD pharmacotherapies (e.g., selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitors) have relatively poor efficacy.<sup>9</sup> There is a link between experiencing a traumatic event and increased cannabis use.<sup>10</sup> Individuals with PTSD may be especially likely to use cannabis to alleviate the PTSD symptoms of nightmares, flashbacks, hyperarousal, and distress. Chronic stress is hypothesized to create a “hypocannabinergic state” that results in impaired fear extinction (as is seen in PTSD), and this state can be alleviated with CB1 receptor agonists.<sup>7</sup>

*Expert Opinion:* Always ask your patients why and for what symptoms they are using cannabis if they are using it non-medically. For those who are using medical cannabis, it is still very useful to be sure and to ask about possible PTSD symptoms. These patients can have very effective treatment without needing to add in antidepressants and antipsychotics. The caution is risk and assessment for cannabis use disorder,<sup>11</sup> as these patients may be more at risk of higher dose use (greater than 5 g/day).

*Patient experience:* War veterans, in particular, tell us they use cannabis to diminish the symptoms of PTSD. They and others with PTSD also report improved sleep, the ability to calm themselves, and that it helps with concentration and overall mood. Many of them report only using cannabis as they had such poor response to many trials of medications.

## CARDIOVASCULAR DISEASE (CVD), HYPERTENSION, DIABETES, ADULT EPILEPSY

Evidence of a statistical association between cannabis use and the triggering of an acute myocardial infarction (AMI) (cannabis smoking), ischemic stroke, or subarachnoid hemorrhage is limited. As well, there is limited evidence of decreased risk of metabolic syndrome and diabetes, and increased risk of prediabetes. No evidence exists to support or refute a statistical association between chronic effects of cannabis use and the increased risk of AMI.<sup>8</sup> To date, there are no reported human trials relating to diabetes or epilepsy.

*Expert Opinion:* Patients may report lowering of blood pressure (BP), a known side effect of cannabis. Caution needs to be used with any patient with unstable cardiovascular disease and, if there is uncertainty, discuss with their cardiologist. All patients should be told to remain on existing medications for any chronic CVD, metabolic, or seizure disorder.

*Patient experience:* Adults frequently report being able to lower BP medications when they have reached stable dosing of medical cannabis. The same can be seen with some diabetics advising us of improved sugars. Some poorly controlled epileptic patients and their family members have reported fewer seizures.

## CONCLUSION

Be sure to use medical cannabis wisely by following appropriate guidelines, assessing your patient's condition, risk of harm, and risk of misuse. Document your assessment, rationale for using cannabis, and any concerns you have, to ensure best practices.

We are at a very exciting place at the beginning of good clinical research into many of the conditions noted in this article. As time progresses, we will get answers to the many potential benefits of medical cannabis. In the meantime, listen to your patients, ask what benefits they see, and what is working for them.

Not every patient will benefit from medical cannabis. As with many drugs, patients will respond differently based

on their genetics and biopsychosocial environment. Some will have excellent results, others will get some response, and there will be a cohort where cannabis does not help.

If you are able, have your patients join a cannabis registry either with a licensed producer or through a provincial registry where they can document some of the uses, dosing strains, and effects of their cannabis.

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**Celeste Thirlwell, MD, FRCPC**

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# MEDICAL CANNABIS: CAN IT BE USED IN DEMENTIA PATIENTS?

## WHAT IS DEMENTIA?

The World Health Organization (WHO) defines dementia as “an umbrella term for several diseases affecting memory, other cognitive abilities and behavior that interfere significantly with a person’s ability to maintain their activity of daily living”.<sup>1</sup> Alzheimer’s disease is widely considered to be the most common form of dementia and is likely responsible for between 60-70% of all dementia cases worldwide.<sup>2</sup> Even though age is considered a risk factor for dementia, dementia cannot be considered a normal part of the aging process. Typical symptoms of dementia include impairment of cognitive function (from simply forgetting memories to forgetting people), worsening ability to communicate, behavioural changes, loss of emotional control, aggression, and loss of motor control. The WHO contends that dementia is a public health priority, especially as approximately 10 million new cases of dementia are seen worldwide every year.<sup>2</sup>

## CANNABIS AND DEMENTIA RESEARCH

Research into the use of cannabinoids in dementia is in its infancy. Traditional pharmacology is no longer the best option to treat the symptoms of dementia, as the risks considerably outweighs the rewards.<sup>3,4</sup> Cannabinoids may be the solution for treating dementia due to their neurobiological and neuroprotective effects. In 2010, Walther et al. stated that “Because of their broad impact on neurotransmission through retrograde signaling and involvement in inflammation, endocannabinoids have been suggested as modulators of various neurodegenerative diseases”.<sup>5</sup> One issue that

has hampered this research field is that different strains of cannabis can have different effects depending on the percentage of tetrahydrocannabinol (THC) and cannabidiol (CBD) contained in the cannabinoids.<sup>6</sup>

