

ECG Findings in Pediatric Patients under the Influence of Marijuana

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**Jeffrey A. Robinson^{1,2}, Sahana Somasegar², Jill K. Shivapour^{1,2}
Christopher S. Snyder^{1,2}**

¹ The Congenital Heart Collaborative, Rainbow Babies and Children's Hospital, Cleveland, OH

² Case Western Reserve University School of Medicine, Cleveland, OH

ABSTRACT

Background: The effects of marijuana on the cardiac conduction system are ill defined. The purpose of this study is to describe the association between electrocardiogram (ECG) findings and positive urine drug screening (+UDS) for marijuana in the pediatric population. **Methods:** A retrospective review was conducted through the electronic medical record from Emergency Department (ED) visits dated 10/13-11/14 of patients ≤ 18 years of age who tested positive for marijuana exposure by +UDS in the ED. **Inclusion criteria included:** 1) +UDS for marijuana performed in the ED and 2) electrocardiogram (ECG) performed on same day as +UDS. Each ECG was overread by a pediatric electrophysiologist, blinded to the results of the UDS. **Results:** There were 174 patients identified in the ED with a +UDS, median age of 15 years (0-18 years); 42% were male. ECG was performed at time of +UDS on 37 (21%) patients. An abnormal ECG finding was identified in 16/37 (43%), of which 15 had a follow-up ECG. Non-specific similar ECG findings were noted on 3/15: 2 ST segment changes and 1 early repolarization. Significant differences were noted on ECGs with +UDS in 12/15 patients, including ST segment changes (4), left ventricular hypertrophy (3), first-degree atrioventricular (AV) block (2), and 1 each: atrial fibrillation, right ventricular hypertrophy, and Mobitz type I second-degree AV block. **Conclusions:** Abnormal ECG findings, including serious conduction and rhythm disturbances, can be identified in pediatric patients under the influence of marijuana. An ECG should be considered on all patients with a positive urine drug screen for marijuana.

Key words: cannabis, marijuana, electrocardiogram, ECG, urine drug screen, adolescents, pediatrics

Marijuana is the most commonly used illicit drug in the United States, and its abuse in children and adolescents has steadily increased in recent years (Singh, 2000). According to recent epidemiologic data, 7.2% of 12-17 year olds are regularly exposed to marijuana (Wall et al., 2011). The issue of legalized marijuana in states across the country has brought the subject of the potential hazards and health consequences of marijuana to the

forefront of public debate; however, the acute and chronic effects of marijuana in the pediatric population are not completely understood.

Marijuana is known to be a mind-altering substance that also has significant effects on cardiovascular and autonomic nervous system function (Beaconsfield, Ginsburg, & Rainsbury, 1972). In particular, symptoms such as palpitations and chest pain have been noted

Corresponding Author: Christopher S. Snyder, Division of Pediatric Cardiology, The Congenital Heart Collaborative, Rainbow Babies and Children's Hospital, 11100 Euclid Ave, MS RBC 6011, Cleveland, OH 44106, Phone: 216-844-8529, Fax: 216-844-5478, email: Christopher.Snyder@UHhospitals.org

during and after the use of marijuana in adults, which have been found to be tachycardia, near-syncope, or syncope (Brust, 1993; Miller et al., 1977). Regardless, the effects of marijuana use in children and adolescents in particular have not been extensively studied. On an anecdotal basis, otherwise healthy adolescents and young adults with no history of cardiac disease have developed acute cardiac symptoms and presented with acute onset of atrial fibrillation after ingesting marijuana (Korantzopoulos, Liu, Papaioannides, Li, & Goudevenos, 2008; Singh, Huntwork, Shetty, Sequeira, & Akingbola, 2014). Here, it has been postulated that acute catecholamine surges in susceptible individuals—particularly those who are naïve to marijuana—could cause atrial fibrillation, as well as some of the more common cardiac symptoms, consequent to adrenergic and mechanoreceptor stimulation of the heart (Brust, 1993; Korantzopoulos, 2014; Miller et al., 1977).

