Variation in heart rate after acute cannabis exposure

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ABSTRACT

Smoking botanical cannabis often produces tachycardia. However, infrequent reports describe bradycardia, particularly with edibles, concentrates, and resins. We compared the rate of tachycardia in patients with acute cannabis exposures from ingestion versus inhalation and botanical versus resins/concentrates/edibles. Prospective data collection instrument inserted into the case notes of the Oregon/Alaska Poison Center over a 17-month period. We excluded cases without a recorded heart rate. 101 patients met inclusion/exclusion criteria. Patients who inhaled cannabis products were more likely than those who ingested cannabis to have tachycardia (84% v 59%; p = 0.024). Amongst ingestions, tachycardia was more frequent with cannabis edibles than resins/concentrates (63% v 40%; p = 0.044). Amongst resin/concentrate exposures, inhalation more often produced tachycardia than ingestion (90% v 40%; p = 0.014). There was no difference in frequency of tachycardia amongst children (<12 years; 48%; 12/25) or adolescents (12-18 years; 77%; 20/26) when compared to adults (18 years; 66%; 33/50). Six percent of patients had bradycardia, and all had significant symptoms of cannabis toxicity. The effects of cannabis exposure on heart rate are variable. Tachycardia is less common after ingestion of cannabis. Bradycardia occurs rarely after cannabis exposure, is associated with severe symptoms, and occurs in all age groups.

Introduction

Cannabis is a plant that contains many cannabinoids including tetrahydrocannabinol (THC) and cannabidiol (CBD). Cannabis is most commonly inhaled as botanical cannabis (dried cannabis flower) or added to food to produce “edibles”. Cannabis may also undergo chemical or mechanical extraction to produce “concentrates” (liquids used in vaporizers) and “resins” (semi-solid substances from which vapors are inhaled, e.g. dabbing). Concentrates and resins may have much higher concentrations of cannabinoids than botanical material.

Smoked botanical cannabis is associated with elevations in heart rate [1–4]. There is a linear relationship between the magnitude of heart rate elevation and the dose of tetrahydrocannabinol (THC), the main psychoactive substance in cannabis [4]. However, patients with cannabis toxicity occasionally have normal heart rates or bradycardia [5–7]. Bradycardia occurs in rat models with exposure to THC [2, 4] and may be due to dose-dependent inhibition of central sympathetic tone by THC [8].

Since the legalization of medical and retail cannabis in multiple states within the United States, non-botanical exposures including edibles, resins, and concentrates have become more common [7]. It is unclear if patients with cannabis exposure due to edibles, resins, and concentrates, develop tachycardia at the same rate as those who smoke botanical cannabis. Since tachycardia, euphoria, and somnolence are findings that physicians may use to diagnose cannabis toxicity, it is important to recognize if variation in heart rate occurs, because tachycardia may not be a reliable diagnostic indicator of cannabis use.

The objective of this study is to determine the frequency of tachycardia in patients with cannabis exposure after ingestion or inhalation of cannabis botanical material, edibles, resins, and concentrates. In addition, we describe the clinical course of those patients who developed bradycardia after cannabis exposure.
**Methods**

This is a prospective observational study of patients with cannabis exposures reported to a regional Poison Center with documented heart rates. Shortly after legalization of retail cannabis in Oregon and Alaska, we added a data collection “keycut” into the case notes of the Oregon/Alaska Poison Center medical record (Toxicall, Computer Automated Systems, Aurora, CO) in all cases of potential cannabis exposure. Poison Center staff recorded data including heart rate at the time of exposure, means of exposure (e.g. inhalation, ingestion), and source (e.g. commercial edible, resin, concentrate, botanical material). Cases arose both from the public who called the Poison Center from home as well as from clinicians in healthcare settings.

