Positive Airway Pressure Therapy for Hyperventilatory Central Sleep Apnea

Idiopathic, Heart Failure, Cerebrovascular Disease, and High Altitude

Shahrokh Javaheri, MD[a,b,c,*], Lee K. Brown, MD[d,e]

KEYWORDS

• Central sleep apnea • Hunter-Cheyne-Stokes breathing • Heart failure • High altitude
• Cerebrovascular disease • Adaptive servoventilation • Bilevel positive airway pressure
• Continuous positive airway pressure

KEY POINTS

- Hyperventilatory central sleep apnea (CSA) and Hunter-Cheyne-Stokes breathing (HCSB) are caused by a temporary failure in the pontomedullary pacemaker generating breathing rhythm, caused by the existence of an apneic threshold for arterial P_{CO_2} confined primarily to non–rapid eye movement sleep.
- Common causes of hyperventilatory CSA/HCSB in adults are congestive heart failure and stroke.
- Diagnosis and treatment of hyperventilatory CSA/HCSB may improve quality of life, and, when associated with heart failure or cerebrovascular disease, reduce morbidity and perhaps mortality.
- Treatment choices for hyperventilatory CSA/HCSB may include exogenous oxygen administration; continuous positive airway pressure; bilevel positive airway pressure (usually with a backup rate); and, more recently, adaptive servoventilation. Another treatment, phrenic nerve stimulation, is currently under investigation but is beyond of the scope of this article.

Financial Disclosures: S. Javaheri has no relevant conflicts of interest. L.K. Brown has participated in advisory panels for Philips Respironics, and is an insurance claims reviewer for Considine and Associates, Inc. He coedits the sleep and respiratory neurobiology section of *Current Opinion in Pulmonary Medicine*, wrote on continuous positive airway pressure treatment of obstructive sleep apnea in UpToDate and on obstructive sleep apnea in Clinical Decision Support: Pulmonary Medicine and Sleep Disorders. He is currently coediting an issue of *Sleep Medicine Clinics* on positive airway pressure therapy. He serves on the Polysomnography Practice Advisory Committee of the New Mexico Medical Board and chairs the New Mexico Respiratory Care Advisory Board.

[a] Sleep Laboratory, Bethesda North Hospital, 10535 Montgomery Road, Suite 200, Cincinnati, OH 45242, USA; [b] The University of Cincinnati, Cincinnati, OH, USA; [c] The Ohio University Medical School, Columbus, OH, USA; [d] Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Internal Medicine, University of New Mexico School of Medicine, University of New Mexico Sleep Disorders Center, 1101 Medical Arts Avenue Northeast, Building #2, Albuquerque, NM 87102, USA; [e] Department of Electrical and Computer Engineering, University of New Mexico School of Engineering, University of New Mexico Sleep Disorders Center, 1101 Medical Arts Avenue Northeast, Building #2, Albuquerque, NM 87102, USA
* Corresponding author. Bethesda North Hospital, 10535 Montgomery Road, Suite 200, Cincinnati, OH 45242.
E-mail address: shahrokhjavaheri@icloud.com

Sleep Med Clin ■ (2017) ■–■
http://dx.doi.org/10.1016/j.jsmc.2017.07.006

INTRODUCTION

Central sleep apnea (CSA) and its variant Hunter-Cheyne-Stokes breathing (HCSB) result when respiratory rhythmogenesis temporarily fails to initiate inspiration or, in the case of HCSB, rhythmogenesis is aberrant in that there is a waning and waxing of inspiratory effort separated by a (usually brief) period of central apnea. This discordant breathing could be the result of varied medical conditions, although even in normal individuals a few central apneas may be observed during polysomnography in the absence of any pathologic condition (physiologic central apnea), particularly on the resumption of sleep; after an arousal or awakening.[1] One important group of disorders causing CSA/HCSB is characterized by the presence of diurnal hyperventilation, or low normal values for arterial P_{CO_2}, and positive airway pressure (PAP) treatment of these disorders is the focus of this article. A comprehensive list of causes of CSA/HCSB, the underlying mechanisms, and other therapeutic options are beyond the scope of this article and have been covered previously.[1–5]

