Cannabis Use Is Associated With Increased Risk for Diabetic Ketoacidosis in Adults With Type 1 Diabetes: Findings From the T1D Exchange Clinic Registry

Gregory L. Kinney,[1] Halis K. Akturk,[2] Daniel D. Taylor,[1] Nicole C. Foster,[3] and Viral N. Shah[2]

Diabetes Care 2020;43:247–249 | https://doi.org/10.2337/dc19-0365

OBJECTIVE

We examined the frequency of diabetic ketoacidosis (DKA) in cannabis users compared with nonusers in the T1D Exchange clinic registry (T1DX).

RESEARCH DESIGN AND METHODS

The association between cannabis use by total substance score for cannabis (TSC) and DKA in the past 12 months was examined using a logistic regression model adjusted for potential confounders among adults in the T1DX.

RESULTS

Of 932 adults with type 1 diabetes, 61 had a TSC >4, which classified them as moderate cannabis users. Adjusting for sex, age at study visit, and HbA_{1c}, cannabis use was associated with a twofold increase in risk for DKA among adults with type 1 diabetes (odds ratio 2.5 [95% CI 1.0–5.9]).

CONCLUSIONS

Cannabis use was associated with an increased risk for DKA among adults in the T1DX. Providers should inform their patients of the potential risk of DKA with cannabis use.

Cannabis is the most commonly used illicit drug in the U.S. (1), and recent legislation has made cannabis legal for either medical or recreational use in more than half of states. Cannabis use among people with type 1 diabetes is not well described in the literature, but evidence from adolescents suggests that it does not differ from the general population (2). Delayed gastric emptying and reduced gut motility as a result of inhibition of the intrinsic cholinergic system have been shown in humans (3). Cannabis hyperemesis syndrome (CHS) has also been implicated in recurrent episodes of diabetic ketoacidosis (DKA) in patients with type 1 diabetes (4). The gastrointestinal effects of cannabis are not broadly recognized, and the primary reason for cannabis use in most users is recreational. Cannabis-induced alterations to gut motility, food absorption, and postprandial glycemic timing may be unexpected and inconsistent for the typical cannabis user with type 1 diabetes. A single-center study from Colorado showed an association between DKA and cannabis use in people with type 1 diabetes compared with non–cannabis users with type 1 diabetes (5). If this association between cannabis use and DKA holds true in the general population of people with

[1]Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora, CO
[2]Barbara Davis Center for Diabetes, University of Colorado Anschutz Medical Campus, Aurora, CO
[3]Jaeb Center for Health Research, Tampa, FL

Corresponding author: Gregory L. Kinney, greg.kinney@ucdenver.edu

Received 20 February 2019 and accepted 2 October 2019

type 1 diabetes, it would represent an important source of injury and costs. Therefore, we used the T1D Exchange clinic registry (T1DX) to study associations between cannabis use and DKA in adults with type 1 diabetes.

RESEARCH DESIGN AND METHODS

Up to 1,000 adults (age ≥18 years) with type 1 diabetes from 69 T1DX centers were invited to complete the Alcohol, Smoking and Substance Involvement Screening Test questionnaire. The primary predictor variable analyzed was the total substance score for cannabis (TSC), which uses a point system to weight responses to six questions assessing substance use behavior and generates a score ranging from 0 to 33, with higher scores indicating more risk. The scores are used to classify participants in terms of a recommended intervention: low risk, no intervention (0–3); moderate risk, brief intervention (4–26); and high risk, intensive intervention (>26) (5). We interpreted the no intervention group to comprise people less exposed to cannabis, and people with higher scores were considered to be more exposed to cannabis. Between-group characteristics were tested by t, χ^2, or Kruskal-Wallis test, depending on the nature of the data. The primary outcome of interest was self-reported hospitalization for DKA in the past 12 months. We examined the association between TSC and DKA by using logistic regression to test for known aspects of type 1 diabetes associated with DKA, including current glycemic control (HbA_{1c}), use of technology (continuous glucose monitoring, insulin pump), missed insulin doses (basal, mealtime), access to care, alcohol use, depression symptoms (through the Patient Health Questionnaire depression scale, which collected data temporally distant from the TSC data collection), age, and sex.

RESULTS

A total of 932 adults with type 1 diabetes responded to this feasibility survey. No participants in this study were classified as intensive intervention. Compared with participants categorized as no intervention (n = 871), cannabis users with moderate risk (brief intervention) (n = 61) were younger (31.0 ± 13.0 vs. 38.2 ± 16.0 years, $P < 0.0001$), were more likely to be male (54.1% vs. 37.9%), reported less academic education (college degree or more 46.7% vs. 61.0%, P = 0.03), reported a younger age at type 1 diabetes diagnosis (12.8 ± 8.8 vs. 16.1 ± 11.9 years, $P = 0.007$), had a higher HbA_{1c} (8.4 ± 1.8% vs. 7.7 ± 1.4%, $P = 0.005$), were less likely to use continuous glucose monitoring (21.3% vs. 34.4%), and were more likely to use tobacco or other substances. There were no differences in race, use of insulin pump, frequency of severe hypoglycemia requiring hospitalization, or alcohol use between the two groups. However, median self-monitoring of blood glucose was lower among the brief intervention group compared with the no intervention group (3.8 vs. 4.9/day, $P = 0.002$). Multivariable logistic regression showed that DKA was associated with a TSC >4 (odds ratio 2.5 [95% CI 1.0–5.9]) adjusted for sex, age at study visit, and HbA_{1c} (Fig. 1). Adjustment for the legal status of cannabis in the state of residence did not alter this association.