The true mechanism of arrhythmia associated with marijuana use may be multifactorial. In addition to increased sympathetic tone, marijuana use has also been associated with bradycardia, as well as first- and Mobitz type I second-degree atrioventricular block (Wenckebach) in otherwise healthy young adults (Akins & Awdeh, 1981). In fact, multiple exposures to marijuana may modulate the sympathetic nervous system, such that chronic users experience decreased sympathetic activation and increased parasympathetic or vagal tone (Middlekauff et al., 2014; Schmid et al., 2010). Previous work has demonstrated that increased parasympathetic activity can be substrate for atrial fibrillation by decreasing both the action potential duration and the atrial refractory period (Coumel, 1994; Pratap & Korniyenko, 2012).

As the use of marijuana among the pediatric population continues to rise, it is important to understand the cardiovascular effects and changes that can be noted on the electrocardiogram of a pediatric or adolescent patient. The purpose of this study is to describe the association between electrocardiogram (ECG) findings and positive urine drug screen (+UDS) for marijuana in pediatric patients presenting to the acute care setting.

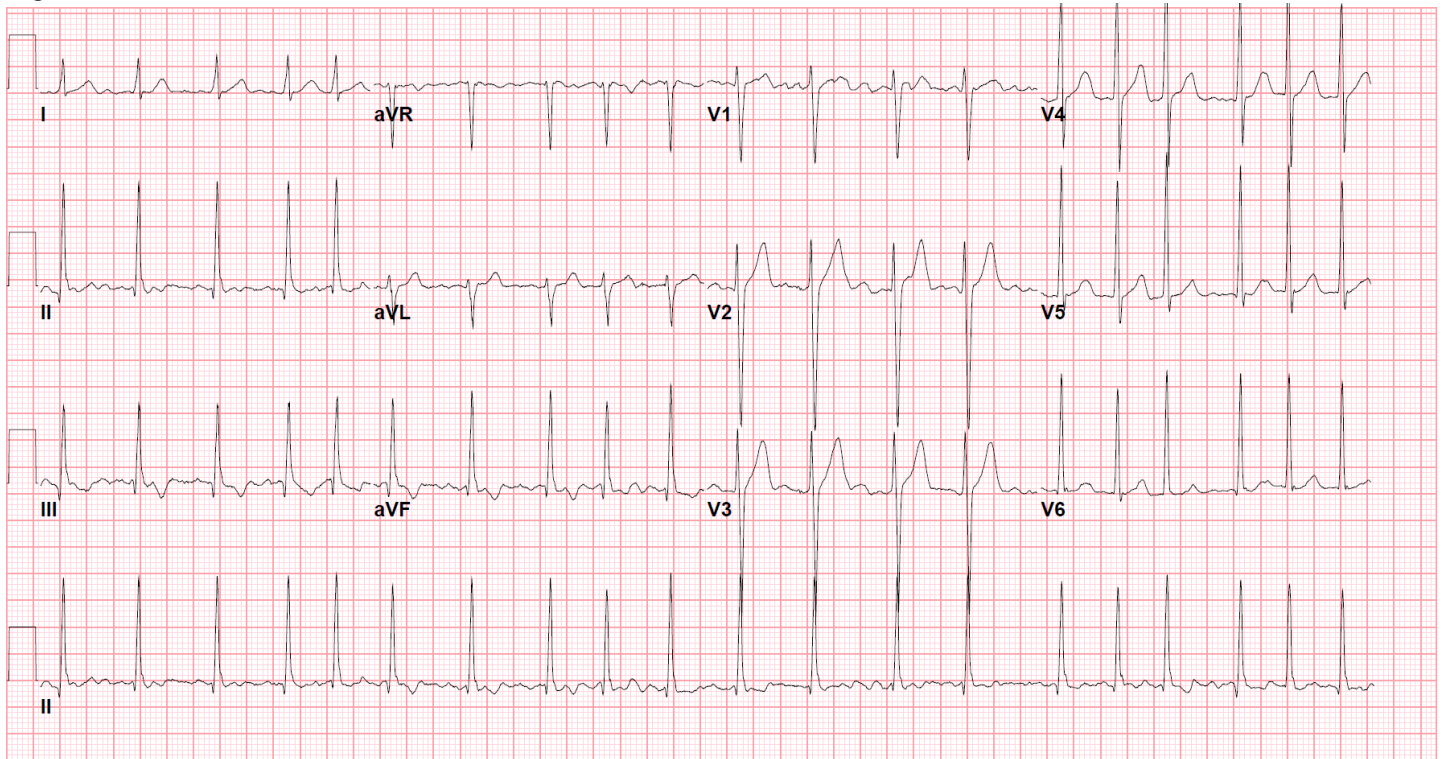
METHOD

This single-center, retrospective chart review complies with the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) for Human Investigation. The Clinical Chemistry database was queried for all +UDS results from the emergency department (ED) in patients ≤ 18 years of age from December 1, 2013, through November 30, 2014. Any ECG that these patients had received on the day of the +UDS for marijuana was obtained from the hospital ECG database (MUSE® Cardiology Information System, version 7.1.1, General Electric Company, Boston, Massachusetts, USA, 2007). Inclusion criteria included both +UDS and ECG performed for any indication during a single ED visit during the study period. For the cohort identified, any additional ECG(s) performed for any indication on any date through November 30, 2014, were obtained from the hospital MUSE ECG database.