## THESE LABORATORY RESULTS HAVE BEEN VERY PROMISING IN DEMONSTRATING HOW CANNABINOIDS COULD HELP TREAT PEOPLE SUFFERING FROM DEMENTIA SYMPTOMS

as well as the possibility of treating the disease itself. Aso et al.,<sup>7</sup> Eubanks et al.,<sup>8</sup> Walther et al.,<sup>9</sup> Ramírez et al.,<sup>10</sup> and Grinspoon and Bakalar<sup>11</sup> explored preliminary laboratory studies and showed that cannabinoids cannot only treat symptoms of Alzheimer’s, but can also interrupt the disease process. Eubanks et al. found a link between the endocannabinoid system and Alzheimer’s disease, which they believe will provide a new focus for the treatment of Alzheimer’s patients.<sup>8</sup> Specifically, Eubanks et al. stated “...AChE inhibitors such as THC and its analogues may provide an improved therapeutic for Alzheimer’s disease, augmenting acetylcholine levels thereby simultaneously treating both the symptoms and progress of Alzheimer’s disease.”<sup>8</sup>

Krishan et al. found in their meta-analysis of existing cannabinoid and dementia research that laboratory studies had yielded exciting results in terms of how useful cannabinoids can be in treating neurodegenerative

diseases.<sup>12</sup> Given the behavioural symptoms of dementia, specifically Alzheimer's disease, cannabinoids may be useful as an antipsychotic replacement. As has been seen in studies for veterans with post-traumatic stress disorder, cannabis has been able to reduce aggression as well as have a calming effect. In fact, Krishan et al. further highlighted that "Neurodegeneration is a feature common to the various types of dementia and the neuroprotective effects of cannabinoids may therefore be beneficial in slowing the progression of these diseases".<sup>12</sup>

Nevertheless, Shelef et al. executed an open-label study of 11 patients with Alzheimer's disease who were treated with medical cannabis oil for 4 weeks and found that there was a significant reduction in patients' symptoms.<sup>3,4,13</sup> Woodward et al. explored how dronabinol could act as an adjunctive treatment for 40 patients with dementia in a retrospective study. The investigators found that these patients had a significant decrease in agitation, as well as improvement in sleep and meal consumption.<sup>14</sup>

Interestingly, researchers at the Salk Institute in a laboratory exploratory model found there was preliminary evidence that cannabis can help to encourage the cellular removal of amyloid beta. Amyloid beta appears to play a major role in the plaque deposits in the brain, a feature of Alzheimer's disease.<sup>15</sup> Even though there has been a growing body of literature surrounding preclinical research into cannabinoids and dementia, this research has yet to play a role in the clinical treatment of dementia patients.

## CLINICAL CASE: WORLD WAR II VETERAN WITH VASCULAR DEMENTIA

These preliminary findings were recently born out in a clinical case of an 88 year-old-World War II veteran with vascular dementia, who had been on standard dementia medications but whose condition continued to deteriorate. His son, who is a veteran who served in Afghanistan, returned to Canada to care for his dementing father. The elderly veteran's condition was severe. He was having nightmares at night and flashbacks during the day of fighting in World War II with uncontrollable anger outbursts. Because of his dementia, it was even harder to de-escalate him. As well, he became cachectic with very poor appetite and was taken to hospital 3 times resulting in doctors reporting that there was little that could be done for the ailing, suffering man other than to, "keep him comfortable." His son turned to cannabis medicine and developed a regimen of care for his father. The

mainstay of treatment was CBD oil microdosed every 3 to 4 hours throughout the day with Indica tea for paranoia and anxiety, which helped to regulate his father's mood and behaviour during the day and improved his appetite; and at night CBD/THC oil 1 hour prior to a set bedtime of 9:00 p.m. with a tea made from a strain of cannabis with high levels of the terpene, myrcene. It took some time to arrive at the correct regimen, but the elderly veteran began to eat again, his physical strength improved, his mood was more regulated, his flashbacks and nightmares were finally controlled, and he slept through the night, allowing his caregiver son to also rest. His son reported, "My dad nearly died 3 times at the hospital and cannabis has saved his life...he has a much better quality of life now."

## FUTURE RESEARCH

Given how dementia is a priority for the WHO, there has been a lack of clinical research in this field of study. There is a growing need for randomized placebo-controlled trials to investigate the relationship between cannabis and dementia, especially as laboratory research has suggested that cannabinoids could be used to treat dementia.<sup>12</sup> The Alzheimer's Society research program does fund research into the study of endocannabinoids and how they can be used to treat Alzheimer's disease. As well, further research is needed to explore how well cannabinoids can manage the behavioural symptoms of dementia.<sup>16,17</sup> Replication of the smaller studies is also needed on a larger scale and for a greater period of observation to fully explore the relationship between cannabinoids and dementia.