Strengths and Limitations

This study is based on self-reported data that may include unmeasured biases, specifically the willingness to report cannabis use in states where cannabis is illegal. We believe that participants' willingness to report other substance use suggests that this effect is not differential because it concerns the reporting of cannabis use. Depression has been shown to increase the risk of DKA, and substance use survey data were collected a few years before the collection of Patient Health Questionnaire depression scale data, making an analysis of the influence of depression on DKA in this population unreliable. The cross-sectional feasibility sample study design and lack of detailed information about diabetes self-management, insulin treatment compliance, and the frequency of DKA also are limitations of this study.

CONCLUSIONS

Cross-sectional analysis of T1DX participants reaffirms the observation of an association between cannabis use and DKA in adults with type 1 diabetes. A recent review of cannabis use in type 1 diabetes identified glycemic control and diabetes emergencies as important topics of interest (6). A suggested biological mechanism, cannabinoid inhibition of gut motility, has been shown in human and animal studies, and the rate of gastric emptying is associated with glycemic excursions (7). Studies with pharmacologic treatment that delays gastric emptying, such as glucagon-like peptide 1 analogs, have been shown to improve glycemic control. However, we hypothesize that unpredictable gastric dysmotility and severity of gastroparesis among cannabis users with CHS may result in suboptimal glycemic control. Moreover, cannabis-induced increase in appetite may result in increased glycemic excursions, and users may experience higher overnight glucose and an altered perception of hypoglycemia because of cannabis impairing their ability to manage diabetes. Studies have also suggested a link between long-term cannabis use and CHS, which is characterized by cyclic episodes of nausea and vomiting and may result in an increased risk for DKA (4). CHS has been observed primarily in heavy cannabis users, and this phenotype was not present in the T1DX participants, limiting our ability to assess CHS and DKA.

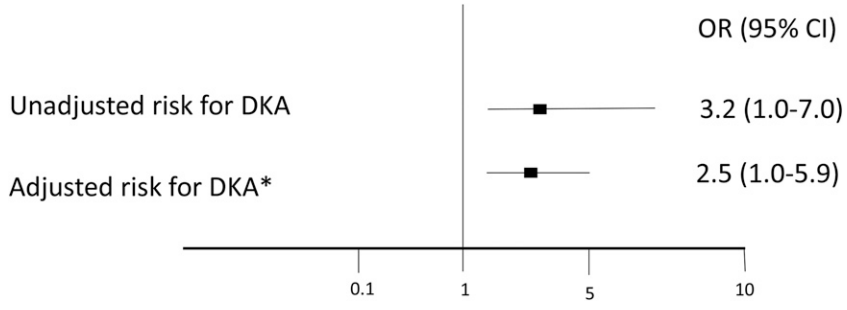

Figure 1—Odds of DKA (*adjusted for age, sex, and HbA_{1c}) among adult cannabis users with type 1 diabetes (Alcohol, Smoking and Substance Involvement Screening Test TSC ≥4) compared with nonusers (TSC <3). OR, odds ratio.

In conclusion, we have found an association between cannabis use and an increased risk for DKA among adults with type 1 diabetes. Our study has important clinical and research implications: Cannabis is a known addictive substance, and this potentially problematic aspect of cannabis use should be assessed in patients with type 1 diabetes. Providers should discuss with their patients who use cannabis the possibility of altered glycemic control, CHS, and DKA. More research is needed to understand the mechanistic link between cannabis use and DKA.

Acknowledgments. The authors acknowledge support from the T1DX, the Barbara Davis Center for Childhood Diabetes, and the Colorado School of Public Health.

Funding. T1DX is funded by the Helmsley Charitable Trust. G.L.K. was supported by faculty development funds through the Department of Epidemiology at Colorado School of Public Health.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

References

1. Hasin DS, Sarvet AL, Cerdá M, et al. US adult illicit cannabis use, cannabis use disorder, and medical marijuana laws: 1991-1992 to 2012-2013. JAMA Psychiatry 2017;74:579–588

2. Potter K, Luca P, Pacaud D, et al. Prevalence of alcohol, tobacco, cannabis and other illicit substance use in a population of Canadian adolescents with type 1 diabetes compared to a general adolescent population. Paediatr Child Health 2018;23:185–190

3. Camilleri M. Cannabinoids and gastrointestinal motility: pharmacology, clinical effects, and potential therapeutics in humans. Neurogastroenterol Motil 2018;30: e13370

4. Gallo T, Shah VN. An unusual cause of recurrent diabetic ketoacidosis in type 1 diabetes. Am J Med 2016;129:e139–e140

5. Akturk HK, Taylor DD, Camsari UM, Rewers A, Kinney GL, Shah VN. Association between cannabis use and risk for diabetic ketoacidosis in adults with type 1 diabetes. JAMA Intern Med 2019;179:115–118

6. Pancer J, Dasgupta K. Effects of cannabis use in youth and young adults with type 1 diabetes: the highs, the lows, the don't knows. Can J Diabetes. 14 May 2019 [Epub ahead of print]. DOI: 10.1016/j.jcjd.2019.05.001

7. Marathe CS, Rayner CK, Jones KL, Horowitz M. Relationships between gastric emptying, postprandial glycemia, and incretin hormones. Diabetes Care 2013;36:1396–1405