Printed 15-lead ECGs were deidentified of personal health information. ECGs were grouped by a study number unique to each patient. Each ECG was separately overread and interpreted by a pediatric electrophysiologist using the MUSE® Cardiology Information System. The pediatric electrophysiologist was blinded to the results of the +UDS. Standard electrocardiographic definitions were used. Repolarization abnormalities were grouped to include non-specific T-wave abnormality, ST segment changes, and early repolarization. ECG findings were then characterized in relation to the date of +UDS for marijuana. Comparisons were then made between ECGs for a single patient performed on the date of +UDS and any performed on a different date.

RESULTS

There were 174 patients identified in the ED with a +UDS, median age of 15 yrs (0-18 yrs); 42% were male. ECG was performed at time of +UDS on 37 (21%) patients. Of these, 21 (57%) patients had a normal ECG on the date of +UDS. An abnormal ECG finding was identified in the remaining 16, of which 15 had an additional ECG performed on another date: either prior to or after the date of the +UDS in the ED. Comparisons were made between each patient's

Figure 1. 17-year-old male, with palpitations, diagnosed with atrial fibrillation.

ECGs. Similar ECG findings were identified in 3 of the patients, regardless of the results of the UDS: 2 with ST segment changes and 1 with early repolarization. The 12 other patients had significant differences in their ECGs while under the influence of marijuana, including ST segment changes (4), left ventricular hypertrophy (3), first-degree atrioventricular (AV) block (2), and one each: atrial fibrillation, sinus bradycardia with Mobitz type I second-degree AV block, and right ventricular hypertrophy.

