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Special Article

Diabetes Canada Position Statement on Recreational Cannabis Use in Adults and Adolescents With Type 1 and Type 2 Diabetes

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Key Messages

- This position statement was developed by Diabetes Canada in response to legalization of recreational cannabis in Canada on October 17, 2018.
- A rapid review of the literature suggests that recreational cannabis use may negatively impact diabetes metabolic factors and self-management behaviours.
- Health-care professionals should discuss recreational drug use with their patients living with diabetes on a regular basis, with a nonjudgmental approach.
- Metabolic parameters and self-care behaviours should be monitored for people with diabetes who regularly use recreational cannabis.

Keywords:
cannabis
diabetes
guidance
ketoacidosis
self-management

A B S T R A C T

Objective: Pursuant to the legalization of recreational cannabis in Canada, a rapid review was undertaken to develop a position statement concerning the effects of cannabis consumption on Canadians living with diabetes.

Methods: An expert committee of 1 adult endocrinologist and 1 pediatric endocrinologist, with the help of coauthors, collaborated to develop the position statement using the same evidence-based principles as the Diabetes Canada Clinical Practice Guidelines (with the exception of an independent methods review). A rapid review was conducted by researchers with the Strategic Patient-Oriented Research Evidence Alliance. The scope of the review was limited to evaluating the effects of recreational cannabis use on: 1) metabolic factors and diabetes complications, and 2) diabetes self-management behaviors in people ≥13 years of age. An informed person with diabetes, Canadian health-care providers and scientific advisors performed independent external reviews.

Results: The review found a limited amount of published or presented literature for the review questions, with gaps in direct evidence linking cessation of cannabis use to improved outcomes in diabetes. However, there were sufficient data to begin developing recommendations for type 1 and type 2 diabetes about education, counseling and management related to recreational cannabis usage.

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Conclusions: This is the first attempt in the world to generate an evidence-based guidance document on the topic of recreational cannabis use and diabetes. It provides guidance for health-care providers, so that they can assist and counsel Canadians living with diabetes on recreational cannabis. Further, higher quality research is required to provide more robust and evidence-informed guidance.

Mots clés :
cannabis
diabète
conseils
acidocétose
prise en charge autonome

R É S U M É

Objectif : Conformément à la légalisation du cannabis récréatif, nous avons entrepris une revue rapide pour élaborer un énoncé de position sur les effets de la consommation du cannabis chez les Canadiens diabétiques.
Méthodes : Un comité d'experts composé de 1 endocrinologue pour adultes et de 1 endocrinologue en pédiatrie, et de co-auteurs, ont collaboré à l'élaboration de l'énoncé de position selon les mêmes principes fondés sur des données probantes que les lignes directrices de pratique clinique de Diabète Canada (à l'exception d'un examen indépendant des méthodes). Les chercheurs ont réalisé une revue rapide en partenariat avec le SPOR (*Strategic Patient-Oriented Research*) Evidence Alliance. La portée de la revue s'était limitée à l'évaluation des effets de la consommation du cannabis récréatif sur: 1) les facteurs métaboliques et les complications associées au diabète; 2) les comportements de prise en charge autonome du diabète chez les personnes de $\geq$ 13 ans. Les personnes renseignées sur le diabète, les prestataires de soins de santé du Canada et les conseillers scientifiques ont réalisé des examens externes indépendants.
Résultats : La revue a permis de trouver un nombre limité de littérature publiée ou proposée sur les questions propres à la présente revue, et les lacunes dans les preuves directes qui établissaient un lien entre l'arrêt de la consommation du cannabis et les issues du diabète. Toutefois, les données étaient suffisantes pour commencer à élaborer des recommandations en matière d'enseignement, de counseling et de prise en charge associées à la consommation du cannabis récréatif lors de diabète de type 1 et de diabète de type 2.
Conclusions : C'est la première fois dans le monde qu'est créé un document qui fournit des conseils fondés sur des données probantes au sujet de la consommation du cannabis récréatif et diabète. Il fournit des conseils aux prestataires de soins de santé de sorte qu'ils puissent aider et conseiller les Canadiens diabétiques sur le cannabis récréatif. De plus, des recherches de qualité supérieure sont nécessaires pour fournir des conseils plus fiables et fondés sur des données probantes.