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# POLICY SCAN: THE USE OF MEDICAL CANNABIS IN PERSONAL CARE HOMES

## ABSTRACT

Medical cannabis refers to the prescription of cannabis to a patient by a healthcare provider, including nurse practitioner or physician, primarily aimed at treating chronic pain syndromes, spastic diseases, etc. Cannabidiol, a compound of cannabis, has been shown to have medicinal properties that can eliminate pain from the body. Cannabis and the medicinal properties remain an active area of enquiry and research.

Canada legalized the use of medical cannabis in October 2018, increasing access of cannabis for both recreational and medicinal purposes. Medical cannabis is purchased from a Health Canada licensed producer and must have a certificate indicating its origin. Seniors living in personal care homes tend to suffer from multi-system disease. The purpose of this study was to evaluate the existing policies on the use of medical cannabis in personal care home facilities located in Newfoundland and Labrador, Canada. This study used SurveyMonkey software to obtain responses from administrators of the 81 personal home care facilities in the province. The data were analyzed using statistical data methods, and inferences, conclusions, and recommendations are outlined.

## BACKGROUND

Medical cannabis is marijuana that a qualified medical practitioner prescribes for patients after a comprehensive assessment.<sup>1</sup> It is primarily prescribed to patients suffering from moderate-to-severe pain from chronic diseases such as cancer.<sup>2</sup> The medicinal use of cannabis has not been adequately tested for possible side effects and interactions with other drugs due to government restrictions.<sup>3</sup> In 2018, Canada legalized the use of medical cannabis; however, there is a lack of policies in many areas regarding its usage.<sup>4</sup> Seniors are the most affected

by chronic pain due to various diseases and illnesses that affect their overall health status.

Despite substantial improvements in access to medical cannabis for Canadians, a great part of the elderly population residing in personal care homes continues to experience limited access.<sup>4</sup> Besides, many personal care homes in Canada have not yet adopted policies on its use within their premises. The purpose of this study was, therefore, to assess medical cannabis policies at personal care homes throughout Newfoundland and Labrador, Canada.

## METHODOLOGY

The purpose of this study was to establish whether there are existing policies put in place by personal care homes in the province of Newfoundland and Labrador, Canada, in relation to the use of medical cannabis within their premises. This study used a purposive sampling method to target all personal care homes in the previously mentioned region. The target population was all 81 personal care homes located in the area. The subjects of the study were the administrative heads of these homes who were in charge of policy formulation in their domain of work.

A survey questionnaire was developed and distributed online to all the research participants to give their responses. Respondents were asked to indicate their level of knowledge of the use of medical cannabis and if there existed any facility policy in relation to medical cannabis. The questionnaires were collected for analysis. The results were analyzed using quantitative data analysis methods and SPSS software. Statistical analyses were also carried out to make inferences, conclusions, and recommendations.

## RESULTS AND FINDINGS

This study was carried out using SurveyMonkey, an online cloud-based survey software, for data collection. The survey questionnaires were distributed, via email, to all administrative contacts for the 81 personal care home facilities for the elderly in the Newfoundland and Labrador regions. By a purposive sampling method done through phone conversations, home administrators were identified and targeted for the survey. They were requested to indicate their level of agreement with the questions by completing the survey questionnaires and returning them for data analysis. The response rate for the study was 77%, with 62 out of the targeted 81 personal care home facilities successfully filling the questionnaires and returning them. This percentage is significant enough to make conclusions and generalizations.

## THERE SHOULD BE DESIGNATED CANNABIS USE AREAS WITHIN THE PROPERTY FOR RESIDENTS WHO HAVE BEEN PRESCRIBED CANNABIS BY THEIR HEALTHCARE PROVIDER.<sup>9</sup>

The administrators were asked if they had a policy on the use of medical cannabis by residents living in their facilities, and 100% of the respondents said that they had no such policy. Depending on whether the facility had a policy or not, the research participants were asked to indicate which statement reflected their attitudes on formulating a policy on cannabis use by residents in the facility. Their responses were: 57% agreed that it was quite important for their facilities to adopt a policy on the use of cannabis within their premises by residents, 14% felt that it was somewhat important to have a policy on cannabis use within their premises, while 29% of the respondents felt that it was not important to have a policy on cannabis use within their premises. The respondents were also asked to indicate their knowledge on the medical use of cannabis, where 43% said they were very knowledgeable, 57% had limited knowledge, whereas none had no knowledge on the use of marijuana for medicinal purposes. Amongst the 62 facilities that successfully filled the questionnaire, 14% were located in urban areas, while 86% were located in rural regions with none located in remote areas.

