ORIGINAL RESEARCH ■ PEER-REVIEWED

Cannabis use in patients with insomnia and sleep disorders: Retrospective chart review

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As medication experts, pharmacists are best suited to consult on the therapeutic applications of cannabinoids. Insomnia is highly prevalent and with the rise of cannabis use, this research is a necessary first step to providing sound care. We want to ensure our patients are using any medication safely and effectively.

ABSTRACT

Background: Medical cannabis has been increasingly used in Canada after being sanctioned by Health Canada in 2001. Insomnia and sleep disorders are among the most common conditions for which patients report using cannabis. Current research shows cannabis may have a beneficial effect in sleep disorders and may improve patient-reported sleep scores.

Methods: A retrospective chart review was conducted at Hybrid Pharm community pharmacy in Ottawa, Ontario, and included patients who were interested in, or already using, medical cannabis for sleep disorders. A qualitative, exploratory approach was taken to evaluate the descriptive efficacy and safety of medical cannabis when prescribed for insomnia or comorbid conditions. The comprehensive data collection also involved investigating the impact of cannabis on other medication used for insomnia.

Results: A total of 38 patients were identified as having adequate follow-up documentation to assess the impact of medical cannabis. At time of data collection, 15 patients (39%) were able to reduce or completely discontinue a prescription medication indicated for sleep. On follow-up, 27 patients (71%) reported a subjective improvement in their sleep or related condition. Only 8 patients (21%) reported any adverse effects from medical cannabis use, and these were manageable and did not require discontinuation of cannabis.

Conclusion: This study highlights the importance of a pharmacist's role in the management of cannabis-based therapy, including ongoing supportive care, follow-up and medication management. *Can Pharm J (Ott)* 2022;155:xx-xx.

Introduction

Cannabis has been used in Canada for medical purposes since being sanctioned by Health Canada in 2001 under the Medical Access Regulation Act.[1] Data on the potential impact of cannabis to treat insomnia remains equivocal, however, with a recent meta-analysis by Bhagavan et al. pointing out that while there are data to show a

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positive effect of cannabis on outcomes in patients living with insomnia, it is still low quality because of small sample sizes and short treatment periods.[2] Indeed, sleep disorders are one of the most common reasons individuals report using cannabis for medicinal purposes, alongside chronic pain and mental health–related disorders.[3]

Sleep is essential for health and involves factors such as quality and duration,[4] and recent research has shown that later sleep timing and greater variability in sleep are associated with adverse health outcomes such as increased risk of depression[5] and cardiovascular diseases.[6-9] Despite advances in pharmacotherapy and psychotherapy, insomnia and sleep disorders remain a significant burden to society. Cannabinoids are gaining acceptance for use as medicines in the treatment of insomnia. Patients often report using medical or recreational cannabis to treat multiple symptoms[10]; patients may be using cannabis for a primary sleep disorder (e.g., insomnia) or secondary to another medical condition or psychiatric condition (e.g., depression, anxiety, chronic pain, fibromyalgia, etc.).[11] Currently, the available pharmacologic treatments for insomnia and sleep disorders include H1-antagonists, benzodiazepines and hypnotics (e.g., zopiclone, zolpidem, etc.). Other medications are used off-label for sleep, including antidepressants (e.g., trazodone, mirtazapine) and second-generation antipsychotics (e.g., quetiapine).[12] However, many of these medications have unwanted adverse effects, including dizziness, cognitive impairment, daytime sedation, weight gain, metabolic syndromes and the potential for addiction and dependency. Many patients who seek medical cannabis for sleep and related disorders have often tried many of these medications and have experienced undesirable side effects.

