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Emergency Department Burden of Nausea and Vomiting Associated with Cannabis Use Disorder: U.S. Trends from 2006 to 2013

Andrea Bollom, BS¹, Jasmine Austrie¹, William Hirsch, BS¹, Judy Nee, MD¹, Daniel Friedlander, MD¹, Johanna Iturrino, MD¹, Sarah Ballou, Ph.D.¹, and Anthony Lembo, MD¹

¹Division of Gastroenterology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts, USA

Abstract

Background & Aims—Chronic cannabis use is associated with nausea and vomiting that may lead to Emergency Department (ED) visits, multiple diagnostic tests, and procedures. The aim of this study was to analyze recent trends in ED visits for vomiting associated with cannabis use disorder between 2006 and 2013.

Methods—Data were obtained from the National Emergency Department Sample (NEDS) records in which vomiting (ICD-9-CM codes 787.01, 787.03, and 536.2) was a primary diagnosis in combination with cannabis abuse or dependence (304.3, 304.30, 304.31, 304.32, 304.33, 305.2, 305.20, 305.21, 305.22, and 305.23) and were seen in the ED between 2006 and 2013. The NEDS collects data from more than 25 million visits in over 950 emergency departments and is weighted to provide national estimates.

Results—The rate of ED visits for vomiting with cannabis use disorder from 2006 compared to 2013 increased from 2.3 to 13.3 per 100,000 ED visits, while the mean inflation-adjusted costs increased 68.5% from \$2,758.43 to \$4,647.62, respectively. Men between the ages of 20 and 29 were the most common group to present to the ED for vomiting with cannabis use disorder. The Midwest and West had the higher rates of ED visits for vomiting with cannabis use disorder compared with the Northeast and South.

Conclusions—ED visits for vomiting associated with cannabis use disorder is common and is associated with significant medical costs. Further research on the role of cannabis use in nausea and vomiting is warranted.

Keywords

Nausea; Vomiting; Cannabis; Emergency Department

Address correspondence and reprint requests to: Anthony Lembo, M.D. Beth Israel Deaconess Medical Center 330 Brookline Ave, Boston, MA 02215. alembo@bidmc.harvard.edu.

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Introduction

Cannabis is the most widely accessible and consumed illicit drug worldwide¹. The number of daily cannabis users in the U.S. increased from 5.1 million in 2005 to 8.1 million individuals in 2013. In that same year there was an estimated 19.8 million previous month users². The most common age group to use marijuana comprises individuals between 18 to 25 years of age³. The vast majority of individuals use cannabis recreationally, however, at prescribed doses cannabis has been reported to help patients suffering from cachexia, cancer, glaucoma, human immunodeficiency virus infection/acquired immune deficiency syndrome, and pain among other conditions⁴. For these reasons, as of July 2016 cannabis is now legal in 25 states and the District of Columbia for medicinal purposes and is legal for recreational purposes in 4 states^{5,6}. The Food and Drug Administration (FDA) had approved two cannabinoids in the U.S. for cancer chemotherapy-induced nausea and vomiting and for patients with HIV or cancer as an appetite stimulant^{7,8}.

There is increasing evidence of potential adverse side effects of chronic cannabis use. In a recent single center study conducted on patients in a tertiary care hospital gastroenterology clinic, there was a 1.47-fold increase in ED visits per year for GI patients with cannabis dependence compared to non-cannabis abusers⁹. Likewise, after the liberalization of medicinal cannabis in Colorado in 2009, the ED visits for cyclic vomiting at two medical centers increased from approximately 36/100,000 ED to 70/100,000 ED visits¹⁰. In addition, patients may present to the ED with nonspecific symptoms that are triggered by cannabis use, including anxiety and panic attacks¹¹. Cannabinoid hyperemesis syndrome (CHS), was first well-described in 2004 by Allen et al¹², by observing 19 patients with chronic cannabis use suffering from cyclical vomiting occurring every few weeks or months, with improvement in symptoms following cessation of cannabis use. Three patients re-challenged themselves with marijuana and relapsed within months. Since then, multiple reports have been published and the disorder has been increasingly recognized^{13–21}. However, the true prevalence of this disorder is unknown. Risk factors for CHS, other than cannabis use are also not known. A study with 98 patients reported that the majority of patients became symptomatic within 1 to 5 years of the beginning of daily cannabis use. Moreover, 32% of patients developed symptoms within the first year of cannabis use²⁰. Discontinuation of cannabis use may relieve CHS symptoms¹², although in general studies are lacking adequate follow-up^{16,20,22}.