At the end of the 17-month study period (December 4, 2015–April 15, 2017), we extracted data for all cases of acute cannabis exposure by searching for the terms “marijuana,” “cannabis,” “THC,” “dab,” “hash oil,” “butane hash oil,” or “BHO” in the substance data field. We used these terms because an expanded database substances list for cannabis products was not yet available in Toxicall during the study period. We excluded cases if they had no exposure to cannabis, the cannabis exposure was non-acute, not a human patient (e.g. animals/pets), if they were exposed to other substances by history (including ethanol, illicit drugs, and nicotine products), and if a numerical heart rate was not documented. A single researcher extracted all data.

We defined botanical cannabis as the flower of the cannabis plant. We defined edibles as products that contained cannabis extracts in a readily edible form (e.g. gummies, brownies, cookies). Commercial products were purchased from a dispensary or retail establishment. Homemade products were cannabis-containing edibles, concentrates, or resins produced in a non-commercial environment (e.g. a home). We divided concentrated cannabis products into either cannabis “concentrates” or “resins”. We defined concentrates as a liquid product prepared for vaporization in a cannabis vaporizer. We defined resins as solid or semi-solid products in which cannabis is extracted using heat and pressure or a hydrocarbon solvent such as butane.

“Heart rate” was the initial heart rate recorded. We defined heart rate as “normal” if it was between the 10th and 90th percentile for age in children, or between 60 and 100 beats per minute in adults (>18 years) [9]. We defined tachycardia as > 90th percentile for age in children or >100 beats per minute in adults. We defined bradycardia as < 10th percentile for age in children or < 60 beats per minute in adults. We reviewed each case and assigned a predominant clinical sign or symptom. We grouped clinical signs and symptoms into central nervous system (CNS) excitation (e.g. agitation, hallucinations, or seizures), sedation (e.g. obtundation, somnolence) and other symptoms (e.g. gastrointestinal symptoms, palpitations, altered mental status/dysphoria, lightheadedness, asymptomatic).

We compared categorical variables using Pearson’s Chi square. We used Fisher’s exact test for data that were sparse (<= 5 observations in any datafield) with alpha of 0.05. We entered data into an Excel database (Microsoft, Redmond, WA). Statistical calculations used Social Science Statistics (available at soscientist.com). The Institutional Review Board of the Oregon Health and Science University approved the study.

**Results**

We screened 228 cases and excluded 127 cases as follows: 11 non-exposures (information call), 8 non-acute (cannabinoid hyperemesis syndrome), 8 non-human (all dogs), 70 co-ingestions, and 30 lacking a documented initial heart rate, leaving 101 patients for analysis. The majority ingested (n = 76) rather than inhaled (n = 25) cannabis products (Table 1).

Patient heart rates were 65% tachycardic (65/101), 30% normal heart rate (30/101), and 6% bradycardic (6/101) (Table 2). Given the small sample size, comparison of clinical signs and symptoms between groups was somewhat limited. Sedation was more common in patients with normal heart rate than in those with tachycardia (43% v 12%) and less common in patients with tachycardia than bradycardia (12% v 67%). CNS excitation was more common in the tachycardic group than in those with normal heart rates (54% v 33%).

Patients who inhaled cannabis products were more likely to have tachycardia than those who ingested cannabis products (84% v 59%; p = 0.024) (Table 1). Of those who inhaled cannabis products, there was no difference in the frequency of tachycardia between those who inhaled botanical products and those who inhaled resins and concentrate products (80% v 90%; p = 0.63).