A case study was also carried out to get the first opinion of some of the residents in the personal care facilities. One resident, who will be identified by her initials as VP for privacy reasons, was a 78-year-old female who had been previously diagnosed with chronic pain secondary to fibromyalgia, occasional insomnia, and anxiety. She had been prescribed several medications commonly used for patients suffering from related conditions. However, her condition never improved, but instead, she suffered from multiple severe side effects from drug interactions.<sup>5</sup> Having read online about the medicinal use of cannabis to reduce pain, her daughter suggested that VP should consider a trial of medical cannabis. The daughter then proceeded to the office of the personal care home administrator to enquire how she could obtain a medical document for medical cannabis for her ailing mother. The administrator was categorical that no residents were allowed to use cannabis in the facility. The administrator also doubtfully expressed concern if cannabis had any known medicinal properties that would improve the health condition of her mother.<sup>6</sup> From this response, VP became upset and disillusioned because she felt that her only chance to potentially improve her health condition was compromised and she would never know what could have happened if she was allowed to use cannabis for therapy in the facility.

## CONCLUSIONS

From the findings, it can be concluded that the majority of the personal care homes in Newfoundland and Labrador have not yet developed policies on the use of medical cannabis by the residents within their premises. Personal care home administrative staff do not possess adequate information regarding the benefits of medical cannabis and how it can significantly improve the health of the seniors.<sup>7</sup> As well, staff do not have the right perceptions and attitudes regarding the medical use of cannabis and need to be trained to improve their knowledge on the health benefits of medical cannabis. Seniors living in personal care home facilities are being denied their right to access medical cannabis. This trend should be reversed as the medical use of cannabis is now legalized in Canada and no one should be denied this fundamental right.<sup>8</sup>

## POLICY RECOMMENDATIONS

Personal care homes need to define and adopt a policy on the use and storage of cannabis specific to their premises. There should be a contract clause requiring

residents to produce a purchase certificate, or medical document, from a legal cannabis licensed producer before they can be permitted to use cannabis within the facility. Residents should be responsible for the storage of cannabis in their personal lockers which should be locked at all times, and free from access by any unauthorized person. Administrative staff should be strictly prohibited from assisting any resident in accessing cannabis with adverse consequences. A policy on medical cannabis use is essential to ensure the safety of all residents in the personal care home cannabis.<sup>10</sup> There is a need to grant senior residents residing in personal care homes limited access to medical cannabis without endangering the safety and security of the rest of residents and members of staff.

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**Dr. Sana-Ara Ahmed, MD, FRCPC**

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# TREATING CHRONIC PELVIC PAIN WITH CANNABINOIDS: A RETROSPECTIVE CHART REVIEW\*

\*This article is based on a poster that was presented at the AAPM (American Academy of Pain Medicine 2019 Annual Meeting and was published in the AAPM Journal, April 2019)

## BACKGROUND

Chronic Pelvic Pain (CPP) is a complex, debilitating disorder in women defined as “intermittent or constant pain in the lower abdomen or pelvis for at least 6 months’ duration, not occurring exclusively with menstruation and not associated with pregnancy” and can be a combination of disease in the gynecologic, urologic, and central nervous systems.<sup>1,2</sup>

The greatest incidence is in women between the ages of 26 and 30. It is estimated that 33-39% of women living in North America will experience pelvic pain at least one point in their lives with as many as 20% of these cases progressing to CPP.<sup>3</sup> There is a wide range of causes for CPP and oftentimes it is difficult to diagnose and treat due to the complexity of the interdependence of varying etiology. Common reproductive system causes are endometriosis, adenomyosis and pelvic adhesions.<sup>3</sup> However, in many women a clinical diagnosis is not often found, and the concept of neurologic and musculoskeletal causes becomes more forefront.<sup>3</sup>

**TABLE 1 – CAUSES OF CHRONIC PELVIC PAIN<sup>1-3</sup>**

<p><b>Reproductive</b> Endometriosis, Endosalpingiosis, Adenomyosis, Pelvic adhesions, Chronic pelvic infections, Ovarian cysts, Residual ovary syndrome, Ovarian remnant Syndrome, Post-hysterectomy pain, Fibroids, Vulvodynia</p>	<p><b>Musculoskeletal</b> Pelvic Ligamentous structures, pelvic muscular (iliopsoas, piriformis, quadrates lumborum, sacroiliac joint, obturator internus, pubococcygeus) Pelvic floor muscle tension/spasm</p>
<p><b>Vascular</b> Dilated pelvic vein/pelvic congestion</p>	<p><b>Spinal</b> Degenerative joint disease, disc herniation, spondylosis, neoplasm of spinal cord/sacral nerve, Coccydynia, degenerative disc disease</p>
<p><b>Gastrointestinal</b> Irritable bowel syndrome, abdominal migraines, recurrent small bowel obstruction, hernias, inflammatory bowel disease</p>	<p><b>Neurologic</b> Neuralgia/cutaneous nerve entrapment (surgical scar in the lower part of the abdomen), iliohypogastric, ilioinguinal, genitofemoral, lateral femoral cutaneous nerve, shingles (herpes zoster infection), spine-related nerve compressions</p>
<p><b>Urologic</b> Chronic (nonbacterial) UTI’s, painful bladder syndrome, interstitial cystitis, nephrolithiasis, urethral syndrome</p>	<p><b>Psychological (Psychosocial/Sexual)</b> Anxiety, depression, physical or sexual abuse, drug addiction/dependence, family problems, sexual dysfunction</p>



