Published in final edited form as:

Pacing Clin Electrophysiol. 2012 July ; 35(7): e206–e209. doi:10.1111/j.1540-8159.2012.03365.x.

Sleep Syncope: Treatment with a Permanent Pacemaker

Jason A. Rytlewski, MD*, John T. Lee, MD*, and Satish R. Raj, MD MSCI*,%

*Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee

%Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, Tennessee

Abstract

Vasovagal syncope usually occurs during upright posture, but Jardine et al. have described a variant that occurs at night. During “sleep syncope”, patients are awakened from sleep with nausea, abdominal cramping or a sense of impending diarrhea, get up, and faint in the bathroom. We report on a patient with recurrent sleep syncope (with physical injury) in whom an asystolic pause was documented during one of her “sleep syncope” spells. Implantation of a dual chamber pacemaker (5 year follow-up) “cured” her of further syncope. This is the 1st report of pacemaker use for this unusual form of reflex syncope.

Keywords

syncope; sleep; pacemaker

Case Presentation

A 41 year old female with no significant past medical history was referred to Arrhythmia Clinic for recurrent syncope. She reported infrequent syncopal episode since her teenage years that occurred with upright posture and light activity. These spells were not associated with any personal injury, prodromal symptoms, precipitants, non-postural or phobia related triggers. She had no faints triggered by pain, needles, phlebotomy or claustrophobia. The patient was unconcerned until she developed a distinctly different “fainting spell” in her early twenties that was not associated with any other life altering or stressful events.

During the newer spells, she would awaken abruptly at night with severe nausea, abdominal cramping and a feeling of impending diarrhea (or a combination of those symptoms). She would get up and go to the bathroom to vomit and sometimes attempt to defecate. Within 20 seconds to 2 minutes, she would faint, often in the absence of a bowel movement. The brief syncopal spells (<2 minutes) were witnessed by her husband on some occasions. There was not any tonic-clonic movement during the spell, and post-spell the patient was mildly diaphoretic, and felt weak, but with a clear sensorium. She would be escorted back to bed without any further difficulty for the remainder of the night. Of note, even if she did not have a bowel movement, the abdominal sensations would resolve.

Since the initial episode of “sleep syncope”, the patient has continued to experienced sleep syncope every 8–12 months. Every episode occurred with the patient awakening from sleep with severe nausea. Some, but not all, of the spells were associated with vomiting or

Correspondence: Satish R Raj MD MSCI Assistant Professor of Medicine and Pharmacology Vanderbilt University School of Medicine AA3228 Medical Center North 1161 21st Avenue South Nashville, TN 37232-2195 Office: (615) 343-6499 • Fax: (615) 343-8649 Satish.raj@vanderbilt.edu.

Conflicts of Interest: None

defecation. Nearly every spell was associated with personal injury, ranging from facial abrasions or lacerations requiring sutures to broken teeth requiring extensive dental repair.

Conventional therapy for reflex syncope, including lifestyle modification, beta blocker therapy and fludrocortisone failed to alter the pattern of sleep syncope. The patient was instructed to maintain a supine posture with these spells, but her ability to do so was limited by her severe nausea and vomiting. The patient denied having a history of tachycardia, conduction system disease, palpitations or current orthostatic symptoms. Baseline electrocardiogram (Figure 1) was unrevealing. Urine tests for pheochromocytoma, carcinoid syndrome and mast cell activation disorder were all negative. She underwent a drug-free 45 minute head-up tilt table test during which she was symptom-free and maintained her blood pressure. Autonomic reflex testing assessing both sympathetic & parasympathetic nervous system tone were also normal.

Given both the negative investigative work-up and her ongoing spells with injury, an implantable loop recorder was placed. After a period of several months the patient experienced another typical “sleep syncope” spell with the cardiac rhythm demonstrated in Figure 2. The recorded rhythm was initially a sinus rhythm, which then markedly slowed, and then there was then a junctional rhythm that slowed, and eventually a 7 second asystolic pause. Due to her recurrent syncope with asystole and physical injury, a clinical indicated dual chamber pacemaker with rate drop response (Medtronic E2DR01) was implanted and programmed with a lower rate limit of 40 bpm. The rate drop response feature would briefly pace rapidly in response to sudden drops in her heart rate suggestive of a neurally mediated spell. Since pacemaker implantation in August 2006 the patient has had 4 nocturnal episodes when she would awaken with her normal prodrome of nausea and abdominal cramping, but no further spells of complete syncope. Of note, most of these prodromal spells were associated with a “rate drop” episode (indicating a neurally mediated spell) and a brief period of ventricular pacing. Unfortunately, intracardiac electrograms could not be recorded during these rate drop episodes.