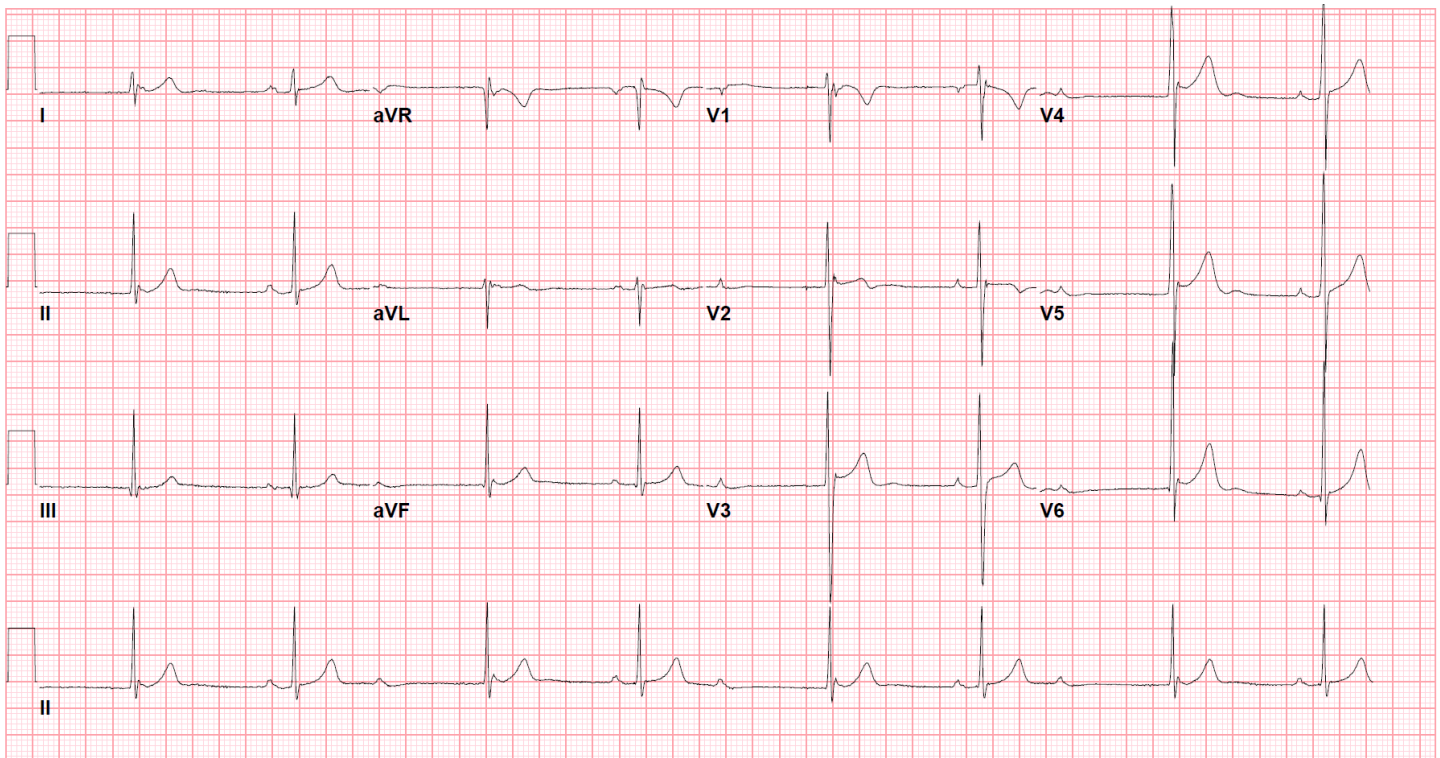
In particular, two cases will be highlighted. First, a 17-year-old athletic, otherwise healthy Caucasian male presented to the ED with new and sudden onset of palpitations. The patient was alert and answered questions appropriately. On physical exam, there was an irregularly irregular heart rhythm with ventricular rate of 112 beats per minute (bpm). ECG confirmed atrial fibrillation (see Figure 1). Initial blood pressure was 154/94 mmHg; however, there was no previous history of hypertension. Body mass index (BMI) was within normal limits for age.

The patient had a prior history of tobacco and alcohol use, as well as distant recreational use of 3,4-methylenedioxymethamphetamine (MDMA). The patient had smoked marijuana occasionally, previously without cardiac symptoms. On the day of presentation, he had exposure to marijuana

from a new source within a few hours of developing palpitations. No other risk factors for atrial fibrillation were identified on history and review of systems. The patient was prescribed oral doses of atenolol and aspirin in the ED. Spontaneous cardioversion and return of normal sinus rhythm occurred several minutes after taking the first doses of these medications. The patient was observed overnight without recurrence of his arrhythmia. Over 2.5 years of follow-up, he continued to use marijuana intermittently, twice developing palpitations with one episode of documented atrial fibrillation.

The second patient was a 14-year-old, otherwise healthy African American male, who presented with new onset of acute chest pain and headache at school. He was transported by ambulance to the ED, where he was noted to be agitated, defiant, and uncooperative. On exam, baseline heart rate was 51 bpm. The patient was appropriately oriented to person, place, and time. There were otherwise no murmurs or any other positive findings on physical exam. On ECG and 24-hour Holter monitor, the patient was found to have a Mobitz type I second-degree AV block (see Figure 2). The patient smoked marijuana on

Figure 2. 14-year-old male, with headache/blurred vision, diagnosed with 2nd-degree atrioventricular block.



a frequent basis as a therapeutic measure to relieve symptoms of anxiety. He had smoked marijuana within a few hours of this acute presentation.