Of those who ingested cannabis products, ingestion of cannabis edibles had a higher frequency of tachycardia than resins and concentrates (63% v 40%; p = 0.044), but were not significantly different from
Table 1. Heart rate in patients with cannabis toxicity from various exposures and sources.

| Exposure | Source | N (N = 101) | Bradycardia, n (%) | Tachycardia, n (%) | Normal HR, n (%) | Mean HR, bpm | Median HR, bpm (IQR) | HR range |
|----------|--------|-------------|--------------------|-------------------|------------------|--------------|----------------------|----------|
| Ingestion | Botanical | 4 | 1 (25) | 2 (50) | 1 (25) | 120 | 130 | 87-140 |
| All Botanicals | 4 | 1 (25) | 2 (50) | 1 (25) | 120 | 130 | 87-140 |
| Commercial Edible | 21 | 1 (5) | 13 (62) | 7 (33) | 107 | 118 | 56-160 |
| Homemade Edible | 24 | 1 (4) | 15 (63) | 8 (33) | 109 | 107 | 55-173 |
| Edible-unknown source | 14 | 0 (0) | 9 (64) | 5 (36) | 112 | 108 | 78-170 |
| All Edibles | 59 | 2 (3) | 37 (63) # | 20 (34) | 109 | 110 | 56-173 |
| Inhalation | Botanical | 15 | 1 (7) | 12 (80) | 2 (13) | 116 | 126 | 50-173 |
| Resin | 7 | 0 (0) | 6 (86) | 1 (14) | 120 | 119 | 98-160 |
| Concentrate | 3 | 0 (0) | 3 (100) | 0 (0) | 130 | 130 | 122-140 |
| All resin & Concentrate | 10 | 0 (0) | 9 (90) @ | 1 (10) | 123 | 123 | 98-160 |
| Total inhalation | 25 | 1 (4) | 21 (84) o | 3 (12) | 119 | 125 | 50-173 |

Table 2. Predominant clinical signs and symptoms according to heart rate.

| CNS excitation, n (%) | Sedation, n (%) | Other symptoms, n (%) |
|-----------------------|------------------|-----------------------|
| Tachycardia n = 65    | 35 (54%)         | 8 (12%)               | 22 (34%) |
|                       |                  |                       | gastrointestinal |
|                       |                  |                       | palpitations     |
|                       |                  |                       | altered mental status |
|                       |                  |                       | lightheaded      |
| Normal Heart Rate n = 30 | 10 (33%)        | 13 (43%)              | 7 (23%) |
|                       |                  |                       | gastrointestinal |
|                       |                  |                       | palpitations     |
|                       |                  |                       | altered mental status |
|                       |                  |                       | lightheaded      |
| Bradycardia n = 6     | 1 (17%)          | 4 (67%)               | 1 (17%) |
|                       |                  |                       | asymptomatic     |
|                       |                  |                       | lightheaded      |

CNS = Central Nervous System.

bottanicals (63% v 50%; p = 0.63) (Table 1). Four toddlers ingested botanical cannabis (cannabis flower); three developed somnolence, one developed agitation, and two were admitted to the hospital for observation. Small sample size of this group limited statistical comparison, and interpretation should be cautious.

Of those who used resins and concentrates, patients with inhalation exposures were more likely to develop tachycardia than those with ingestions (90% v 40%; p = 0.014).

Children were less likely to develop tachycardia (< 12 years; 48%) than adolescents (12-18 years; 77%) or adults (> 18 years; 66%). (Table 1)

Six patients (6%) had bradycardia, following five ingestions (one botanical, two edibles, two resins) and one botanical inhalation (Table 3). Ages ranged from 13 months to 87 years. There were two toddlers (ages 13 months and 2 years), two adolescents (ages 15 years and 16 years) and two geriatric patients (ages 70 years and 87 years). There was no difference in the rate of bradycardia amongst children < 12 years (8%; 2/25), adolescents (12-18 years; 8%; 2/26), or adults (> 18 years; 4%; 2/50). All patients who developed bradycardia had CNS sedation or agitation that were likely to lead to an ED visit independently (Table 3). Blood pressure was marginally low in several patients.
and high in others (Table 3). No adult or adolescent patient developed a heart rate lower than 50 beats per minute. However, one 13-month old child developed a heart rate of 50 beats per minutes without hypotension. No patient developed bradycardia with hypotension. There were no ventricular dysrhythmias and one case of atrial fibrillation with rapid ventricular response.