Introduction

Recreational cannabis (marijuana) was legalized in Canada on October 17, 2018. Canada is the second country, after Uruguay, to legalize recreational use of cannabis. Although the federal minimum age to use cannabis in Canada is 18 years, and all but 2 provinces (Alberta and Quebec) suggest 19 years as minimum age of use, the National Cannabis Survey reported in February 2019 that the highest prevalence of recreational consumption was among those 15 to 24 years old (18%) (1). Moreover, 15% of those $\geq$15 years old reported cannabis use (including use of marijuana, hashish, hash oil or any other preparation of the cannabis plant) in the past 3 months, an increase of almost 3% from previous estimates in 2012 (1,2). Half of those individuals (7%) who reported using cannabis in 2018 indicated they exclusively use this substance for nonmedical purposes (i.e. recreational consumption). Furthermore, 19% of the survey respondents indicated that they anticipate using cannabis in 2019, 4% higher than the consumption rates reported in 2018; up to 33% of current cannabis users anticipated increasing their cannabis use in the next year (1).

It is highly probable that consumption rates of cannabis (for recreational use) were under-reported in surveys and questionnaires in the past because of its illicit drug status until October 2018. It is expected that this under-reporting bias may change with legalization and greater acceptability of recreational cannabis use in Canada. Separately, and importantly for this Diabetes Canada position statement, use of recreational cannabis, specifically among Canadians living with diabetes, is unknown. Future surveys, specifically those performed among people living with diabetes, may be immensely informative in this regard.

In 2019, the prevalence of diabetes in Canada is close to 10%, and it is estimated that >1.5 million individuals are living with undiagnosed diabetes (3). Within the next decade, it is expected that the prevalence of diabetes will jump to >11% and costs associated with diabetes are expected to rise to $39 billion.

Cannabis plants produce a unique family of compounds called cannabinoids (4). Of these, the major psychoactive compound is trans-delta-9-tetrahydrocannabinol (THC). Cannabis contains high levels of THC, as well as other psychoactive chemicals, which produce the "high" users feel when inhaling or ingesting the drug. THC is associated with psychosis, anxiety and depression symptoms, along with potential for exacerbation of underlying psychiatric disorders. Several authors reported effects on memory, cognition, motor function, reaction time and psychomotor performance. Two other compounds, tetrahydrocannabivarin and cannabidiol, may have less psychoactive and possibly more medicinal properties; however, the published literature available has been considered to have low quality of evidence and may suffer from industry bias in reporting (5–7). Limited research has shown a potential link between cannabis use and changes in metabolic factors, and knowledge of these associations among health-care providers is lacking. Cannabis use may be associated with alterations in caloric intake and body mass index values or may interfere with self-management behaviours in youth living with type 1 diabetes mellitus (T1D) (8,9).

Following the recent cannabis legislation, Diabetes Canada commissioned a rapid review to examine and appraise existing evidence on the effects of recreational cannabis use in people with diabetes. The timely rapid review and synthesis, with the intent of generating clinical recommendations, enables Diabetes Canada to

inform and guide best practices among health-care providers for the care of persons with diabetes in Canada based on the currently available evidence. The intent of this Diabetes Canada position statement is to formulate evidence-based recommendations on counselling, glucose monitoring and management approaches for people with diabetes living in Canada who intend to, or are considering, using cannabis recreationally. This position statement is meant to serve as a guide for Canadian health-care providers to help maintain the health and safety of their patients.

Although the recommendations in this position statement are based on a rapid review and clinical expertise, the lack of high-quality research studies is acknowledged, especially with regard to intervention studies directly linking cessation of cannabis use to diabetes management–related behaviours and clinical outcomes. The limited availability of robust evidence warrants the urgent need for further research on this topic.