The cannabis flower contains more than 120 different phytocannabinoids, with delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD) being the most studied cannabinoids of interest.[12] Cannabis, specifically with strains containing higher levels of THC, is known to have a dose-dependent effect on sleep.[13] THC acts on the CB1 receptors in the central nervous system and can yield a biphasic effect on sleep[14] such that THC, at lower doses, can reduce sleep onset latency and has been associated with greater ease of falling asleep, increased slow-wave sleep and increased total sleep time.[15-17] At higher doses, THC-predominant cannabis has demonstrated a reduction in total rapid eye movement (REM) sleep and REM density.[18]

CBD, the second most abundant cannabinoid found in cannabis, has been shown to have a dual effect on sleep latency. At lower doses, CBD can have a stimulating effect; however, at higher doses, it can have more of a sedating effect. It can increase total sleep time and decrease the frequency of arousals during the night. Overall, cannabis may have a short-term benefit on improving sleep time, where evidence has shown reductions in sleep onset latency.[19]

Based on the available evidence, THC and THC derivatives, used either alone or in combination with CBD, have been shown to improve self-reported sleep scores.[20] Because of the preliminary evidence from small-scale randomized controlled trials suggesting cannabis can provide treatment benefits in sleep disorders, along with the downfalls of current pharmacologic therapy, it is reasonable to conduct a review of patients using cannabis for sleep and assess their sleep scores, along with other measures of improvement or adverse effects of cannabis use.

Methods

The primary objective of this chart review was to evaluate the descriptive efficacy and safety of medical cannabis in patients with insomnia. The secondary objective was to identify specific medical cannabis products used for the treatment of insomnia and observe their effects on the utilization and discontinuation of other prescription medications in patients.

Design

A retrospective chart review of patients who indicated they were interested in using, or already using, recreational or medical cannabis for sleep or related disorders was conducted at Hybrid Pharm. The data collection was conducted through a comprehensive chart review of patients seen at Hybrid Pharm community pharmacy in Ottawa from January 2019 to July 2020, and who indicated they were seeking cannabis for insomnia and had received a medical document for cannabis.

Patients (inclusion/exclusion criteria) and recruitment

The inclusion criteria included patients who had received a medical cannabis document either from a clinician at Hybrid Pharm or from another prescriber. Patients were identified by investigators to be included in the analysis if there was adequate follow-up documentation regarding their cannabis use. Patients excluded from this study consisted of recent patients with a short duration of use, defined as less than 3 months of medical cannabis use from date of consultation at Hybrid Pharm. Further exclusion criteria included inadequate documented follow-up to assess efficacy and safety or patients who were not seeking cannabis for insomnia or sleep conditions.

Outcomes

The primary efficacy endpoints were subjective patient-reported improvements in sleep and a reduction in prescription medication use for sleep disorders. Secondary endpoints included adverse effects of cannabis and types of medical cannabis products used.

Follow-up

Patients were reassessed by a nurse practitioner 3 months after starting medical cannabis, once their initial medical document had expired. Pharmacists also conducted follow-up appointments with the patients to assist in medication counselling, including product selection, dosing, side effects and drug interactions. Electronic databases, consisting of patient

questionnaires and charts, community pharmacy patient profiles and health care professional documentation found in Kroll Pharmacy Management Software, AdvancedCare and CannScript, were all used to collect information. Self-reported diagnosed conditions on initial intake questionnaire can be seen in Table 1. The patient onboarding questionnaire contained in the AdvancedCare platform was a descriptive form completed individually by the patient. It included the Insomnia Severity Index (ISI), which was used to determine baseline insomnia severity as well as assess improvement, medical conditions and general open-ended questions regarding previously tried therapies and impact on quality of life. The ISI is a validated 7-item self-report with adequate psychometric properties that captures the nature, severity and impact of insomnia.[20]

Upon renewal, patients report on a recall period of "last month" using a 5-point Likert-type scale with the following dimensions: severity of sleep onset, sleep maintenance and early morning awakening problems, sleep dissatisfaction, interference of sleep difficulties with daytime functioning, noticeability of sleep problems by others and distress caused by the sleep difficulties. As indicated by Bastien et al., "The total score is interpreted as follows: absence of insomnia (0-7); subthreshold insomnia (8-14); moderate insomnia (15-21); and severe insomnia (22-28).[20] Ethics approval for this retrospective chart review was obtained from the Research and Ethics Board at the Children's Hospital of Eastern Ontario (CHEO).