Furthermore, it has been postulated that particular disease states (i.e. endometriosis) which damage internal organs and lead to somatic pain can, over time, also develop into neuropathic pain.<sup>4</sup> Likewise, nerve entrapments in the pelvic floor region and abdominal region should be considered as these are more likely to occur in post-surgical patients still suffering with CPP. It has been my experience that once a woman has been diagnosed with CPP the likelihood of neuropathic pain contributing to the overall pain experience is very high.<sup>4</sup>

Causes of pelvic floor nerve entrapment can be from

- intra-abdominal or pelvic adhesions or
- edema around nerves or
- damage from surgical procedures

By following a clinical examination that is based on location of primary onset of pain symptoms, specific pain generators can be identified and subsequently treated.<sup>4</sup> These pain generators are often peripheral nerves that contribute to pelvic floor and lower abdominal pain which are: Ilioinguinal, Iliohypogastric, Genitofemoral, Pudendal & Lateral cutaneous nerves. Targeted pain control of these nerves via ultrasound guided nerve blocks is a mainstay of my clinical practice.

**TABLE 2 – PERIPHERAL NERVES OF PELVIC REGION<sup>4</sup> (ADAPTED FROM APTE)**

Nerve	Origin	Localization of Pain	Characteristics of Pain
<b>Ilioinguinal &amp; Hypogastric Nerve</b>	originates from L1 to L2 and converges on dorsal horn structures shared with the proximal fallopian tubes and uterine fundus. It enters the inguinal canal approximately 2 cm medial to the anterior superior iliac spine to travel along the canal.  located between the internal oblique and transverse abdominis muscles	the medial groin, the labia majora or scrotum, and the inner thigh	burning, tingling paresthesia, deep achy pain like visceral pain and sharp stabbing pains
<b>Genitofemoral Nerve</b>	Passes through the psoas muscles and originates from L2 and branches into (1) genital nerve (2) femoral nerve above the inguinal ligament in pelvis	genital branch provides sensation to the labia majora and mons pubis  femoral branch provides sensation in the middle anterior thigh	Burning pain in vulva Pain and deep ache down middle anterior thigh and inability to relax pelvic floor muscles
<b>Pudendal Nerve</b>	Originates from the anterior branches of the ventral rami from S2 to S4. Exits the pelvis via greater sciatic foramen and re-enters the pelvis thru the lesser sciatic foramen, passing between sacrospinous ligament anteriorly and sacrotuberous ligament posteriorly and wraps behind the ischial spine	both motor and sensory fibers to the genital area from the anal and perirectal area up to the clitoris or penis.	Symptoms include burning pain in the genital area. Severe pain with intercourse symptoms decrease when sitting on a toilet seat. Urinary incontinence, urgency or frequency, as well as pain with bowel movement and constipation
<b>Lateral Cutaneous Nerve</b>	Originates from L2 to L3 and courses inferolaterally in the iliacus muscle to pass under the inguinal ligament. May pass behind or through the inguinal ligament	Also known as meralgia paresthetica, LCN provides sensory for upper outer thigh	produces burning, aching pain and numbness/ paresthesia in the upper outer thigh

Secondly, women experiencing CPP also suffer from secondary chronic pain related diagnoses such as fibromyalgia, post-traumatic stress disorder, general anxiety disorder, depression and sleep disorders. Clinical challenges become more pronounced in accurately diagnosing the cause of pelvic pain due to the central hyper-sensitization of the nervous system secondary to the influence of concurrent affective mood disorders.<sup>5-6</sup>

In clinical chronic pain practice, the combination of neuropathic pain and anxiety states or depression results in the additional diagnosis of pain related functional sleep disorder. Functional sleep disorders are defined as problems with the quality, timing and amount of sleep, which, in turn, cause problems with functioning and distress during the daytime.<sup>7-8</sup>

## THE ENDOCANNABINOID SYSTEM

Understanding the endocannabinoid system (ECS) is the first step in recognizing when cannabinoid medicine can be used to treat functional sleep disturbances due to pain. The ECS is an ancient, ubiquitous signalling system found in most complex vertebrates. The endocannabinoid system is comprised of cannabinoid receptors (CB1/CB2), cannabinoid molecules (lipid ligands called endocannabinoids) and enzymes that create and break down endocannabinoids in order to regulate a variety of responses in our bodies, particularly for homeostasis.<sup>9</sup> The role of the ECS is briefly summarized as the system that regulates “relaxation, appetite, sleep, memory & immunity” implicating it in pain relief, mood management, physical movement, appetite, sleep cycles, extinction of traumatic memories, immunomodulation, neuroprotection and immuno-surveillance.<sup>9-10</sup> Simply put: if our organ systems make up the body’s symphony, the endocannabinoid system is the conductor coordinating body functions.