IDIOPATHIC CENTRAL SLEEP APNEA

This is a rare polysomnographic finding in individuals otherwise thought to be free of comorbidities. There are multiple causes of CSA in otherwise asymptomatic individuals and some may have unrecognized disorders that might be the cause of the so-called idiopathic CSA. Examples include asymptomatic carotid artery stenosis and left ventricular systolic dysfunction. These potential causes of CSA, and others, were not systematically investigated in most reports of idiopathic CSA. Therefore, before any specific therapy for CSA with PAP devices or with pharmacologic therapy is contemplated, appropriate testing for a potential cause should be undertaken and, if found, appropriately treated. For example, surgical treatment of carotid artery stenosis may be all that is needed to eliminate what was considered idiopathic CSA. The HCSB variant of CSA has occasionally been reported to be idiopathic, but it is likely that one of the underlying causes mentioned earlier could have been present but not identified.

There are no systematic studies on PAP therapy in idiopathic CSA. If no cause is found, the authors recommend a trial of continuous PAP (CPAP) as the first treatment modality. If ineffective, we recommend pharmacologic therapy. Bilevel PAP devices in spontaneous mode (bilevel PAP-S) should not be used to treat CSA whatever the underlying disorder, because these devices could result in worsening of central apnea by increasing ventilation, reducing the prevailing arterial P_{CO_2} below the apneic threshold for P_{CO_2}, and creating a vicious cycle of worsening CSA.[6] This phenomenon was reported in a patient with idiopathic CSA treated with bilevel PAP-S.[7] If bilevel PAP is used, a backup rate (timed mode) should always be used (bilevel PAP-S/T). However, the new generation of adaptive servoventilators (ASVs)[8] should in theory be most effective and comfortable but no data exist specifically for this modality in patients with truly idiopathic CSA.

HEART FAILURE

Sleep disordered breathing (SDB), both obstructive and CSA/HCSB, commonly occurs in individuals with left ventricular dysfunction, which may be both systolic and diastolic. Most commonly CSA/HCSB occurs in patients with heart failure with reduced ejection fraction (HFrEF) and those with heart failure with preserved ejection fraction (HFpEF). However, CSA/HCSB caused by left ventricular dysfunction often manifests the unique pattern of periodic breathing described as HCSB.[2] The pattern of HCSB is characterized by central apneas that occur between decrescendo-crescendo ventilatory efforts. Importantly, as in the case of obstructive sleep apnea (OSA), central apneas also result in hypoxia alternating with reoxygenation, changes in arterial P_{CO_2}, and recurrent arousals. Furthermore, central apneas are associated with excessive negative swings in intrathoracic pressure during the hyperventilatory phase of the cycle, also bearing similarity to those that occur in OSA. These adverse consequences of CSA/HCSB are generally of a lesser degree compared with those accompanying OSA. However, multiple studies have shown that, compared with patients with heart failure without central sleep apnea, those with CSA do have adverse consequences, most likely caused by the creation of a hyperadrenergic state. This hyperadrenergic state has been shown using a variety of techniques, including muscle sympathetic nerve activity, plasma and urinary norepinephrine measurements, and heart rate variability. In addition, multiple randomized clinical trials, mostly incorporating small numbers of patients, have shown that attenuation of CSA/HCSB by PAP therapy, including CPAP and ASV, as well as by nocturnal oxygen administration, attenuates the hyperadrenergic state imposed by central SDB.[3] This article reviews the studies with CPAP and adaptive servoventilation; the authors do not recommend the use of bilevel PAP-S for CSA, as noted earlier. Virtually all studies using a PAP device, specifically CPAP