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Marijuana use in adults admitted to a Canadian epilepsy monitoring unit

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ABSTRACT

Objectives: Epidemiologic evidence supporting antiseizure properties of cannabis is limited and controversial. We determined the prevalence of marijuana use and its perceived effects in patients with and without epilepsy.
Methods: Information was collected over 14 months from consecutive adult patients admitted to an epilepsy monitoring unit using a 27-item anonymous questionnaire. Patients with cognitive impairment unable to understand the questions or give informed consent and readmissions were not recruited. Subjects were divided into 4 groups, those with epileptic seizures, those with psychogenic nonepileptic seizures (PNES), those with both epileptic and PNES, and those with other nonepileptic events. Patients with exclusively epileptic seizures were compared with those with exclusively PNES.
Results: From 310 patients, 18 undiagnosed cases were excluded leaving a cohort of 292 patients with median age 35 (range: 27–49) years; 57.2% female. Epilepsy was documented in 190 (65.1%), PNES in 64 (21.9%), and both types of seizures in 26 (8.9%). Median duration of seizure disorder was longer (2 [1–9] vs. 13 [5.7–25] years; $p < 0.001$) and seizure frequency lower (daily or weekly in 62.3% vs. 44.9%; $p = 0.03$) in patients with epilepsy compared with those in patients with PNES. Overall, 166 (57%) had tried marijuana, and 36.2% used it over the past year. Utilization was 57.1% in sole epilepsy and 64.1% in sole PNES, but daily use was more likely in epilepsy (59% vs. 33.3%). Estimated mean dose was 1 g/day. Marijuana use was associated with tobacco smoking ($p < 0.001$) but not alcohol use. Eight patients used other street drugs. Improvement in seizures was perceived by 84% in those with epilepsy and 72.7% in those with PNES. In the 2 groups, stress was decreased in 84.9% and 88%, sleep improved in 77.3% and 88%, and memory/concentration was better in 32% and 28%, respectively. Antiepileptic drug side effects were decreased in 53.2% of marijuana users. Perceived effect on epileptic seizures correlated with effect on stress ($r = 0.35$, $p = 0.004$). Adverse effects of marijuana were mild and reported in 30.7% but included possible seizure precipitation in 5 patients with epilepsy.
Significance: Patients with uncontrolled epilepsy or nonepileptic events had a high rate of marijuana use with associated perceived improvements in seizure control, stress, sleep, and drug side effects. Stress reduction may contribute to the perceived impact of marijuana on seizures and nonepileptic events in adults.

1. Introduction

One-third of people with epilepsy have continuing seizures despite optimal medical treatment [1]. Cannabis was one of the few drugs thought to be effective for treatment of epilepsy in the 19th century but lost favor when it became illegal in the 20th century. However, interest in this substance in epilepsy has recently increased again. As modulators of neuronal excitability, cannabinoids, the active neuropharmacological component of marijuana, are well poised to affect the initiation, propagation, and spread of seizures [2]. A number of studies, primarily of 9-tetrahydrocannabinol (Δ9-THC) and cannabidiol (CBD), in animal models of epilepsy have provided evidence of potential antiseizure activity [3].

However, the epidemiologic evidence supporting antiseizure properties of cannabis in humans is limited and controversial as proper drug trials were discouraged (until very recently) since marijuana is an illegal substance in most jurisdictions [4–6]. Although medical organizations continue to advise caution in using marijuana for medical purposes, patients with seizures and their families lobbying for this alternative treatment, encouraged by prominent media attention to dramatic improvements in some children with intractable epilepsy, [7,8] have led to changes of legislation against marijuana and clinical trials providing evidence for efficacy of cannabis in children and young adults with uncontrolled epilepsy due to Dravet and Lennox–Gastaut syndromes [9–11].

Canada legalized and introduced a regulatory system specifically for medicinal marijuana as treatment for seizures and other conditions in 2001. The "Marijuana for Medical Purposes Regulations" allow patients to possess marijuana for medicinal purposes if prescribed by a physician or nurse and obtained through licensed suppliers.

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A general range of 0.5–3 g of cannabis per day for medical use is reasonable according to Health Canada. The drug is legally approved in Canada only as the crushed plant components meant to be smoked, although other routes of administration are under challenge in the courts [6,12]. In this context, the number of patients authorized to use marijuana for a number of medical conditions in Canada has grown from approximately 500 people in 2002 to more than 26,000 in 2012 [13].

We aimed to determine the prevalence and sociodemographic characteristics of marijuana users among patients admitted to our epilepsy monitoring unit (EMU), to assess the perceived impact on seizures, to evaluate the effects on stress and sleep, and to determine perceived adverse effects of the drug. We also analyzed these same parameters in a group of patients found after investigation not to have epilepsy.