Functional sleep disturbances secondary to pain and anxiety are challenging to manage for the chronic pain specialist due to the inherent risk of pharmaceutical misuse by patients. In my chronic pain practice, the translation of the current knowledge on cannabinoid medicine has evolved into a safe prescribing alternative to the combination treatment of opioids, tricyclics and anti-convulsants for managing the secondary symptoms of anxiety and functional sleep disturbances caused by complex pelvic pain in women.

The use of phytocannabinoids (1) delta-9-tetrahydrocannabinol (THC) and (2) cannabidiol (CBD) are well established as modalities for treating neuropathic pain, inflammation, anxiety, post-traumatic stress disorder & functional sleep disturbances.<sup>11-14</sup> Likewise, the extensively researched monoterpene myrcene is found to have sedative properties and is the prominent sedative terpene in the *Cannabis sativa* plant.<sup>15-16</sup>

## CHART REVIEW: BASELINE CHARACTERISTICS, METHODOLOGY AND RESULTS

We conducted a retrospective chart review of female medical cannabis patients receiving ultrasound guided ilioinguinal & genitofemoral nerve blocks between August 2017 and December 2017. All patients received initial treatment from a Health Canada approved licensed producer of medical cannabis via the Access to Cannabis for Medical Purposes Regulations (ACMPR). We present a case series of treating functional sleep disturbances using high myrcene medical cannabis strains with THC content greater than 15% in both dried flower and sublingual oil form as primary treatment prior to initiating ultrasound guided nerve blocks for complex pelvic pain in women.

Three women ages 36 – 42 were identified with severe pelvic pain, anxiety, depression & insomnia. Brief Pain Inventory (BPI) indicated prior treatment with poly-pharmacy of long and short acting opioids, anti-convulsants, TCA anti-depressants, SSRI anti-depressants, laxatives/diuretics and anti-psychotics with VAS pain scores still ranging between 8-10 on a daily basis.

At three months follow up, there was a reduction in VAS pain scores by 30% with use of medical cannabis for treating anxiety, pain and insomnia. At six months follow up, the decision to initiate targeted ultrasound-guided nerve blocks for genitofemoral and ilioinguinal neuralgia was based upon the following criteria:

1. minor improvement in VAS pain scores or
2. inability to reduce poly-pharmacy or
3. the need for diagnostic and therapeutic value from a nerve block to confirm or refute diagnosis by other medical specialists

## AFTER 9 MONTHS OF COMBINED TREATMENT OF MEDICAL CANNABIS AND TARGETED NEUROPATHIC PAIN TREATMENT, VAS PAIN SCORES REMAINED IMPROVED BY 30% OR MORE AND THE NUMBER OF PRESCRIPTION PAIN MEDICATIONS WAS REDUCED ALSO BY 30%.

Treating complex chronic pelvic pain with medical cannabis for functional sleep disturbances had the following three core treatment outcomes: (1) VAS pain score consistently reduced by 30%; (2) Harm reduction of pharmaceuticals, particularly opioids; (3) Improved accuracy of pelvic pain diagnosis with confirmation by allied medical specialists.

**Patient 1** successfully weaned off of dependency on poly-pharmacy by using vaporized dried flower CBD: THC 1:1 at night and CBD oil 25 mg during the day. A suspected diagnosis of missed endometriosis was made after a diagnostic ilioinguinal/hypogastric block in office resulted in significant pain control. Recently she elected to undergo vaginal hysterectomy after recommendation by gynaecology confirming the diagnosis. We have discontinued interventional nerve blocks.

**Patient 2** successfully treated anxiety and insomnia with balanced CBD:THC oil 5:5 mg TID and high myrcene THC oil 5 mg at night. Within 5 months of medical cannabis treatment, she was diagnosed by an ER physician for nephrolithiasis and hydronephrosis. She underwent urologic surgical treatment and has reduced her 3 different types of opioids to morphine 5 mg PO TID. We have discontinued iliopsoas blocks performed by another pain clinic which in the past have resulted in local anesthetic toxicity. She continues with ilioinguinal/hypogastric nerve blocks and genitofemoral nerve blocks 3 times a year to maintain her opioid dose at 15 mg a day.

