Sleep apnea and severe bradyarrhythmia – an alternative treatment option: a case report

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Abstract

Introduction: Sinus arrest, atrio-ventricular block, supraventricular, and ventricular arrhythmias have been reported in patients with sleep apnea syndrome. The arrhythmias usually occur during sleep and contribute to the cardiovascular morbidity and mortality, and the treatment of sleep apnea usually results in the resolution of the brady-arrhythmias. Weight loss, continuous positive airway pressure (CPAP), oral appliances, and upper airway surgery are the recommended treatments, however, compliance and efficacy are issues.

Case presentation: A 58-year-old Arab man presented with recurrent presyncope. He was subsequently diagnosed with sleep apnea associated with frequent and significant sinus pauses. He presented a treatment challenge because he refused continuous positive airway pressure and pacemaker, however, he was successfully treated with theophylline.

Conclusion: Frequent and significant sinus pause associated with sleep apnea was successfully treated with theophylline in our patient when the standard treatment of care was refused.

Keywords: Bradycardia, Sinus arrest, Sleep apnea, Theophylline
demonstrated both central and OSA: Epworth score 7, sleep latency of 17 minutes, Apnea–Hypopnea Index (AHI) of 98/hour, arousal index of 49/hour and lowest oxygen saturation at 78% on room air (Table 1).

Overnight CPAP was started and the telemetry showed sinus bradycardia with a minimum heart rate of 30 beats per minute with infrequent pauses of less than 3 seconds. However, he refused to continue to use the CPAP.
| Symptoms | Weight (kg) | 24-hour Holter monitor | Polysomnography | Theophylline level $^1$ |
|----------|------------|------------------------|----------------|-------------------------|
|          | Max sinus pause (seconds) | Total number of sinus pauses | Min/max/Average HR (beats/minute) | |
| Prior to presentation (2008 until 2011) | Presyncope twice a year for 3 years | 115 | – | – | Not on treatment | – |
| At presentation (September 2011) | Presyncope once a month for 3 months | 119 | 22 | 71 | 49/119/85 | Not on treatment | Epworth score 7 |
| | | | | | | Sleep latency of 17 minutes | |
| | | | | | | AHI of 98/hour | |
| | | | | | | Arousal index of 49/hour | |
| | | | | | | Lowest oxygen saturation at 78% on room air | |
| 5-month follow up | None | 120 | 6 | 18 | 61/125/93 | 11.11 | Not done |
| 6-month follow up | None | 122 | 5 | 5 | 68/124/94 | 13.0 | Not done |
| 7-month follow up | None | 126 | None | None | 71/128/92 | 14.4 | Epworth score of 11 |
| | | | | | | Sleep latency of 28 minutes | |
| | | | | | | AHI of 96/hour | |
| | | | | | | Arousal index of 43/hour | |
| | | | | | | Lowest oxygen saturation at 78% on room air | |
| 14-month follow up | None | 123 | None | None | 69/123/90 | 11.4 | Not done |
| 19-month follow up | None | 129 | 2.9 | 3 | 67/115/82 | 14.6 | Epworth score of 11 |
| | | | | | | Sleep latency of 48.5 minutes | |
| | | | | | | AHI of 83/hour | |
| | | | | | | Arousal index of 42.8/hour | |
| | | | | | | Lowest oxygen saturation at 75% on room air | |
| 29-month follow up | None | 130 | None | None | 65/110/81 | Not done | Not done |

$^1$AHI = Apnea-Hypopnea Index; HR = Heart rate; Max = Maximum; Min = Minimum.

$^*$Therapeutic level is between 10 and 20mcg/mL in plasma [4].
upon discharge. In addition, he was offered a pacemaker and he refused. A trial of theophylline 200mg twice daily was initiated and he was discharged from our hospital and encouraged to initiate a weight reduction program.

At follow up, he had no further episode of presyncope with infrequent short or no pauses at therapeutic theophylline levels (Table 1). A follow-up sleep study revealed improvement in the central element of his sleep apnea, however, his AHI did not significantly improve; such results are expected with theophylline therapy (Table 1).

Discussion
Sleep apnea syndrome has been associated with cardiovascular complications including hypertension [1], heart failure [2] and cardiac arrhythmia [3]. Observational studies have shown that treating sleep apnea syndrome can decrease blood pressure [1], reduce cardiac arrhythmia [3] and decrease cardiovascular mortality [4]. Noninvasive positive pressure ventilation effectively decreases the incidence of sleep apnea-associated arrhythmia [3]; however, not all patients can tolerate it and compliance is an issue [5]. We report the case of a patient who presented with presyncope most likely secondary to sleep apnea-induced brady-arrhythmia. He was started on beta-blockers after his CABG, which could have made his brady-arrhythmia worse and contributed to increasing presyncope. However, while he was an in-patient and off his metoprolol he continued to have significant sinus pause. He did not tolerate CPAP and refused a pacemaker so, as a last resort, theophylline treatment was started and he reported complete resolution of his symptoms. A Holter monitor documented a decrease in both the frequency and duration of sinus pauses. We initiated theophylline based on its effectiveness in treating brady-arrhythmia in the setting of post-cardiac transplant [6] and spinal cord injury [7]. The mechanism of brady-arrhythmia in sleep apnea syndrome is hypothesized to be due to the activation of the diving reflex by hypoxemia and apnea, with reflex activation of the cardiac vagal nerve. This induces severe nocturnal bradycardias, especially during rapid eye movement sleep [8]. Theophylline is a nonselective phosphodiesterase inhibitor that also competitively blocks adenosine receptors resulting in central nervous system and cardiovascular stimulation. Theophylline also increases the respiratory drive and it has been used in patients with central sleep apnea due to left ventricular dysfunction before CPAP and is still recommended in patients who cannot tolerate CPAP [9]. For OSA, theophylline has been shown to mildly reduce obstructive events but is associated with sleep disruption and therefore it is not recommended [9]. The limitations and side effects of theophylline result from its narrow therapeutic index, traditionally between 10 and 20mcg/mL [4] in plasma. Theophylline is metabolized in the liver through the cytochrome P450 system and consequently is implicated in several drug interactions with commonly prescribed drugs, which may increase serum concentrations of theophylline [10].

Conclusions
We report a case of treating sleep apnea-induced bradyarrhythmia with theophylline when standard treatment of care was refused. Further studies are needed to determine the safety and efficacy of theophylline for treating sleep apnea-induced bradyarrhythmias to ensure the benefits outweigh the risks.

Consent
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Abbreviations
AHI: Apnea–Hypopnea Index; CABG: Coronary artery bypass surgery; CPAP: Continuous positive airway pressure; OSA: Obstructive sleep apnea.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
AD was the major contributor and provided care to the patient. AD also conceived the case report, collected information and wrote the manuscript. SO, SMAF, AAAA and AL contributed in the preparation, editing and revision of the manuscript. WA assisted with data collection. FA contributed in the preparation, editing and revision of the manuscript. All authors have read and approved the final manuscript.

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