Recently, the Rome IV Criteria defined CHS as the presence of all of the following symptoms: (i) stereotypical episodic vomiting similar to cyclic vomiting syndrome (CVS) in regards to onset, duration, and frequency; (ii) symptomatic after chronic cannabis use; (iii) relief of episodes upon cessation of cannabis use²³. These symptoms should be fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis. The observation that prolonged hot baths or showers provides temporary relief of symptoms also supports the diagnosis. Patients with CHS sometimes also experience epigastric or periumbilical abdominal discomfort or pain¹⁶.

The purpose of this study was to analyze the national trends in the rates of ED visits for nausea and vomiting associated with cannabis use disorder in the United States. No previous

study has evaluated nausea and vomiting prevalence in the presence of cannabis use disorder in the ED on a nation-wide scale from 2006 to 2013.

Methods

This study extracted data from the Nationwide Emergency Department Sample (NEDS)²⁴ from the Healthcare Utilization Project (HCUP)²⁵, which is maintained by the Agency for Healthcare Research and Quality (AHRQ). The NEDS is the largest publicly available emergency department all-payer database in the United States (US). The 2006 NEDS contains data from about 26 million ED visits from over 950 hospitals weighted to approximate over 120 million ED visits, and the 2013 NEDS contains data on 30 million ED visits at 947 hospitals that are weighted to provide national estimates for 135 million ED visits²⁵. The NEDS includes national ED information regarding patient and hospital demographics, as well as inpatient admissions rates, and ED and inpatient procedures and associated costs, among others. Summary statistics on trends and population rates for these data are available for free on HCUPnet, offered by AHRQ. Individual years of the NEDS are available for purchase, and include patient specific cost data and further diagnoses. We analyzed ED trends for vomiting and cannabis use disorder in 2006 and 2013 using ICD-9-CM codes 787.01, 787.03, and 536.2 for vomiting, and codes 304.3, 304.30, 304.31, 304.32, 304.33, 305.2, 305.20, 305.21, 305.22, and 305.23 for cannabis abuse and cannabis dependence. The DSM-IV-TR had separate diagnoses for cannabis abuse and cannabis dependence, but combines them into one disorder in DSM-V, cannabis use disorder, which we will refer to in this paper²⁶. Cannabis use disorder is defined as a consequential trend of cannabis use that results in at least two of the following symptoms: (i) cannabis use for a long period of time, (ii) unsuccessful attempts to limit cannabis use; (iii) a significant amount of time dedicated to activities related to cannabis use; (iv) craving cannabis; (v) cannabis use resulting in negligence towards responsibilities; (vi) continued cannabis use after experiencing the negative effects of cannabis; (vii) activities are limited due to cannabis use; (viii) cannabis use in perilous environments; (ix) cannabis use even after experiencing cannabis related side-effects; (x) tolerance, and (xi) withdrawal²⁶. Despite extensive criteria for diagnosis, previous research has shown that this disorder is as accurately diagnosed as other drug use disorders²⁷.