Cessation of marijuana use was recommended and the patient was seen for follow-up in outpatient clinic several days later. There, baseline ECG was sinus rhythm. An exercise stress test was performed on a treadmill with a standard Bruce ramp protocol. Resting heart rate was 48 bpm and normal sinus rhythm was documented by ECG. Heart rate increased to 187 bpm at peak exercise, with likewise appropriate blood pressure response to exercise. There was no additional arrhythmia or significant ectopy noted throughout exercise or during recovery. On most recent follow-up, the patient continued to use marijuana on a regular basis; repeat ECG demonstrated Mobitz type I second-degree AV block.

DISCUSSION

The prevalence of abnormal ECG findings and arrhythmias (including atrial fibrillation and second-degree AV block) are largely unknown in the general pediatric population. As such, a wide

differential diagnosis should be considered in the acute care setting. History and physical exam should guide subsequent evaluation, with consideration of urine drug screening for marijuana, especially when other risk factors for an arrhythmia are absent.

Dating back to the 1970s, several prospective studies in humans have described increases in both heart rate and blood pressure associated with acute exposure to marijuana, attributed to modulation of the autonomic nervous system (Beaconsfield et al., 1972; Roth et al., 1973; Weiss et al., 1972). The heart rhythm abnormalities associated with these early prospective studies in humans were essentially limited to isolated, multifocal premature ventricular contractions (PVCs) and repolarization abnormalities (Kochar & Hosko, 1973; Miller et al., 1977; Pratap & Korniyenko, 2012; Weiss et al., 1972). Subsequent manuscripts have raised concern for second-degree AV block (Akins & Awdeh, 1981), atrial fibrillation (Aryana & Williams, 2007; Charbonney et al., 2005; Korantzopoulos et al., 2008; Korantzopoulos, 2014; Kosior et al., 2000; Singh et al., 2014; Singh, 2000), and cardiac asystole (Menahem, 2013). Likewise, coronary artery vasospasm leading to acute myocardial

infarction has been associated with exposure to either marijuana or synthetic cannabinoid derivatives (Arora et al., 2012; Charles et al., 1979; Collins et al., 1985; Deharo et al., 2013; Ghannem et al., 2013; Gunawardena et al., 2014; McKeever et al., 2015; Mir et al., 2011; Mittleman et al., 2001).

This study highlights the occurrence of potentially concerning arrhythmias presenting in patients with +UDS for marijuana. Strict causation and effect could not be demonstrated by the data collected. In particular, concurrent illicit substances were not queried in conjunction with the +UDS for marijuana. Comparison ECGs (those not performed on the date of the +UDS for marijuana) could have been performed at any time, from birth of the patient up until the end of the study period. Similarly, marijuana status (either by history or urine drug screening) was unknown for comparison.

This study was performed at a single, large academic medical center. The patients in this cohort were evaluated and managed in the ED; pediatric cardiology was not consulted in all cases for clinical decision-making. Likewise, there was no standard outpatient follow-up employed during this period of study for patients. As such, any follow-up examination or cardiac imaging performed by pediatric cardiology based on abnormal ECG findings was not evaluated in this study to confirm the presence of right or left ventricular hypertrophy, as detected by abnormal screening criteria on ECG.

It is inherent to clinical research that a larger or multi-centered controlled trial would be necessary to further support any ECG changes resulting directly from marijuana ingestion. Such information would benefit the ability of the medical community to most effectively educate patients and the general public about any potential cardiac risks associated with marijuana exposure. In the meantime, clinicians should consider marijuana in the differential diagnosis for any child or adolescent patient presenting with unexplained arrhythmia or repolarization abnormalities.

Conclusion

Marijuana use may cause ECG abnormalities, including atrial fibrillation, second-degree AV block (Mobitz I, Wenckebach), and repolarization

abnormalities. Marijuana exposure should be considered in the differential diagnosis for children or adolescents who have arrhythmias identified in the acute care setting. We recommend performing a urine drug screen for all pediatric patients who present to the emergency department with unusual arrhythmia or ECG abnormality.

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