**Patient 3** successfully weaned off of multiple NSAIDs, stomach protection agents and belladonna suppositories by using CBD oil 50 mg during the day & 10 mg THC oil at night to manage anxiety & depression secondary to pain. The initiation of US-guided ilioinguinal and GFN blocks has greatly improved her quality of life.

## DISCUSSION

Urogynecological pain is often misunderstood and misdiagnosed in female patients with concurrent diagnoses of generalized anxiety disorder, fibromyalgia, and insomnia. We were able to make distinctions in patient care by accurately guiding patients to relevant urgent care and need-based surgical procedures to alleviate the root cause of their complex pelvic pain by initiating medical cannabis as primary treatment. Further investigation is recommended to establish the potential of initiating high myrcene medical cannabis strains as a primary treatment for chronic pain associated sleep disturbances. This will be in order to differentiate better the need for peripheral nerve blocks for the neuropathic component of pelvic pain. We believe that the combination of medical cannabis and nerve blocks provides an important paradigm shift and non-opioid option for treatment of chronic pelvic pain in women.

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## RESEARCH CORNER: CANNABIS IN THE TREATMENT OF HEADACHES, MIGRAINES, AND ANXIETY, AND IT'S IMPACT ON OPIOID AND PRESCRIPTION SUBSTANCE USE

Nothing teaches patience quite like conducting human health research. Research on individuals demands determination, attention to detail, and humility, with the outcome of all that planning, and perseverance not being known for weeks, months, or years, depending on the study design.

In the best of cases, research is a labour of love, with the reward not being monetary, nor typically taking the form of awards or prizes. More often than not, the modest outcome is the publication of results in a peer-reviewed journal and an acknowledgement from a few fellow academics that all that hard work was not for naught. Sometimes the world notices and perhaps even changes. Much of the time a new reference is added to a PubMed search and the world goes on.

Regardless of the impact, academics do this formal dance because we understand and accept this is how new scientific knowledge is formed; not with rare and dramatic eureka moments, but with the slow stacking of evidence on a scale that delicately balances one way or the other. Science is rarely absolute, but an honest and earnest debate of ideas, and of ways to challenge the same via research and the publication of findings.

In this article, it's my pleasure to present triplets born of this laboured academic process: 3 new publications stemming from the Tilray Patient Survey 2017 (TPS17). They are the result of collaborations between Tilray

and academics across Canada and the US, and their findings, while limited, may add to our understanding of the impact of medical cannabis on pain and headaches, anxiety, and the use of opioids and other substances. The Tilray Patient Survey 2017 is a 239-question instrument distributed online in January 2017 to authorized medical cannabis patients across Canada, ultimately gathering 2,032 complete responses. The study included a number of academic collaborations, including the contribution of validated questions specific to headaches and migraines by neurologist Dr. Eric Baron from Cleveland Clinic, as well as instruments specific to anxiety by Dr. Michael Van Ameringen from McMaster University.

The first article is titled Patterns of medicinal cannabis use, strain analysis, and substitution effect among patients with migraine, headache, arthritis, and chronic pain in a medicinal cannabis cohort and was published in the Journal of Headache and Pain.<sup>1</sup> Baron provided the ID Migraine™ questionnaire, a validated instrument used to predict the probability of migraine in patients. Patients who self-identified as migraine or headache sufferers filled out the questionnaire, and then were compared with the general patient population to identify patterns of use specific to this sub-population. Overall, 505 patients (24.9%) identified headaches as a symptom for which they used cannabis, with 75 citing it as a primary condition. Based on the analysis of the ID Migraine™, 88% (n = 445) of headache patients were

treating probable migraine with cannabis. Prescription substitution in headache patients included opiates/opioids (43.4%), antidepressants/anti-anxiety medications (39%), nonsteroidal anti-inflammatories (21%), triptans (8.1%), anticonvulsants (7.7%), and muscle relaxers (7%).

Perhaps the most interesting finding of the study came from a sub-analysis of the strain preferences identified by this patient population. Hybrid strains were preferred by headache sufferers, as well as most pain groups, with OG Shark, a high tetrahydrocannabinol (THC)/low cannabidiol (CBD) strain with predominant terpenes  $\beta$ -caryophyllene and  $\beta$ -myrcene, most preferred in the headache and ID Migraine™ groups. The researchers suggest this could be due to the analgesic, anti-inflammatory, and antiemetic properties of THC, coupled with the known anti-inflammatory and analgesic properties of  $\beta$ -caryophyllene and  $\beta$ -myrcene. To the best of my knowledge, this is the first time a specific strain and associated terpene and cannabinoid profile has been statistically identified with the treatment of a primary condition like headache/migraine/pain, and this could point the way to more specific cannabis-based treatments for these conditions in the future. There appears to be keen interest in this, as the article is amongst the top 10 most popular at this journal with over 9,000 accesses to date!