Methods

Two review questions were developed by the Diabetes Canada Professional Section Expert Committee members working on a volunteer basis (H.S.B. and C.H.): Among people ≥13 years who have T1D or type 2 diabetes mellitus (T2D), what are the effects of recreational cannabis use on: 1) Metabolic factors and/or diabetes complications? and 2) Diabetes self-management behaviours? Further questions that relate to other physical or psychological effects of cannabis (or its components), including potential medicinal benefits or nondiabetes complications, other than the 2 specific questions just described for this review, were not considered. This focused scope of the review was chosen because of the short timelines involved and the need to make this position statement available to Canadian health-care providers as soon as possible after legalization.

The rapid review methodology will be published elsewhere. Briefly, the methods entailed compiling a protocol and work plan based on the 2 questions by the Strategic Patient-Oriented Research (SPOR) Evidence Alliance in consultation with Diabetes Canada. The protocol was registered in the PROSPERO database (CRD42019122829). A search strategy was conducted in Medline, Embase and PsycINFO to identify experimental, quasiexperimental or observational studies (with the exception of case studies/case series) including people ≥13 years of age with any type of diabetes or prediabetes who used cannabis (any constituents) in any product form (inhaled, brewed, eaten) for recreational purposes compared with nonuse of cannabis. The outcomes of interest were metabolic factors related to diabetes, such as glycated hemoglobin (HbA1C), complications (decreasing renal function, DKA) or diabetes self-management behaviours.

All screening, data abstraction and risk-of-bias appraisal were conducted by pairs of reviewers working independently. A summary report was generated by the SPOR Evidence Alliance and approved by Diabetes Canada experts (10).

Subsequently, based on the summary report and the extracted studies, this position statement and guidance recommendations were generated by Diabetes Canada authors. Each recommendation was reviewed, graded and then approved with 100% consensus. Grading of recommendations was based on the best available evidence, as well as on applicability to the Canadian population, and followed the methods used by the *Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada* (2018 Guidelines) (11). However, unlike the 2018 Guidelines, the position statement did not undergo an independent review process to assess the accuracy of grading of the evidence. In addition, the assigned grading was lowered if any of the following conditions existed: 1) evidence was not applicable to the Canadian population, 2) findings from relevant (and equally rigorous) studies on the topic were conflicting and/or 3) specific subgroups of interest were not well represented in a study.

Independent external reviewers, including a person living with diabetes, a family physician, a certified diabetes educator, a scientific advisor, a diabetes specialist and a substance-abuse psychiatry specialist, provided critique and suggestions for the development of this position statement.

Results

Rapid review

The results of the rapid review itself will be published elsewhere. Briefly, the rapid review included 2 full-text articles and 4 conference abstracts after screening 1,848 citations and 59 full-text articles. All of the 6 studies reported on diabetes metabolic factors among cannabis users specifically, with 1 of these studies also focusing on diabetes self-management behaviours. In addition, 1 study provided information on the association of diabetes ketoacidosis (DKA) with drug use (including cocaine, cannabis and alcohol).

Effect of recreational cannabis use on glycemic control parameters in diabetes

Five studies (12–16) reported statistically significantly worse glycemic control among a total of 1,004 participants with T1D who consumed cannabis, although usage frequency was indicated in only 1 study (12). Although these studies consistently suggest worsening of glycemic control (HbA1C) for cannabis use, exact quantification of the effect size of this harm could not be determined due to either disparate reporting or lack of reporting (categorization of HbA1C, rather than mean HbA1C) in these publications.