Study Variables

We included patients with a primary diagnosis of vomiting alone, persistent vomiting or nausea with vomiting as defined by HCUPnet as the first-listed diagnosis on a medical record. This was determined to be the principal reason for the ED visit. Out of the patients with a primary diagnosis of vomiting, we analyzed how many also had cannabis abuse (305.2x) or cannabis dependence (304.3x) coded during their ED visit as well as one of their other 14 listed diagnoses. We used STATA/MP 14.1 to analyze patient statistics including age, sex, primary payer, residence (large, medium, or small metropolitan, large fringe (suburb) or micropolitan), and median income for zip-code (low or not low). Hospital characteristics were also obtained from using STATA/MP 14.1 and HCUPnet and included region (Northeast, Midwest, South, or West), location (metropolitan or non-metropolitan), trauma center designation, and teaching status. We used STATA/MP 14.1 to analyze the

2006 and 2013 NEDS datasets for associated costs, inpatient admission information and other diagnoses²⁵.

The variables included in this study are defined according to HCUPnet. Demographic data by zip code collected by Claritas defined the median income of a patient's zip code. The lowest income quartile ranged from \$1–\$37,999 (low), while the three highest income quartiles were defined as \$38,000 and above (not low). A “large central” residence specifies metro areas considered cores of large cities with a population of 1 million or more. A “large fringe” residence specifies suburbs of large cities with a population of 1 million or more. “Medium and small metro” residences specifies metro areas that have a population less than 1 million but greater than 50,000. “Micropolitan and noncore” residences refer to rural counties that have a population below 50,000. The American Hospital Association (AHA) Annual Survey determines teaching hospital status if a hospital has an AMA-approved residency program, Council of Teaching Hospitals (COTH) membership, or 0.25 or higher ratio of residents and full-time equivalent interns to beds. American Hospital Association (AHA) Annual Survey of Hospitals determines hospital ownership.

Statistical Analysis

The rate of vomiting and cannabis ED visits per 100,000 ED visits in 2006 was calculated for all patient and hospital characteristics by dividing the number of vomiting and cannabis ED visits in each category by the total number of ED visits within that respective category, then multiplying by 100,000. For example, the rate of vomiting and cannabis ED visits per 100,000 ED visits for the 20–29 age group in 2006 was calculated by dividing the number of vomiting and cannabis ED visits in the 20–29 age group (1,147) by the total number of ED visits for the 20–29 age group (18,226,784), then multiplying by 100,000. The rate of vomiting with cannabis ED visits per 100,000 residents in 2006 was calculated with age group populations taken from US Census divided by the number of vomiting with cannabis ED visits in each category by the total number of the respective age group's population, then multiplying by 100,000.

The cost data for 2006 and 2013 were calculated from the source files of the respective NEDS databases using STATA/MP14.1. Individual payer costs were calculated from the percentage of total vomiting and cannabis ED visits paid by each payer, multiplied by the aggregate cost of vomiting and cannabis ED visits in 2013. All costs were adjusted for inflation and reported in terms of 2015 dollars using the CPI inflation calculator²⁸.

Results

We identified 2,915 patients in 2006 who presented to the ED with a primary diagnosis of vomiting and also had cannabis use disorder. In contrast in 2013 we identified 17,904 patients. The rate per 100,000 ED visits for vomiting with cannabis use disorder was 2.4 in 2006 and 13.3 in 2013 (Figure 1), while the rate of ED visits per 100,000 ED visits for vomiting without cannabis use increased from 1,141 in 2006 to 1,435 in 2013, a 24.9% increase.

Costs

The mean ED cost per patient for vomiting and cannabis use disorder increased by 68.5% from \$2,758 in 2006 (95% CI 2,643 – 2873 s.d.= \$2,755) to \$4,648 (95% CI 4,534 – 4,762 s.d.= 6,530), in 2013. In contrast, the mean cost for all ED visits in the US increased by 76.9% from \$1,540 (95% CI 1539–1541 s.d.=2,205) in 2006 and \$2,724 (95% CI 2,723–2,725 s.d.=4,132) in 2013. The total aggregate cost for ED visit with vomiting and cannabis use disorder was \$8,039,570 (95% CI 7,704,345 – 8,377,710 in 2006 and \$83,210,988 (95% CI 81,176,736 – 85,258,848) in 2013. All costs were inflation adjusted to 2015 dollars.