Results

At the time of data collection, a total of 159 patients had indicated on the patient intake form that they were seeking cannabis for insomnia. Of 159 patients, 38 were identified as having adequate follow-up to assess the impact of medical cannabis (Table 2).

Patient demographics

At the initial point of contact at Hybrid Pharm, 39% of patients were taking a prescription medication indicated for sleep disorders when they began using medical cannabis (Table 3). At baseline, the mean ISI score was 15.4 (±5.2), which is indicative of moderate insomnia.

On the initial patient onboarding questionnaire, 87% of patients reported that their sleep disorder affected their daily routine, affecting quality of life. Patients were often seeking alternative therapies, including medical cannabis. Of the 38 patients included, 23 patients had reported previous or current cannabis use, either obtained recreationally or from a prior medical cannabis document from a licensed producer. Recreational cannabis was defined as use of cannabis not obtained directly from a licensed producer with a medical document. Medical cannabis was defined as cannabis authorized by a prescriber with a medical document and obtained from a Health Canada–licensed producer. Thirteen patients indicated they had never tried recreational or medical cannabis before and were therefore cannabis naive.

TABLE 1 Self-reported diagnosed conditions on initial intake questionnaire from Hybrid Pharm ($N = 38$)

Condition	*n*
Anxiety/stress disorders	18
Depression	12
Chronic pain	13
Sleep disorders	11
Migraines	7
PTSD	6
Cancer	4
ADD/ADHD	4
Fibromyalgia	3
Psoriasis	3
Eating disorders	1
COPD	1
IBS	1
Spinal cord injury/disease	1
Crohn's disease/colitis	1
Epilepsy	1
Arthritis	1

Patients were able to select more than 1 condition. PTSD, posttraumatic stress disorder; ADD/ADHD, attention-deficit disorder/attention-deficit hyperactivity disorder; COPD, chronic obstructive pulmonary disease; IBS, irritable bowel syndrome.

TABLE 2 Documentation of patients self-identified as interested in seeking or already using cannabis for a sleep disorder

Documentation	*n*
Adequate follow-up to assess endpoints	38
Inadequate documentation to assess endpoints	21
No follow-up documented	73
No medical document for cannabis or follow-up	27

The average duration of follow-up was 100.9 ± 60.4 days (data not shown). Upon follow-up with either a pharmacist or nurse practitioner at Hybrid Pharm, 21% of patients reported being able to reduce their prescription medication use, while 18% were able to completely discontinue prescription medications used for sleep or related comorbid conditions. These

TABLE 3 Baseline characteristics of patients included in the retrospective chart review ($N = 38$)

Baseline characteristics	*n*
Currently taking prescription medication indicated for sleep disorders	15
Reported using specifically for insomnia	7
Reported using primarily for depression or anxiety	5
No indication specified	3
Number of patients reporting that sleep disorder and/or related medical/psychiatric conditions were affecting their life daily	33
Previous cannabis use	23
Recreational cannabis	14
Medical cannabis	9
Cannabis naïve (no previous cannabis use)	13

Patients could be identified with multiple baseline characteristics. Recreational cannabis = cannabis used without a medical document authorized by a prescriber; medical cannabis = cannabis authorized by a prescriber and purchased from a Health Canada–licensed producer of medical cannabis products.

included benzodiazepines, benzodiazepine receptor agonists (i.e., zopiclone) and antidepressants (i.e., trazodone). Patients also reported using medications such as benzodiazepines and trazodone less frequently for sleep. Benzodiazepines are often associated with adverse effects, including the development of tolerance, risk of abuse and cognitive impairment, especially in older adults.[5] Eleven patients reported taking antidepressants such as trazodone, mirtazapine, doxepin or quetiapine for a concurrent diagnosis of depression or anxiety or, more commonly, for sleep.