In their retrospective cohort study, Akturk and colleagues (12) compared cannabis users with T1D to nonusers with T1D. The mean HbA1C level was higher (8.4% [standard deviation, 2.0%] vs 7.6% [standard deviation, 1.6%], respectively; $p<0.01$), with no difference in reported severe hypoglycemia events among cannabis users (21 of 134 [15.6%] vs 64 of 316 [20.3%], respectively; $p=0.17$). Cannabis users maintained a mean 0.41% higher HbA1C level than nonusers after adjustment for insulin delivery method, income and age (95% confidence interval, 0.38 to 0.43).

Effect of recreational cannabis use on diabetes complications

Winhusen and colleagues (17) conducted a case–control study with >1.2 million people, including 1,184 participants with T2D, who used cannabis. In their analysis, the risks of developing several diabetes complications (peripheral arterial occlusion, myocardial infarction and renal disease) were found to be statistically higher among participants with T2D who used cannabis.

Worse renal parameters were also observed for cannabis users with T1D in a cohort study involving 132 participants, where smoking cannabis was weakly, but statistically significantly, correlated with not only a higher HbA1C ($r=0.30$, $p<0.01$), but also a higher albumin/creatinine ratio ($r=0.22$, $p<0.05$) (16).

Effect of recreational cannabis use on risk of DKA in T1D

In the aforementioned study by Akturk and colleagues (12), the primary outcome was DKA hospitalization during the preceding 12 months. All self-reported DKA hospitalizations were confirmed by medical record review. However, the possibility of an underreporting bias for self-reported DKA events is a limitation of their study. Among adults with T1D in the study, cannabis use within the

previous 12 months was associated with an almost doubled risk of DKA compared with no cannabis use (entire cohort odds ratio, 1.98; 95% confidence interval, 1.01 to 3.91), with the authors suggesting a mechanistic link that cannabinoid alteration of gut motility may cause hyperemesis, hence leading to an increased risk for DKA in T1D (12,18).

Isidro and colleagues (19) also investigated the association between recreational drug use and DKA in a retrospective examination of records from an urban teaching hospital in Spain. Cocaine, followed by cannabis and alcohol, was the drug most frequently consumed in this T1D study population. More than half of the patients admitted for DKA had used 2 or more different drugs and 20.6% of the episodes in total were shown to be related to substance abuse. During the study, the mean number of hospital admissions for DKA was 1.4±1.3 for nonusers and 3.6±3.1 for any drug users ($p<0.001$). In the multivariate logistic regression analysis, drug use was associated with a higher probability of readmission ($p<0.001$; odds ratio, 9.5; 95% confidence interval, 2.5 to 15.3); although there was a high prevalence of simultaneous polysubstance consumption, a multivariate logistic regression analysis of the influence of each individual drug on the likelihood of readmission could not be performed.

Effect of recreational cannabis use on diabetes self-care behaviours

Wisk and colleagues (15) conducted a cross-sectional study to estimate the impact of substance use (including cannabis) and self-management behaviours on glycemic control in 138 college students with T1D. Students 17 to 25 years of age, from universities and colleges across 30 states and Washington, DC, in the United States and Canada self-reported their substance use behaviours, diabetes self-management and burden and most recent HbA1C level. The researchers discovered, after multivariable analyses, that students who smoked cannabis more frequently experience higher HbA1C and were less likely to achieve glycemic targets, independent of blood glucose testing and diabetes burden. However, no specific analysis on substance use and self-management behaviours was reported in the study. As in all cross-sectional studies, causality cannot be inferred and it is likely that social determinants of health play a significant role in this domain.

