CLINICAL VIGNETTE

Sleep Apnea and Bradyarrhythmia: Pacemaker or not?

Eugenia Wen, M.D., Joanne Bando, M.D. and Ramin Tabibiazar, M.D

.

Introduction

Cardiac arrhythmias during sleep are common due to sleep state dependent autonomic nervous system activity, especially in patients with cardiovascular disease. Though malignant arrhythmias are generally less common during sleep, 15% of fatal ventricular arrhythmias still occur resulting in sudden nocturnal death. Bradyarrhythmias, sinus pauses greater than 2 seconds, and atrioventricular conduction delays commonly occur during sleep in young and healthy individuals without cardiac disease. Impressively long sinus pauses up to 9 seconds in 4 healthy athletes without cardiac disorder were reported by Guilleminault et al in 1984[1]. In patients with significant obstructive sleep apnea, even more dramatic conduction blockade can occur, with ventricular asystoles up to 15.6 seconds reported [2].

Case Report

A 66-year-old man with known history of duodenal ulcer presented to the ED with melena, severe progressive weakness, and dyspnea. He was transfused 2 units of PRBCs and admitted to the telemetry unit for monitoring. Overnight, he developed crampy abdo-minal discomfort with an associated 6.8-second pause on monitor with ventricular asystole. The patient denied palpitations, dizziness, or lightheadedness. His admission 12 lead EKG showed 1st degree AV block with a PR interval of 220 miliseconds. The telemetry event strip revealed sinus slowing with lengthening PR interval prior to high-grade AV block with ventricular asystole duration of 6.8 seconds. Nocturnal 2:1 AV block with narrow QRS was noted. The consulting cardiologist recommended sleep disorders consultation for assessment of possible sleep related breathing disorder causing the nocturnal bradyarrhythmia. On questioning, the patient reluctantly acknowledged being diagnosed with obstructive sleep apnea 15 years ago at an outside facility by polysomnogram. He had classic symptoms and signs of obstructive apnea with nocturnal arousals with snoring and choking, observed apnea, daytime fatigue, increased neck circumference, oral crowding and elevated BMI of 45 as well as hypertension. He tolerated CPAP use poorly due to mask discomfort and abandoned its use shortly after starting. He subsequently lost 50 lbs with decrease in his severity of symptoms. He continues to experience nocturnal arousals with nocturia, snore arousals and mild daytime fatigue. Loud snoring and apneic episodes continue to be observed by his wife. His Epworth sleepiness scale score was elevated at 13/24. He has no history of nodding off at stoplights, motor vehicle accidents related to loss of vigilance, or daytime or nocturnal palpitations. He has no history of myocardial infarction, stroke, or thyroid disorders.

Full overnight polysomnography studies were performed. Initial baseline study showed severe OSA with elevated apnea hypopnea index of 68/hour (normal <5/hr) and maximal desaturation of 86%. CPAP was initiated during the second half of night with persistent obstructions and development of complex apnea. EKG showed the presence of frequent PVC's and second degree AV block, both type I and II. Arrhythmias were noted during all stages of sleep, REM and non-REM. Second night polysomnography study was performed 2 nights later for BiPAP titration. BiPAP at 19/15 cmH2O, which was the maximum pressure tolerable to patient, in combination with a lateral decubitus sleeping position reduced airway obstruction, however, snore arousals (indicating mild, residual disease) persisted. The patient's oxygenation was maintained above 94% through the night. On EKG, second degree AV block and complete heart block with ventricular asystole up to 9 seconds were noted primarily during REM sleep.

Discussion

Cardiac rhythm is controlled by the sympathetic and parasympathetic system output during sleep. The autonomic nervous system in turn is affected by circadian rhythm and sleep states. Parasympathetic system output follows circadian cycle with higher output at night, peaking between 2-5 am and lower during daytime. Sympathetic system output is modulated by sleep stages: high output during wake, low output in NREM sleep and variable output during REM sleep. Parasympathetic tone predominates at night since NREM sleep occupies 80% of total sleep time. Thus bradycardias and conduction delays commonly occur during sleep[3].
From Adlakha and Shephard's summary of cardiac arrhythmias in normal sleep, nocturnal arrhythmias vary according to age and sex in young adults[4].

