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Prolonged Ventricular Asystole: A Rare Adverse Effect of Hydrocodone Use

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

EF 1 **Sivakumar Sudhakaran**
BEF 2 **Saherish S. Surani**
EF 1 **Salim R. Surani**

1 Department of Medicine, Texas A&M University Health Science Center, College Station, TX, U.S.A.
2 Research Assistant, Pulmonary Associates of Corpus Christi, Aransas Pass, TX, U.S.A.

Corresponding Author: Salim R. Surani, e-mail: srsurani@hotmail.com
Conflict of interest: None declared

Patient: Female, 56
Final Diagnosis: Ventricular asystole
Symptoms: Dizziness • headache • near-syncope • weakness
Medication: —
Clinical Procedure: —
Specialty: Cardiology

Objective: Unusual clinical course





Background: Prolonged ventricular asystole is a rare vagal reaction caused by hydrocodone use. Sinus bradycardia is a characteristic presentation of the vasovagal response; examples of other presentations include arrest or atrioventricular block. Physicians need to be aware of ventricular asystole due to vagally-mediated atrioventricular block caused by hydrocodone or other opiates.

Case Report: We present a case of prolonged ventricular asystole in a young patient due to a vasovagal reaction caused by the hydrocodone found in the hydrocodone/acetaminophen combination.

Conclusions: Ventricular asystole can be a rare complication of hydrocodone found in hydrocodone/acetaminophen. Physicians need to be aware of this adverse effect, rather than resorting to expensive diagnostic interventions.

MeSH Keywords: Arrhythmias, Cardiac • Heart Arrest

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/891214>

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Background

The vasovagal response is characterized by inappropriate cardiac slowing and arteriolar dilatation. Vasovagal responses reflect autonomic neural changes; bradycardia results from sudden augmentation of efferent vagal activity, and hypotension results from sudden reduction or cessation of sympathetic activity and relaxation of arterial resistance vessels [1]. An acute vasovagal response may range in presentation from a temporary loss of consciousness (vasovagal syncope) to vagally-mediated atrioventricular (AV) block [2]. Vasovagal syncope is the most common form of syncope and has a lifetime cumulative incidence of 35% [3]. Recurrent syncopal episodes are common, and cost the U.S. roughly \$2.4 billion in hospital-related admissions [4]. Therapeutic strategies for management of extreme vasovagal episodes remain somewhat limited due to its complex pathophysiology [5], but current evidence strongly suggests that genetic factors play a role. Family aggregation studies have repeatedly shown that individuals with vasovagal syncope more frequently have affected family members with vasovagal syncope than unaffected controls. Furthermore, evidence provided by a twin study showed significantly higher concordance rates in monozygous versus dizygous twins for syncope associated with vasovagal triggers. Molecular genetic studies have identified the first locus for vasovagal syncope in an autosomal dominant family on chromosome 15q26 [6]. An exaggerated vasovagal response may present due to a wide variety of clinical determinants. We here present a case and brief discussion of prolonged ventricular asystole of vasovagal etiology due to the hydrocodone found in the hydrocodone/acetaminophen combination.

Case Report

A 56-year-old female patient presented in the emergency department (ED) complaining of weakness, intermittent nausea, dizziness, and near-syncope. Past medical history was significant for lower extremity and plantar foot pain, requiring hydrocodone/acetaminophen. In the ED, the patient reported waking up about 3 or 4 times throughout the night with headache, nausea, retching, and feelings of near loss of consciousness. The patient reported her last dose of hydrocodone/acetaminophen was taken the night prior to presentation. Initial electrocardiogram on presentation was unremarkable, displaying normal sinus rhythm with normal PR interval and QRS duration (Figure 1). Heart rate was within normal limits at 68 beats/min (bpm). A short while later, while still in the ED, the patient subsequently had several episodes of nausea and retching closely followed by diaphoresis and ventricular asystole for about 6–8 s (Figure 2). Each asystolic episode spontaneously resolved back to normal sinus rhythm. The patient was quickly given isoproterenol for sinus bradycardia, which

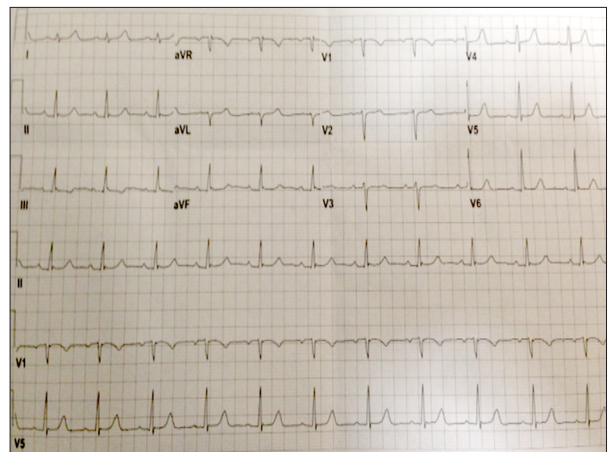


Figure 1. Electrocardiogram showing normal sinus rhythm with rate of 68 bpm, PR interval of 182 milliseconds (ms) and QRS duration of 96 ms.