The types of medical cannabis products used were based on the data collected, either from self-reported patient information during follow-up or recommendations made by the pharmacist or nurse practitioner: 34% reported using a CBD-only oil, while 21% of patients reported using a combination product of a THC:CBD oil, of varying concentrations. Many patients were using multiple medical cannabis products, with high-concentration CBD oil during the day and a THC:CBD (1:1) oil at night. Approximately 29% reported using at least 2 different types of cannabis oils, although this number may be higher, as a confirmed list of all products patients were using was not available. This included a high-CBD oil and a combination THC:CBD oil. Patients were often recommended to start CBD oil initially for use at bedtime if sleep was the main indication. Although smoking was discouraged, 3 patients reported that rapid onset via inhalation was more beneficial

TABLE 4 Medical cannabis products used by patients at Hybrid Pharm ($N = 38$)

Results	*n*
Cannabis oil products used:	
CBD-only oil	13
Combination THC-CBD oil	8
≥2 different cannabis oils	11
Routes of administration:	
Ingestion (oils)	37
Smoking/vaporization	3
Concentrated dosage forms (e.g., dabs, shatter)	1

Patients were exposed to multiple products and routes of administration.

before sleep, where they reported using inhalation methods such as vaporization, dabbing and shatter (Table 4). These patients were typically cannabis experienced and often used vaporization and alternative methods in addition to regularly dosed cannabis oils.

Based on follow-up documentation from the health care practitioners, 71% of patients reported subjective improvement in their sleep or related medical condition with cannabis, which was a primary efficacy endpoint. The degree of improvement varied, with some patients reporting a mild improvement, such as taking less time to fall asleep or sleeping longer through the night. Moreover, 26% reported a very significant improvement in their sleep or comorbid symptoms. Thirteen percent of patients reported that their symptoms and sleep level were the same and had no change with cannabis use (see Table 5 for efficacy and safety endpoints). Upon follow-up, based on anecdotal evidence, these patients were taking a dose that was too low to provide benefit for sleep or the medical cannabis product was inappropriate. Some patients reported their concurrent medical conditions, such as chronic pain, were improved with cannabis; however, their sleep may not have been affected to the same degree. This was often due to improper dosing and may have been improved with additional counselling and patient education. In addition, 2 patients reported worsening of sleep with medical cannabis. One of these patients was cannabis naive. The other patient reporting a worsening of sleep had previously smoked and vaporized recreational cannabis daily while also using a concentrated THC resin. They reported that the medical cannabis products recommended did not provide the same effect on pain relief and insomnia as the recreational product did.

Patients were assessed for the development of any adverse effects from cannabis during follow-up appointments. Of the 38 patients included, 66% reported no adverse effects from

TABLE 5 Efficacy and safety endpoints identified in patients using medical cannabis for sleep disorders ($N = 38$)

Endpoint	*n*
Efficacy endpoints	
Subjective improvement in sleep or related medical condition with cannabis use	27
Very significant subjective improvement in sleep or related medical condition with cannabis use	10
No change in sleep disorder or related medical conditions with cannabis use	5
Worsening sleep disorder or medical condition with cannabis use	2
Reduced prescription medication use	8
Discontinued prescription sleep medication	7
Safety endpoints	
No adverse effects reported	25
Mild adverse effects	8
No data of adverse effects	5

their cannabis use. Twenty-one percent of patients reported mild adverse effects, including diarrhea and acid reflux with cannabis oil, increased anxiety with higher THC concentrations and "brain fog." These adverse effects were often manageable with either a change in cannabis product, adjustment of THC:CBD concentrations, alternative dosage formulations or a dose reduction. While some patients chose to discontinue cannabis use for other reasons, no patients specifically discontinued medical cannabis due to an intolerable adverse effect.