Discussion

Until a few years ago, the dogma was that reflex fainting did not occur in the supine position in the absence of an obvious trigger (e.g. phlebotomy). This case is an example of a phenomenon recently reported by Krediet et al.¹ known as “sleep syncope”. The differential diagnosis of nocturnal episodes of syncope includes sleep paralysis, epilepsy, vertebrobasilar migraines, hypnagogic hallucinations, systemic mastocytosis, carcinoid, pheochromocytoma, visceral edema and panic attacks. The classic description from patients is that they are awakened from their sleep with gastrointestinal symptoms, including nausea, abdominal cramping and a sense of impending diarrhea.

The initial case series of sleep syncope included 13 patients. Every patient awakened suddenly from sleep with severe nausea prior to their syncopal spell¹. Unlike our patient, the initially cohort of patients were predominantly tilt positive (7/9), and bradycardia was only documented in 5 patients due to limited ambulatory monitoring. Jardine et al.² compared the spells of patients with sleep syncope to those with non-sleep syncope. Sleep syncope patients had a higher incidence of phobia-triggered syncope and syncope while horizontal than the non-sleep syncope patients. There were no differences in the muscle sympathetic nerve activity responses to head-up tilt testing, and the authors concluded that sleep syncope was a subtype of vasovagal syncope.

Most recently, Busweiler et al.³ have reported on characteristics on 54 patients with sleep syncope. They found that 75% of their patients with sleep syncope described specific

phobias (such as phlebotomy), and they hypothesized that an exaggerated fear response may contribute to the overall condition³. Their patients were predominately women and usually experienced their first syncopal event in adolescence. Our patient lacked any specific phobia but did begin experiencing syncopal episodes in adolescence.

There has not been adequate monitoring in these patients to know definitely whether the bradycardia precedes or follows the gastrointestinal symptoms. Our patient described gastrointestinal symptoms for 20 seconds to 2 minutes prior to syncope. Given that we documented asystole lasting ~10 seconds, it is not likely that the bradycardia preceded the gut symptoms. Unlike true situational defecation syncope, however, most of her syncopal spells occurred in the absence of a bowel movement.

It is postulated that acutely increased vagal tone might be an important mechanism of syncope in “sleep syncope”. Increased vagal tone could also explain the gastrointestinal symptoms that are almost universal in this population. Vagal activity will increase gut motility and could present with abdominal cramping, nausea and a sense of impending diarrhea. Vagal discharge could initial lead to gastrointestinal symptoms that are then followed by cardioinhibition. Proposed mechanisms for the apparent hypervagotonia associated with sleep syncope include: a centrally mediated increase in vagal activity during deeper phases of Non-REM sleep, or perhaps a focal peri-insular seizure leading to a sudden & transient increase in vagal outflow. If isolated hypervagotonia is the sole mechanism of syncope, then in theory a medication such as atropine could acutely treat such an episode, although this is entirely impractical to administer. Given this patient's apparent response to pacing, isolated asystole might be the sole mechanism of syncope in this case. This is not always the case. Recently, Krediet et al.⁴ demonstrated that in a patient with carotid hypersensitivity and an asystolic response, total peripheral resistance also fell with a delayed recovery of blood pressure even after resumption of a normal heart rate.

Clinical trials of permanent pacing for recurrent vasovagal syncope have been disappointing to date. While early randomized trials that randomized patients with vasovagal syncope to unblinded pacemaker implantation or standard of care showed early promise⁵⁻⁷, more recent studies in which such patients all underwent pacemaker implantation and were blinded to pacing therapies on or off showed a more modest to no benefit^{8,9}. These data point to a large “expectation effect” that patients with vasovagal syncope experience when they know that they are being treated with a pacemaker¹⁰. The ISSUE 2 investigators¹¹ have reported that patients with recurrent syncope with asystole who receive a pacemaker had less syncope than those syncope patients without asystole. While raising hopes of more optimal patient selection, ISSUE 2 was unblinded, and more definitive data should be forthcoming from the properly blinded ISSUE 3 study¹². Even if ISSUE 3 study is positive, careful consideration is required before implanting a permanent pacemaker into these typically young patients, given the risks of mechanical failures, multiple lifetime generator changes, and the potential negative effect of RV pacing.