**Discussion**

We found that, among cases of acute cannabis exposure reported to a poison center, tachycardia is most common in patients who inhale cannabis. This is consistent with decades of research that identifies tachycardia after inhalation of botanical material. Fewer than half of those who ingested resins or concentrates and fewer than two-thirds of patients who ingested edibles, developed tachycardia. As edibles, resins, and concentrates become more common, providers should anticipate that patients might maintain normal heart rates despite other evidence of cannabis toxicity. In addition, tachycardia is not an absolute component of the toxidrome for cannabis exposures.

Only a small percentage of our patients developed bradycardia (6%). While we would expect 5-10% bradycardia in healthy individuals given our heart rate definitions, it is remarkable that patients developed bradycardia while intoxicated with a drug that has been broadly associated with tachycardia. Bradycardia occurred mainly in patients with severe toxicity that included significant CNS sedation (Table 3). We hypothesize that bradycardia may be a symptom consistent with high doses of THC. Ingestion of edibles, resins, and concentrates may expose the user to a larger dose of cannabinoids than smoking botanical cannabis. Further, bradycardia has occurred in hospitalized volunteers who ingested THC for prolonged periods [10]. These subjects had impaired circulatory response to exercise, Valsalva maneuver, and cold pressor testing. The authors hypothesized that THC has a dose-dependent biphasic effect on the cardiovascular system, with predominately sympathetic activity at low to moderate doses and parasympathetic effects at higher doses.

Our study has several limitations. Healthcare professionals and the public voluntarily provide poison center information, and this may introduce significant bias. Healthcare providers caring for patients with unusual presentations (e.g. bradycardia) may be more likely to consult a poison center. Additionally, we obtained data from two states with availability of fully legal retail and medicinal cannabis, which may not be representative of cases that are seen in states without full legalization. Some small data sets limited statistical evaluation, in particular in cases with bradycardia, and this limits evaluation of these cases. Finally, we used initial heart rate recorded. It is possible that heart rates recorded later in the patient’s medical care were different and would have altered the analysis.

**Conclusions**

Tachycardia is common amongst patients who inhale cannabis (botanical, resins or concentrates), but is less common amongst those who ingest edibles, resins, or concentrates. Bradycardia is also less common in children than in adolescents. Bradycardia infrequently occurs during cannabis toxicity, and its mechanism is not known. Clinicians should be aware that patients with CNS sedation from ingestion of cannabis products may not reliably develop tachycardia. Normal or slow heart rates do not exclude cannabis as a cause of CNS effects, particularly in children.

### Table 3. Clinical characteristics of patients who developed bradycardia.

| Age  | Type | Exposure | HR (bpm) | BP (mmHg) | Symptoms | Disposition | Notes |
|------|------|----------|----------|-----------|----------|-------------|-------|
| 2yo M | Botanical | Ingestion | 87 | 125/53 | Somnolent | ED, then discharged | Family member’s cannabis
| 70yo M | Botanical | Inhalation | 50 | 150 syst | Dizzy, lightheaded, vertigo | ED, then discharged | First time use; cannabis naive |
| 87yo F | 6-8 commercial brownies (unknown dose) | Ingestion | 56 | 99/51 | Somnolent, altered mental status. In ED, developed atrial fibrillation with rapid ventricular rate. | Admit ward | |
| 16yo M | Homemade brownie | Ingestion | 55 | 87/33 | Paranoia, agitation, nausea | ED, then discharged | |
| 15yo M | Resin | Ingestion | 50 | 102/80 | Somnolence, syncope, vomiting | ED, then discharged | Dab given by friend |
| 13mo M | Resin | Ingestion | 50 | 105/49 | Obtundation, seizure | Admit ward | Parent’s dab |

HR = heart rate.
BP = blood pressure.
yo = year old.
mo = month old.
M = male.
F = female.
bpm = beats per minute.
ED = emergency department.
Disclosure statement

No potential conflict of interest was reported by the authors.

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