Discussion

Sleep-related disorders represent one of the most common uses for cannabis products. Our review of patients using cannabis products for sleep showed that 71% of patients reported a subjective improvement in their sleep, with 39% of patients reducing and/or discontinuing prescription therapy. Twenty-one percent of patients experienced manageable dose-dependent adverse effects, which did not result in discontinuation of medical cannabis therapy.

Most patients we identified during this chart review indicated they had been diagnosed with an anxiety/stress disorder. Anxiety can often affect a patient's sleep, and both anxiety and stress often occur concurrently. Indeed, anxiety and sleep are top conditions cited by patients as indications for their cannabis use, along with pain[14]; the current findings dovetail with this previous research, as many of the patients in this chart review reported using cannabis for sleep, anxiety and chronic pain. Many patients reported reduced anxiety at night, which helped them fall asleep. Not only did this retrospective investigation demonstrate a subjective improvement in patients' quality and quantity of sleep and related symptoms, but it also demonstrated that many patients were able to discontinue prescription medications previously taken for sleep and anxiety. This had other improvements in their overall health, such as reduced side effects of medications and improved psychological well-being. Importantly, this review of chart data demonstrated that patients presenting to a pharmacy for treatment are able to completely discontinue insomnia medications, or reduce their use from nightly administration to as-needed administration, with the use of medical cannabis.

Adverse events and clinical implications

There were few adverse effects reported by patients, with only 21% of patients reporting any. None of the side effects reported were intolerable, and they often responded to therapy modification. Pharmacist and practitioner interventions were able to improve the efficacy and ameliorate the adverse effects of cannabis. These recommendations included titrating to an appropriate dosage or switching to an alternative product. Most of the adverse effects reported responded to a change in dose or product. For some patients, high concentrations of THC were reported to activate states of anxiety, euphoria, general stimulation and feeling "high," and for some, this was described as an adverse effect. However, these undesirable side effects were manageable and mitigated by recommendations from the pharmacist or prescriber to either switch to an alternative cannabis product or to reduce the dose. In addition, while patients were cautioned regarding smoking, some patients found this route of administration particularly helpful for sleep. The rapid onset and quick effect of smoking cannabis was cited by patients as helping reduce sleep onset latency.

This study highlights the importance of health care practitioner medication management, including proper dosing, product selection and adverse event mitigation. Most patients, 34%, used CBD-dominant ingestible products.

Study limitations

There were limitations to the current study. This was a retrospective chart review, and as a result, it was not possible to determine causation, only association. Although an initial 159 patients were identified as seeking cannabis for insomnia, there was a limited sample size of 38 patients due to a lack of follow-up data, which reduces the applicability of the current findings. Many of the patients included in this analysis were motivated to try cannabis or were already using medical or recreational cannabis with good effect, and this may have introduced bias, as the patients included in the analysis were likely more willing and motivated for medical cannabis to be effective. The ISI

scores were collected at baseline; however, there were no follow-up scores for the vast majority of patients, so it was not possible to compare scores over time. This indicates a possible area of future study. By looking at objective measures of sleep, including the ISI, it would be possible to better quantify the beneficial impact of medical cannabis on sleep. In addition, other scores such as the Brief Pain Inventory and Generalized Anxiety Scale–7, for patients with chronic pain and anxiety, respectively, would provide more objective data on the impact that cannabis may have on these conditions. Since insomnia, chronic pain and anxiety are often comorbid conditions, it is important to evaluate the response of cannabis on these medical and mental health conditions as well. Given the limitations of this study, the results are only hypothesis generating and unfortunately cannot inform current practice. While there appears to be a benefit for cannabinoids for sleep, larger randomized controlled trials are needed to provide clear data to change practice.