Demographics

Age—The 20–29 year age group had the highest rate of ED visits for vomiting with cannabis use disorder per 100,000 ED visits with 6.8/100,000 in 2006 and 39.0/100,000 in 2013 (Figure 2). The lowest rate of ED visits per 100,000 ED visits for vomiting with cannabis use disorder, but the greatest increase between the years, was the 30–39 year old age group with 4.0/100,000 in 2006 and 23.4/100,000 in 2013 (Figure 2). All of the age groups displayed increases in rates of ED visits for nausea and vomiting with cannabis use disorder.

Gender—Men presented to the ED for vomiting with cannabis use disorder at a higher rate than women in both 2006 and 2013 (Figure 3). The rate of ED visits for men in 2006 was 3.0/100,000 ED visits and it increased to 16.8/100,000 ED visits in 2013. The rate of ED visits for women increased in line with that of men from 1.9/100,000 ED visits in 2006 to 10.3/100,000 ED visits in 2013.

Geographical Region—In 2006, the Midwest had the highest rates of ED visits for vomiting with cannabis use disorder (3.1/100,000 ED visits) and the North had the lowest rates (1.5/100,000 ED visits). However, in 2013 patients in the West had the highest rates of ED visits for vomiting with cannabis use disorder in 2013 (22.8/100,000 ED visits) and the Northeast had the lowest rates (8.7/100,000 ED visits). The greatest increase between 2006 and 2013 was in the West.

The patients living in the “Large Fringe Metro (suburbs)” had the highest increase in ED visit rates for vomiting and cannabis use disorder (Table 1). For the “suburbs” the rates increased from 1.6/100,000 to 11.8/100,000 for 2006 and 2013. “Medium and Small Metro” had the lowest rates of increase rising from 3.1/100,000 to 11.9/100,000 for 2006 and 2013, respectively. The ED visit rates for vomiting with cannabis use disorder across varying locations were similar for 2006 and 2013.

Discussion

Using a comprehensive nationwide database of ER visits we found that there are a significant number of patients presenting to the ED with the primary diagnosis of vomiting associated with cannabis use disorder, with a six fold increase from 2006 to 2013. Men between the ages of 20 and 29 represent the most common group seen in the ED for vomiting associated with cannabis use disorder. The total aggregate costs (adjusted for

inflation to 2015 dollars) associated with these ED visits was in excess of \$80 million dollars in 2013.

There are several likely explanations for the dramatic increase in ED visits for nausea and vomiting associated with cannabis use between 2006 and 2013. There is increasing awareness and acceptance of cannabis use and therefore patients may be more likely to report its use. Likewise, there is also increasing awareness about the association between chronic cannabis use and recurrent vomiting and therefore physicians may be more likely to ask patients about cannabis use. It is also possible that the rise in ED visits related to cannabis use may potentially be contributed by the increase in delta-9-tetrahydrocannabinol (THC) potency, which has increased from 1–5% in the late 1960s to as high as 10–15% at present²⁶. Additionally, the number of individuals in the United States using cannabis has increased²⁹ along with the types and quantities.¹¹ Finally, it is possible that the increase is confounded with increasing rates of opioid use given its association with nausea and vomiting.³⁰

The mechanism whereby chronic cannabis use results in severe vomiting remains unclear. The active ingredient in cannabis, THC, binds to cannabinoid receptors 1 and 2 (CB1 and CB2), which affect the nervous system, enteric plexus, and the body's immune system. It has been reported that cannabis slows gastric emptying, which may promote nausea and vomiting^{12,16,20,31}. Additionally, it is also believed that the buildup of lipophilic THC in cerebral fat may manifest itself as toxic in some individuals which can promote vomiting³². Also, genetic variations in hepatic drug transforming enzymes in susceptible individuals may cause high levels of cannabis metabolites thereby promoting the development of vomiting¹⁶.