The second article is titled Cannabis use behaviors and prevalence of anxiety and depressive symptoms in a cohort of Canadian medicinal cannabis users, and was published in the Journal of Psychiatric Research.<sup>2</sup> Prof. Michael Van Ameringen, from McMaster University, provided a few validated instruments used to assess for anxiety/anxiety disorders; namely, the Generalized Anxiety Disorder 7-item, Patient Health Questionnaire-9, Mini-Social Phobia Inventory, and panic disorder/agoraphobia Diagnostic and Statistical Manual of Mental Disorders criteria. Findings from these instruments showed that the prevalence rate of anxiety in this population was very high. Overall, 43.7% (n = 888) of this population cited anxiety as a symptom which they treated with cannabis, and 63.4% met screening criteria for  $\geq 1$  disorders: 45.6% potentially qualifying for generalized anxiety disorder, 42.4% for social anxiety disorder, 25.7% for major depressive disorder, and 25.7% for panic disorder/agoraphobia.

## THE FINDINGS SUGGEST THAT MOST OF THESE PATIENTS FOUND CANNABIS HELPFUL IN TREATING THEIR ANXIETY, WITH 92% REPORTING IT IMPROVED THEIR SYMPTOMS

despite continuing to report symptoms of moderate-level severity. In fact, greater cannabis use was associated with higher symptom severity, suggesting that either increased symptoms led to greater use, or that despite higher rates of use, symptoms persisted.

Nearly half (49%) of respondents reported using cannabis as a substitute for a nonpsychiatric (53.7%) or psychiatric medication (46.3%) (see Table 1). Although there's been much interest in the use of CBD in the treatment of anxiety and other mental health issues, high THC strains were most often rated as anxiolytic by this patient population.

**Table 1. Proportion of the ANX Sample Replacing a Prescribed Medication with Medicinal Cannabis (n = 888).**

Drug Class	%
Antidepressants	23.8
Opioid	19.2
Benzodiazepine	15.8
NSAIDs	6.1
Antiepileptic	5.0
Sedative-hypnotic	4.2
General analgesic	3.9
Psychostimulant	3.7
Antipsychotic	3.0
All others	15.3

NSAIDs=nonsteroidal anti-inflammatories

In light of the high percentage of patients citing the use of medical cannabis in the treatment of anxiety and mental health issues, and ongoing questions in regard to both the positive and negative impacts of THC and CBD on psychiatric disorders, more rigorous research in this therapeutic area is clearly justified.

The third paper stemming from the TPS17 is titled Medical cannabis patterns of use and substitution for opioids & other pharmaceutical drugs, alcohol, tobacco, and illicit substances; results from a cross-sectional survey of authorized patients, and was published in the Harm Reduction Journal.<sup>3</sup> Overall, pain and mental health conditions accounted for 83.7% of all respondents (n = 1,700), and researchers found a very high rate of self-reported substitution for prescription drugs (69.1%, n = 953), as well as alcohol (44.5%, n = 515), tobacco (31.1%, n = 406), and illicit substances (26.6%, n = 136). Opioid medications accounted for 35.3% of all prescription drug substitution (n = 610), followed by antidepressants (21.5%, n = 371) (see Table 2). Perhaps of most significance to public health, of the 610 mentions of specific opioid medications, patients report total cessation of use of opioid medication in 59.3% (n=362) of cases.

**Table 2. Breakdown of Drugs Substituted with Cannabis Prescription Drugs**

	<u>(n, %)</u>
1. Opiates/opioids	610; 35.3%
2. Anti-depressant/anti-anxiety	371; 21.5%
3. Non-opioid pain medications	189; 10.9%
4. Anti-seizure medications	149; 8.6%
5. Muscle relaxant/sleep aids	140; 8.1%
6. Benzodiazepines	75; 4.3%
7. Stimulants	59; 3.4%
8. Antiemetics	24; 1.4%
9. Antipsychotics	18; 1%

These results support other recent publications suggesting that cannabis can reduce the use of – and associated harms associated with – more dangerous substances such as alcohol, tobacco, opioids, and illicit substances, potentially resulting in improved patient outcomes and overall public health.<sup>4-7</sup> Encouragingly, the article has been accessed nearly 3,000 times, so perhaps some of these findings will ultimately find their way into public policy to address the ongoing opioid overdose crisis.

While there is still so much to learn about the therapeutic potential of cannabis, through ongoing collaborations on innovative observational and clinical

studies, patients, academics, and healthcare providers are slowly and diligently filling the gaps of knowledge. The progress is long, slow, and systematic, but it is progress, nonetheless. We now know more about medical cannabis today than we did yesterday, and there is no doubt we'll know still more tomorrow.

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