Recommendations

1. Health-care professionals should engage their patients in discussion about substance use on a regular basis, with a nonjudgmental approach [Grade D, Consensus].
2. Use of recreational cannabis is not recommended for adolescents and adults with diabetes [Grade D, Consensus]. The safety of recreational cannabis has not been demonstrated, whereas regular cannabis use is associated with worsening of glycemic control [Grade D, Level 4 for type 1 diabetes (16); Grade D, Consensus for type 2 diabetes], more diabetes-related complications [Grade D, Level 3 for type 1 diabetes (16); Grade D, Level 4 for type 2 diabetes (17)] and poorer self-care behaviours, such as adequate glucose monitoring, adherence to medications, compliance with dietary and physical activity recommendations, etc [Grade D, Consensus].
3. People with T1D should avoid recreational cannabis use because of the increased risk for DKA [Grade D, Level 4 (12,19)]. Management of DKA associated with cannabis consumption should be based on the 2018 Guidelines chapter, "Hyperglycemic Emergencies in Adults" (20) [Grade D, Consensus].
4. For adults with T1D or T2D who intend to use cannabis recreationally, individualized assessment and counselling should be offered to inform them of the general risks of cannabis with a focus on harm reduction and reduction of the risk for potential deleterious effects on diabetes management and complications [Grade D, Consensus for all]. This assessment should include:
   a. Risk stratification based on anticipated frequency, method, type and dose of recreational cannabis consumption and polysubstance use.
   b. Review of adverse impact on diabetes metabolic and self-management parameters from previous consumption (if any).
   c. Formulation of an individualized treatment plan, discussion about the importance of adherence to anti-hyperglycemic medications and/or insulin, dietary and physical activity recommendations, frequency of self-monitoring of blood glucose and scheduled contacts with health-care provider(s).
   d. Consideration of referral to local substance-use services for motivational interviewing, individual or group therapy and support, as appropriate.
5. People with type 1 or type 2 diabetes should be offered education on and encouraged to read public information available through resources from various Canadian health authorities about general risks of cannabis use, to reduce the risk of non–diabetes-related adverse effects of cannabis consumption [Grade D, Consensus].

Discussion

This position statement is the first evidence-based guidance document worldwide on the topic of recreational cannabis use in diabetes. It provides guidance for health-care providers so that they can assist Canadians living with diabetes on this issue. Cannabis use may be increasingly accepted with legalization in Canada and health-care providers need to be aware of the current state of evidence. The best available evidence was utilized to formulate recommendations, using a standard grading system. The literature search revealed significant knowledge gaps, which highlights the need for further high-quality research in this field, including more studies performed within the Canadian population.

It is important to note that this position statement did not address the risks and benefits of medical cannabis (or the specific compounds THC, tetrahydrocannabivarin, cannabidiol, etc) for people with diabetes—either in terms of efficacy for management of painful diabetes neuropathy or adverse effects on glycemic control and metabolic parameters.

The majority of evidence included in the review (5 of 6 studies) did not consider or report the route of administration for marijuana (smoking vs vaping vs edibles), which may have different risks for people with diabetes. Smoking cessation is a key pillar of diabetes management because of increased risk for cardiovascular disease. Edibles containing carbohydrates may present an additional challenge for glycemic control, in addition to the appetite-stimulating effects of cannabis.

This position statement has focused on risks specific to people with diabetes. Clearly, other risks associated with recreational cannabis use, such as psychiatric disorders, perturbations in neurologic development in adolescents, lung disorders, intoxication, risk-taking behaviour, impairment of driving ability and risk for motor vehicle accidents, other substance abuse and illegal procurement of drugs, etc, are highly relevant for people with diabetes. We recommend readers to refer to guidelines and recommendations for recreational cannabis use in the general population, such as the lower-risk cannabis-use guidelines for adults and youth (see https://www.cps.ca/en/documents/position/cannabis-children-and-youth and https://www.canada.ca/en/services/health/campaigns/cannabis/health-effects.html) (21).

Conclusions

Overall, this Diabetes Canada position statement calls for caution on recreational cannabis use with T1D and T2D, while highlighting the need for further health-care provider and patient education on the associated risks. Sustained education and dissemination efforts for the recommendations included in this position statement may assist Canadians living with diabetes in managing their condition safely. Timely updates to the recommendations included in this position statement may be considered in the future as further evidence is generated on this important issue of cannabis use with diabetes.

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Author Contributions

All authors actively discussed the content of the manuscript, drafted portions of the manuscript, critically revised the completed manuscript and approved the final version for submission.

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