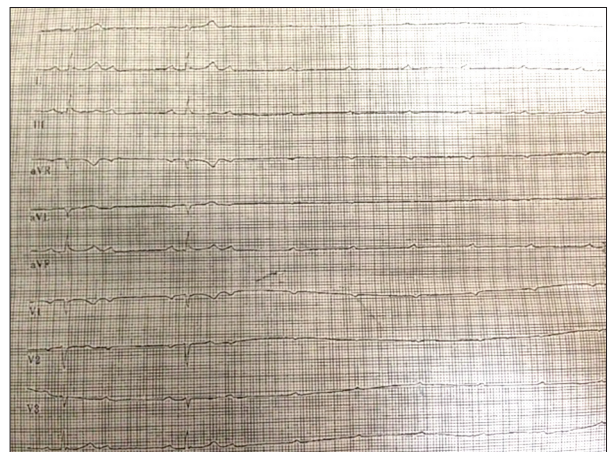


Figure 2. Rhythm strip showing normal sinus rhythm and then P wave followed by no QRS complex (ventricular asystole).

resulted in a heart rate of 150 bpm with normal sinus rhythm and no blocks. The patient's laboratory data showed no evidence of electrolyte imbalance, with sodium, potassium, calcium, and magnesium levels all within normal ranges. The patient was on no medications aside from hydrocodone/acetaminophen, which she had taken for the first time prior to her presentation to the ED. She had no history of hypertension, peripheral vascular disease, or cerebrovascular events. Furthermore, the patient reported no history of an enlarged heart or cardiac murmur. Cardiovascular, respiratory, gastrointestinal, genitourinary, musculoskeletal, and endocrine system functions were all within normal limits.

The patient was admitted and kept under observation with telemetry monitoring. An echocardiogram showed normal ejection function, with no pericardial effusion. In addition, there were no signs of regional wall motion or valvular abnormalities.

Hydrocodone/acetaminophen was discontinued, and the nausea was resolved. Moreover, there were no episodes of AV-block, asystole, or other arrhythmias during her 48 h of observation on telemetric monitoring. The patient was completely asymptomatic at the time of discharge, and was scheduled for follow-up in 2 weeks.

Discussion

Vagally-mediated AV block is defined as a paroxysmal AV block, localized within the AV node, associated with slowing of the sinus rate. All types of second-degree AV block, ranging from pseudo-Mobitz II block to complete AV block, may be present [2]. As exhibited in this case, the vagal response can be extreme enough to alter conduction of the AV node and, consequently, ventricular automaticity [7,8]. Typical forms of vagally-mediated AV block include carotid sinus massage, tilt-induced syncope, spontaneous neural syncope, and emotional distress [2]. Ventricular asystole as a vagal response to hydrocodone has not been well characterized in the literature to date.

The diagnostic impression of this case was based on a variety of factors. There were neither previous episodes nor a family history of syncope or near-syncope. Furthermore, there was no history of cardiac arrhythmias. Alternatively, there was no evidence to suggest an intrinsic conduction system disease, as isoproterenol administration caused pronounced sinus tachycardia of over 150 bpm. Additionally, the patient's initial electrocardiogram displayed a normal sinus rhythm (Figure 1), with no AV conduction abnormalities. A diagnosis of vagally-mediated AV block was made based on the simultaneous depression of sinus node function, as well as AV conduction (with ventricular asystole) [2] (Figure 2). Moreover, these near-syncope episodes occurred only after taking hydrocodone/acetaminophen and resolved spontaneously after discontinuing the drug. After careful evaluation, these episodes of prolonged ventricular asystole are most likely due to a pronounced vasovagal response caused by the hydrocodone found in the hydrocodone/acetaminophen combination.

There is a consensus that syncope due to vagally-mediated AV block should be diagnosed and managed as neurally-mediated

(vasovagal) syncope, according to European guidelines [9]. For patients with unexplained syncope or an ambiguous history of vasovagal syncope, a tilt table test may help support a diagnosis [9]. There are a number of different tilt table protocols, each with variations in the initial stabilization phase, duration of tilting (20–45 min) and application of pharmacological agents [10,11]. The symptoms and treatment strategies for vasovagal episodes are quite varied. Common symptoms include nausea, diaphoresis, epigastric discomfort, dizziness, blurred vision, and pallor [12]. Therapeutic strategies include β -blockers, disopyramide, scopolamine, theophylline, ephedrine, etilefrine, midodrine, clonidine, and serotonin reuptake inhibitors [9]. Currently, the limited data derived from placebo-controlled trials offers no convincing data to support the use of one drug over another as a first-line therapy. Consequently, non-pharmacological treatment options such as tilt training are a fundamental first step of all treatment pathways to avoid any potentially harmful effects from the drugs mentioned above [13]. However, when vagally-mediated AV block is encountered as an asymptomatic (or near syncopal) episode, the European guidelines on pacing make no distinction between vagally-mediated and intrinsic AV block [14]. Finally, in severe cases of asystole, the use of permanent cardiac pacing may be necessary [15].

Conclusions

Prolonged ventricular asystole due to hydrocodone or other opiate medications is a rare outcome of the vasovagal response. Syncope due to vagally-mediated AV block should be managed as vasovagal syncope, but placebo-controlled trials offer no convincing data to support the use of one drug over another as a first-line therapy [13]. A small percentage of patients will require electrophysiological assessment to determine if a cardiac pacemaker is needed for management of persistent vasovagal asystole [15]. Ultimately, it is important to understand that prolonged ventricular asystole may be seen as an acute vasovagal response from hydrocodone to insure timely management in the clinical setting.

Conflicts of interest

None.

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