2. Subjects and methods

A self-administered anonymous 27-item questionnaire (see Supplementary material) was given to all consecutive adult patients admitted to our 8-bed EMU over a 14-month period. Patients with cognitive impairment unable to understand the questions or give informed consent for participation were not recruited, and readmitted patients were excluded. Questions addressed demographics, severity of epilepsy, and marijuana and other drug use. Those using marijuana were asked about perceived effect of marijuana on seizures, stress, sleep, memory, and antiepileptic drug (AED) side effects using a 7-item Likert scale from "not effective" or "worse" to "very effective" or "improved". Since medical marijuana can be legally prescribed for seizures and other conditions in Canada, subjects were also asked how they accessed the drug if they were using it. The study was approved by the Western University ethics committee.

Subjects were divided into groups based on video-EEG recording of events: those with exclusively epileptic seizures, those having exclusively psychogenic nonepileptic seizures (PNES), those with both epileptic and PNES, and those having other nonepileptic events such as convulsive syncope, migraine, and sleep disorders [14]. Those in whom a diagnosis could not be made were excluded from the study. Patients with exclusively epileptic seizures were compared with those with exclusively PNES.

The estimated grams per day of cannabis were calculated according to Health Canada recommendations and an approximate 0.5 to 1 g of drug per marijuana joint.

2.1. Statistical analysis

Analyses were performed using the statistical package SPSS (Chicago, Ill., USA, version 17.0). Statistical significance for intergroup differences was assessed by the Pearson χ^2 or Fisher's exact test for categorical variables. Statistical correction for multiple comparisons was applied when required using the Holm procedure. Normality for continuous variables was assessed with the Kolmogorov–Smirnov test. For continuous variables that were non-normally distributed, values were expressed as medians [interquartile ranges (IR)], and statistical significance for intergroup differences was assessed using Mann–Whitney tests. For variables that were normally distributed, values were expressed as means ± SD, and significance was assessed using ANOVA or Student's t test. The correlations between continuous variables were determined with Spearman coefficient. A value of $p < 0.05$ was considered statistically significant. A logistic regression analysis was used to identify factors that would predict marijuana use in the last year including age, gender, work status, current use of tobacco, and seizure frequency. Results were expressed as adjusted hazard ratios and corresponding 95% confidence intervals.

3. Results

The study sample consisted of 310 patients. An additional 21 patients refused to participate. After investigation in the EMU, epileptic seizures were confirmed in 190 (62.3%), PNES in 64 (21%), both epilepsy and PNES in 26 (8.5%), and other causes in 12 (3.9%). In 18 cases (5.8%), the etiology could not be confirmed because no seizures were recorded. These were excluded from further analysis leaving the studied cohort of 292 patients with a median age of 35 (range: 27–49) years; 57.2% female. Thirty-seven point three percent were working or in school, 30.5% on disability, and 33.9% unemployed or retired. Fifty-two point three percent were university- or college-educated. The frequency of seizures was daily or weekly in 50.3% and the median duration of seizure disorder was 9 years (range: 3–22). Baseline characteristics of the study population are summarized in Table 1.

Those with exclusively PNES were more likely to be female (75%; $p < 0.001$), had seizures for a shorter period of time (2 [1–9] vs. 13 [5.7–25] years; $p < 0.001$), and had a higher frequency of seizures (daily or weekly in 62.3% vs. 44.9%; $p = 0.03$) than those with exclusively epileptic seizures. Otherwise, there were no demographic differences between the two groups. The majority of patients with epilepsy had intractable focal seizures and were being assessed for surgical management. Some admitted for diagnostic workup or medication changes had generalized or mixed focal/generalized epilepsy.

3.1. Marijuana usage

Of the studied cohort of 292 diagnosed patients, 166 (57%) had tried marijuana, and 105 (36.2%) were actively using it in the last year. Median duration of use was 8 (2.9–14) years. Nine of the 18 excluded undiagnosed patients had also used the drug. The frequency of use among active users was daily in 52.9%, weekly in 19.2%, and less often in 27.9%. Mean dose was 1 g per day mainly through smoking (87%). Other forms of administration included vaporizer (37%), ingestion in food (14.6%), and in capsule form (4.9%). Hashish was used by 10.6%. Multiple means were tried by 46 patients (37.4%). Two patients

Table 1
Baseline characteristics of the study sample (n = 292).

Gender (female)	167 (57.2%)
Age (years)	35 (27–49)
Urban (vs. rural)	210 (71.9%)
Work (14 patients counted in two categories)	
Working	92 (31.5%)
School	27 (8.9%)
Working and/or school	109 (37.3%)
Unemployed	74 (25.3%)
Retired	25 (8.6%)
Disability	89 (30.5%)
Education	
Grade school	19 (6.6%)
High school	118 (41.1%)
College	92 (32.1%)
University	58 (20.2%)
Years of seizures	9 (3–22)
Seizure frequency last year	
Daily	62 (21.8%)
Weekly	81 (28.5%)
Monthly	96 (33.8%)
<1/month	45 (15.8%)
Ever used marijuana	166 (57%).
Using marijuana in last year	105 (36.2%)
Used other street drugs in the past year	8 (2.8%)
Smoke cigarettes	85 (29.2%)
Drink alcohol	124 (42.9%)
Diagnosis	
Epilepsy	190 (65.1%)
Psychogenic nonepileptic seizures	64 (21.9%)
Both	26 (8.9%)
Other diagnosis	12 (4.1%)