A pacemaker was implanted in our patient due to the frequency of symptoms, the severity of injury with syncope, and her lack of response to medical therapies in the setting of ILR documented asystole. Since her permanent pacemaker implantation, our patient has experienced 4 discrete prodromal spells that were associated with activation of the “rate drop response” feature with ventricular pacing; suggesting that acute bradycardia or asystole might still be recurring. Over a follow-up period of 5 years, she has had no further frank syncope. Given that the gastrointestinal symptoms might be a marker of hypervagotonia, patients with sleep syncope may represent a subset of vasovagal syncope that may have a salutary response to permanent pacemaker implantation. This hypothesis requires prospective validation.

Acknowledgments

Funding: SRR is supported by grant R01 HL102387 from the National Institutes of Health (Bethesda, MD, USA) and the Paden Dysautonomia Fund (Vanderbilt University).

Reference List

1. Krediet CT, Jardine DL, Cortelli P, Visman AG, Wieling W. Vasovagal syncope interrupting sleep? *Heart*. 2004; 90:e25. [PubMed: 15084573]
2. Jardine DL, Krediet CT, Cortelli P, Frampton CM, Wieling W. Sympatho-vagal responses in patients with sleep and typical vasovagal syncope. *Clin Sci (Lond)*. 2009; 117:345–353. [PubMed: 19281451]
3. Busweiler L, Jardine DL, Frampton CM, Wieling W. Sleep syncope: important clinical associations with phobia and vagotonia. *Sleep Med*. 2010; 11:929–933. [PubMed: 20817601]
4. Krediet CT, Jardine DL, Wieling W. Dissection of carotid sinus hypersensitivity: the timing of vagal and vasodepressor effects and the effect of body position. *Clin Sci (Lond)*. 2011; 121:389–396. [PubMed: 21595633]
5. Connolly SJ, Sheldon R, Roberts RS, Gent M. The North American Vasovagal Pacemaker Study (VPS). A randomized trial of permanent cardiac pacing for the prevention of vasovagal syncope. *J Am Coll Cardiol*. 1999; 33:16–20. [PubMed: 9935002]
6. Ammirati F, Colivicchi F, Santini M. Syncope Diagnosis and Treatment Study Investigators. Permanent cardiac pacing versus medical treatment for the prevention of recurrent vasovagal syncope: a multicenter, randomized, controlled trial. *Circulation*. 2001; 104:52–57. [PubMed: 11435337]
7. Sutton R, Brignole M, Menozzi C, Raviele A, Alboni P, Giani P, Moya A. Dual-chamber pacing in the treatment of neurally mediated tilt-positive cardioinhibitory syncope : pacemaker versus no therapy: a multicenter randomized study. The Vasovagal Syncope International Study (VASIS) Investigators. *Circulation*. 2000; 102:294–299. [PubMed: 10899092]
8. Connolly SJ, Sheldon R, Thorpe KE, Roberts RS, Ellenbogen KA, Wilkoff BL, Morillo C, et al. Pacemaker therapy for prevention of syncope in patients with recurrent severe vasovagal syncope: Second Vasovagal Pacemaker Study (VPS II): a randomized trial. *JAMA*. 2003; 289:2224–2229. [PubMed: 12734133]
9. Raviele A, Giada F, Menozzi C, Specchia G, Orazi S, Gasparini G, Sutton R, et al. A randomized, double-blind, placebo-controlled study of permanent cardiac pacing for the treatment of recurrent tilt-induced vasovagal syncope. The vasovagal syncope and pacing trial (SYNPACE). *Eur Heart J*. 2004; 25:1741–1748. [PubMed: 15451153]
10. Sud S, Massel D, Klein GJ, Leong-Sit P, Yee R, Skanes AC, Gula LJ, et al. The expectation effect and cardiac pacing for refractory vasovagal syncope. *Am J Med*. 2007; 120:54–62. [PubMed: 17208080]
11. Brignole M, Sutton R, Menozzi C, Garcia-Civera R, Moya A, Wieling W, Andresen D, et al. Early application of an implantable loop recorder allows effective specific therapy in patients with recurrent suspected neurally mediated syncope. *Eur Heart J*. 2006; 27:1085–1092. [PubMed: 16569653]
12. Brignole M. International study on syncope of uncertain aetiology 3 (ISSUE 3): pacemaker therapy for patients with asystolic neurally-mediated syncope: rationale and study design. *Europace*. 2007; 9:25–30. [PubMed: 17224418]

Figure 1.
12 lead electrocardiogram of patient.

Figure 2.

Implantable loop recorder tracing during an episode of sleep syncope. Over the span of 2 minutes (shortly before 5am), the patient's rhythm changed from a sinus rhythm to sinus bradycardia, to a junctional rhythm with isorhythmic dissociation, to ventricular asystole with occasional junctional escape beats and then ventricular escape beats before the junctional rate and finally the sinus rate sped back up again.