The findings of this study do not exclude potential anti-emetic benefits of cannabis or that the many of the patients were using cannabis to treat their nausea and vomiting. THC has been shown to selectively act on CB1 receptors in dorsal vagal complex to inhibit emesis³³. An internet survey of patients with CVS found that nearly half of the patients who used cannabis reported improvement in nausea, appetite, general well-being, stress and vomiting³⁴. A recent meta-analysis that included 3 trials found cannabinoids to be associated with improvement in nausea and vomiting due to chemotherapy though the evidence was low-quality³⁵. Thus, at present the role of cannabis for the management of chronic nausea and vomiting remains controversial particularly in light of the potential of cannabis to affect other brain functions and cause side effects³⁶.

This study has several limitations. First, this study relies on ICD-9 billing codes which may not always be accurate. CHS is not well recognized by many ED physicians and therefore even the 2013 rates may not accurately represent the number of ED visits and therefore likely grossly underestimate the true problem. There may be a lack of identification of associated symptoms such as abdominal pain. Second, a causal relationship cannot be definitely established between cannabis use disorder and vomiting. In 2006, when there was a primary diagnosis of vomiting the most common secondary diagnoses were: tobacco use disorder, diarrhea, dehydration, cocaine abuse, hypertension, potassium deficiency, alcohol abuse, abdominal pain, esophageal reflux, and epigastric pain. In 2013, the most common

secondary diagnoses were: tobacco use disorder, abdominal pain, hypertension, diarrhea, potassium deficiency, anxiety, dehydration, esophageal reflux, major depressive disorder, and asthma. Third, though the NEDS provides a representation of the U.S. population it only collected information from 24 states in 2006 and 30 states in 2013. As demonstrated by differences in the laws regarding medical marijuana and even the legalization of marijuana, states differ with regard to acceptance and stigma of marijuana use. Therefore there are likely to be differences among the states in the awareness of the association between cannabis and vomiting and the likelihood of patients to accurately report cannabis use disorder.

Conclusion

This study found a significant number of patients presenting to the ED with nausea and vomiting in the presence of cannabis use disorder, as well as the huge cost burden associated with these ED visits. Further research is needed to diagnose patients presenting to the ED with CHS and formulate a standardized regimen of treatment. Furthermore, research is needed about the dosing and potency of cannabis, as well as safety practices for patients and providers.

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Figure 1.
The rate of emergency department (ED) visits with a primary diagnosis of vomiting associated with cannabis use disorder per 100,000 ED visits in 2006 and 2013.

Figure 2.
The rate of emergency department (ED) visits with a primary diagnosis of vomiting associated with cannabis use disorder in each age group per 100,000 ED visits in 2006 and 2013.

Figure 3.
The rate of emergency department (ED) visits with a primary diagnosis of vomiting associated with cannabis use disorder by gender per 100,000 ED visits in 2006 and 2013.

Table 1

The number and rates of ED visits with a primary diagnosis of vomiting as well as those with a primary diagnosis of vomiting and a secondary diagnosis of cannabis use disorder coded in 2006 and 2013