	Age 23-27, men	Age 22-28, women	Age 60-85, normal
Sinus pauses (>1.5 seconds)	68%	36%	2%
Nocturnal Sinus Bradycardia (HR<40 bpm)	24%	8%	2%
1st degree AVB	8%	12%	
2nd degree AVB	6%	4%	1%

As an example of autonomic system impact on nocturnal cardiac rhythm, REM sleep-related bradyarrhythmia syndrome was proposed by Janssen and colleagues in 2007. Sinus arrests with duration ranging from 7.0-15.0 seconds were observed only during phasic REM sleep in otherwise healthy young individuals with no medical conditions including sleep apnea syndrome. Most of them had daytime symptoms of chest pain, dizziness, malaise or syncope during physical exertion. These sinus pauses are felt to be secondary to abnormal, exaggerated parasympathetic output during phasic REM sleep when the autonomic system is least stable. All of the patients were treated with pace-maker placement[3].

In the classic study by Guilleminault et al who looked at 400 patients with OSA, 48% had significant nocturnal arrhythmia with 18% bradyarrhythmia, 11% sinus arrest, and 8% AVB[5]. From Japan, a more recent study by Abe and colleagues included 1350 patients with OSA diagnosed by PSG testing. Significant increase in incidence of sinus bradycardias (12.5% with OSA vs. 2.3% normal, $p=0.036$), sinus pause (8.7% with OSA vs. 2.3% normal, $p<0.001$) was noted[6]. Sleep Heart Health Study reported increase in incidence of PVC and NSVT, but not sinus pauses, in patients with OSA[7]. Roche et al noted increase in prevalence of nocturnal paroxysmal asystole in patients with OSA as well as increase in prevalence of sinus bradycardias and pauses in association with increase in severity of OSA as measured by AHI and oxygen desaturation[8].

In patients with obstructive sleep apnea, repetitive pharyngeal collapse, resultant hypoxemia and arousals cause disturbances in autonomic system output. Arousals from NREM sleep to wake can cause surges in sympathetic output with tachyarrhythmia as well as rise in blood pressure. Prolonged apnea and hypoxemia is postulated to cause reflex increase in cardiac vagal tone, slowing cardiac conduction[3]. Thus either tachyarrhythmia or bradyarrhythmia may occur, depending on predominant autonomic system output. Becker et al. reported oxygen desaturation to 72% was a precondition to heartblock[9]. Koehler and colleagues did not find a threshold SaO2 below which conduction heartblock occurred with overall 56% of bradyarrhythmias occurring below saturation of 72%. Interestingly, the same study data also showed 87% of sinus arrest occurred below oxygen saturation of 72%[2].

The combination of apnea and hypoxemia is required to produce significant bradycardia[9,10]. This physiologic response is seen not only during sleep but also in the wakefulness state. The deceleration in heart rate can be seen in normal individuals with hypoxemia during breath holding. The combined effect of hypoxemia and cessation of breathing results in bradycardia, which is mediated by the autonomic nervous system. Carotid body stimulation by hypoxemia without lung inflation results in a high degree of vagal tone and eventual bradycardia[9,10]. Conversely, normal individuals who experience hypoxemia during sleep demonstrate acceleration in their heart rate as long as hypopnoea is present[9,10]. Hypoxemia is also required to produce bradycardia when there is diminution of respiratory movement. In individuals with short apneic episodes without hypoxemia or in individuals with prolonged apnea but no hypoxemia due to breathing enriched oxygen,

bradycardia is not observed[9,10]. When administering supplemental oxygen during sleep in patients with apnea, apneic episodes may prolong in duration but bradycardia usually improves[9,10].

Treatment

Positive airway pressure (PAP) therapy has been shown to be highly effective in abolition and reduction of bradyarrhythmias. In the Abe study, sinus bradycardia ($p<0.001$) and sinus pauses ($P=0.004$) were reduced by CPAP therapy. No pacemakers were needed for treatment of bradyarrhythmia after PAP therapy[6]. In the Becker study, 17 patients with OSA without established cardiac disease or conduction disorder were started on CPAP therapy. Sixteen patients had resolution of bradyarrhythmia[9]. Koehler's study showed improvement and resolution of bradyarrhythmia in 12/16 patients with 4 patients requiring pacemaker placement. Of the 4 requiring pacer, 1 was non-compliant with PAP therapy and 3 had persistent sinus pauses >5 seconds despite effective PAP treatment[2]. Harbison reported 6/6 patients with sinus pause/AV block had resolution of bradyarrhythmia with PAP treatment alone[11]. Thus in patients with bradyarrhythmias who are at risk for OSA, overnight polysmonography should be performed prior to pacemaker implantation, especially in younger individuals without underlying cardiac disease. Permanent pacemakers should be considered if significant bradyarrhythmia or pauses persist after adequate treatment trial with PAP therapy.