Conclusion

Our review of cannabis use in patients with sleep disorders suggests some benefits, with a subjective patient-reported improvement in insomnia and a decrease in use of prescription hypnotics. While this study provides some important insights into medical cannabis and sleep disorders, it is a low level of evidence because of the nature of the study. Overall, ongoing clinical trials of cannabinoids in patients living with insomnia are integral to ensuring evidence-based decisions on the role of cannabinoid therapies in the treatment of sleep disorders. ■

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References

1. Marihuana Medical Access Regulations. Justice Laws Website. Government of Canada. Available: https://laws-lois.justice.gc.ca/eng/regulations/sor-2001-227/index.html (accessed Mar. 26, 2020).
2. Bhagavan C, Kung S, Doppen M, et al. Cannabinoids in the treatment of insomnia disorder: a systematic review and meta-analysis. *CNS Drugs* 2020;1-12.
3. Hazekamp A, Ware MA, Muller-Vahl KR, Abrams D, Grotenhermen F. The medicinal use of cannabis and cannabinoids—an international cross-sectional survey on administration forms. *J Psychoactive Drugs* 2013;45(3):199-210.
4. Chaput JP, Gray CE, Poitras VJ, et al. Systematic review of the relationships between sleep duration and health indicators in school-aged children and youth. *Appl Physiol Nutr Metab* 2016;41(6 suppl 3):S266-82.
5. Ashton CH. Pharmacology and effects of cannabis: a brief review. *B J Psych Int* 2001;178(2):101-6.
6. Slavish DC, Taylor DJ, Lichstein KL. Intraindividual variability in sleep and comorbid medical and mental health conditions. *Sleep*. 2019;42(6):zsz052. doi:10.1093/sleep/zsz052
7. Abbott SM, Weng J, Reid KJ, et al. Sleep timing, stability and BP in the Sueño ancillary study of the Hispanic community health study/study of Latinos. *Chest* 2019;155(1):60-8.
8. Liu Y, Wheaton AG, Chapman DP, Cunningham TJ, Lu H, Croft JB. Prevalence of healthy sleep duration among adults—United States, 2014. *MMWR Morb Mortal Wkly Rep* 2016;65:137–41.
9. Baglioni C, Battagliese G, Feige B, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. *J Affect Disord* 2011;135(1):10-9.
10. Bertisch SM, Pollock BD, Mittleman MA, et al. Insomnia with objective short sleep duration and risk of incident cardiovascular disease and all-cause mortality: Sleep Heart Health Study. *Sleep* 2018;41(6):zsy047.
11. Walsh Z, Callaway R, Belle-Isle L, Capler R, Kay R, Lucas P, et al. Cannabis for therapeutic purposes: patient characteristics, access and reasons for use. *Int J Drug Policy* 2013;24(6):511-6.
12. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. *Chest* 2014;146(5):1387-94.
13. Kim D. Insomnia. *Compendium of Therapeutics for Minor Ailments*. Ottawa, ON: Canadian Pharmacists Association; 2018. Available: https://myrxtx-ca.proxy.lib.uwaterloo.ca/print/new/documents/MA_CHAPTER/en/insomnia_minor (accessed Jul. 16, 2018).
14. Health Canada. For health care professionals: cannabis and cannabinoids. 2018. Available: https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html (accessed Oct. 17, 2020).
15. Babson KA, Sottile J, Morabito D. Cannabis, cannabinoids and sleep: a review of the literature. *Curr Psychiatry Rep* 2017;19(4):23.
16. Hanlon EC, Tasali E, Leproult R, et al. Sleep restriction enhances the daily rhythm of circulating levels of endocannabinoid 2-arachidonoylglycerol. *Sleep* 2016;39(3):653-64.
17. Schierenbeck T, Riemann D, Berger M, Hornyak M. Effect of illicit recreational drugs upon sleep: cocaine, ecstasy and marijuana. *Sleep Med Rev* 2008;12(5):381-9.
18. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet* 2003;42(4):327-60.
19. Kuhathasan N, Dufort A, MacKillop J, Gottschalk R, Minuzzi L, Frey BN. The use of cannabinoids for sleep: a critical review on clinical trials. *Exp Clin Psychopharmacol* 2019;27(4):383-401.
20. Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Med* 2001;2(4):297-307.