	2006 Vomiting and Cannabis (N, (%))	2006 Vomiting (N, (%))	2013 Vomiting and Cannabis (N, (%))	2013 Vomiting (N, (%))	2006 ED Visits for Vomiting and Cannabis per 100,000 visits	2013 ED Visits for Vomiting and Cannabis per 100,000 visits
ED Visits for Vomiting and Cannabis per 100,000 population	2,915 (100)	1,369,942 (100)	17,904 (100)	1,922,448 (100)	2.4	13.3
Mean Cost of ED Visits (in 2015 US \$)	1.0	459.1	5.7	608.0		
Total Cost of ED Visits	\$2,758 (95% CI: 2,643–2,874)		\$4,648 (95% CI: 4,534 – 4,762)			
	\$8,039,570 (95% CI: 7,704,345 – 8,377,710)		\$83,217,792 (95% CI: 81,176,736 – 85,258,848)			
Mean Age	30.1	27.3	31.0	27.6		
Age Group	10–19	433 (14.9)	135,793 (9.9)	182,165 (9.5)	3.2	14.8
	20–29	1,234 (42.3)	231,511 (16.9)	7,883 (44.0)	6.8	39.0
	30–39	643 (22.1)	149,864 (10.9)	4,282 (23.9)	4.0	23.4
	40–49	395 (13.6)	129,363 (9.4)	2,321 (13.0)	2.4	13.7
	50+	208 (7.1)	264,847 (19.3)	1,523 (8.5)	0.6	3.2
Sex	Male	1,647 (56.5)	545,134 (37.8)	10,177 (56.8)	3.0	16.9
	Female	1,268 (43.5)	824,719 (60.2)	7,727 (43.2)	1.9	10.3
Payer	Medicare	211 (7.2)	183,494 (13.4)	1,457 (8.1)	0.9	4.8
	Medicaid	852 (29.2)	421,316 (30.8)	5,161 (28.8)	3.2	13.5
	Private Insurance	682 (23.4)	498,579 (36.4)	4,570 (25.5)	1.6	12.4
	Uninsured	989 (33.9)	204,571 (14.9)	5,532 (30.9)	4.8	24.1
	Other	116 (4.0)	56,742 (4.1)	868 (4.8)	1.8	13.5
Median Income for Zipcode	Low	1,259 (43.2)	419,663 (30.6)	5,930 (33.1)	3.4	13.0
	Not Low	1,656 (56.8)	923,245 (67.4)	11,974 (66.9)	2.1	13.9
Patient Residence	Large central metro	809 (27.7)	341,143 (24.9)	7,160 (40.0)	2.9	18.9
	Large fringe metro (suburbs)	467 (16.0)	311,727 (22.8)	3,357 (18.8)	1.6	11.8
	Medium and small metro	1,171 (40.2)	464,214 (33.9)	4,996 (27.9)	3.1	11.9

		2006 Vomiting and Cannabis (N, (%))	2006 Vomiting (N, (%))	2013 Vomiting and Cannabis (N, (%))	2013 Vomiting (N, (%))	2006 ED Visits for Vomiting and Cannabis per 100,000 visits	2013 ED Visits for Vomiting and Cannabis per 100,000 visits
	Micro-politician and noncore (rural)	449 (15.4)	246,282 (18.0)	2,284 (12.8)	369,766 (19.2)	1.9	8.8
Teaching Status	Nonteaching	1,477 (50.7)	780,526 (57.0)	8,991 (50.2)	1,111,978 (57.8)	2.1	11.9
	Teaching	1,438 (49.3)	589,416 (43.0)	8,914 (49.8)	810,470 (42.2)	3.0	15.1
Location	Non-metropolitan	449 (15.4)	246,282 (18.0)	2,245 (12.5)	369,766 (19.2)	2.0	9.4
	Metropolitan	2,466 (84.6)	1,117,084 (81.5)	15,320 (85.6)	1,541,130 (80.1)	2.5	13.8
Trauma Center Designation	Not a trauma center	1,693 (58.1)	902,278 (65.9)	7,839 (43.8)	805,272 (41.9)	2.1	13.2
	Trauma center	1,222 (41.9)	467,664 (34.1)	10,065 (56.2)	1,117,176 (58.1)	3.2	13.3
Region	Northeast	345 (11.8)	208,586 (15.2)	2,251 (12.6)	263,495 (13.7)	1.5	8.7
	Midwest	855 (29.3)	308,683 (22.5)	4,771 (26.6)	431,702 (22.5)	3.1	15.5
	South	1,105 (37.9)	571,517 (41.7)	5,302 (29.6)	802,874 (41.8)	2.4	9.9
	West	609 (20.9)	281,156 (20.5)	5,580 (31.2)	424,377 (22.1)	2.8	22.8

* inflation adjusted for inflation in 2015 dollars

** percentages may not equal 100 due to missing data or small subsets

*** CI, confidence interval; ED, emergency department