Conclusion

Our patient has underlying cardiac conduction disorder with 1st degree AVB which worsens during sleep to high grade complete block without ventricular escape rhythm. Although strong data document resolution or improvement of heart block with correction of airway obstruction with PAP therapy alone, our patient did not fit in to the same category as most of the study patients who responded to PAP therapy, placing him at increased risk for cardiac arrest. The decision was made to place a pacemaker for treatment of his high grade AV block with ventricular asystole. After pacer placement, the patient did not follow up as scheduled and subsequently was lost to follow up.

REFERENCES

1. **Guilleminault C, Pool P, Motta J, Gillis AM**. Sinus arrest during REM sleep in young adults. *N Engl J Med*. 1984 Oct 18;311(16):1006-10. PubMed PMID: 6384778.
2. **Koehler U, Fus E, Grimm W, Pankow W, Schäfer H, Stammnitz A, Peter JH**. Heart block in patients with obstructive sleep apnoea: pathogenetic factors and effects of treatment. *Eur Respir J*. 1998 Feb;11(2):434-9. PubMed PMID: 9551750.
3. **Holty JE, Guilleminault C**. REM-related bradyarrhythmia syndrome. *Sleep Med Rev*. 2011 Jun;15(3):143-51. Epub 2010 Nov 4. Review. PubMed PMID: 21055981.
4. **Adlakha A, Shepard JW Jr**. Cardiac arrhythmias during normal sleep and in obstructive sleep apnea syndrome. *Sleep Med Rev*. 1998 Feb;2(1):45-60. PubMed PMID: 15310512.
5. **Guilleminault C, Connolly SJ, Winkle RA**. Cardiac arrhythmia and conduction disturbances during sleep in 400 patients with sleep apnea syndrome. *Am J Cardiol*. 1983 Sep 1;52(5):490-4. PubMed PMID: 6193700.
6. **Abe H, Takahashi M, Yaegashi H, Eda S, Tsunemoto H, Kamikozawa M, Koyama J, Yamazaki K, Ikeda U**. Efficacy of continuous positive airway pressure on arrhythmias in obstructive sleep apnea patients. *Heart Vessels*. 2010 Jan;25(1):63-9. Epub 2010 Jan 21. PubMed PMID: 20091401.
7. **Mehra R, Benjamin EJ, Shahar E, Gottlieb DJ, Nawabit R, Kirchner HL, Sahadevan J, Redline S;** Sleep Heart Health Study. Association of nocturnal arrhythmias with sleep-disordered breathing: The Sleep Heart Health Study. *Am J Respir Crit Care Med*. 2006 Apr 15;173(8):910-6. Epub 2006 Jan 19. PubMed PMID: 16424443; PubMed Central PMCID: PMC2662909.
8. **Roche F, Xuong AN, Court-Fortune I, Costes F, Pichot V, Duverney D, Vergnon JM, Gaspoz JM, Barthélémy JC**. Relationship among the severity of sleep apnea syndrome, cardiac arrhythmias, and autonomic imbalance. *Pacing Clin Electrophysiol*. 2003 Mar;26(3):669-77. PubMed PMID: 12698666.
9. **Zwillich C, Devlin T, White D, Douglas N, Weil J, Martin R**. Bradycardia during sleep apnea. Characteristics and mechanism. *J Clin Invest*. 1982 Jun;69(6):1286-92. PubMed PMID: 7085875; PubMed Central PMCID: PMC370201.
10. **Zwillich CW**. Sleep apnoea and autonomic function. *Thorax*. 1998 Oct;53 Suppl 3:S20-4. Review. PubMed PMID: 10193356; PubMed Central PMCID: PMC1765913.
11. **Harbison J, O'Reilly P, McNicholas WT**. Cardiac rhythm disturbances in the obstructive sleep apnea syndrome: effects of nasal continuous positive airway pressure therapy. *Chest*. 2000 Sep;118(3):591-5. PubMed PMID: 10988177.

Submitted on June 19, 2012