Nocturnal Oxygen Therapy in the Management of Mild Cheyne-Stokes Respiration in Stable Congestive Heart Failure

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Congestive Heart Failure

Congestive heart failure (CHF) is a global term for the physiological state in which cardiac output is insufficient for the body's needs. Nearly six million Americans currently suffer from heart failure and there are about 670,000 new cases of heart failure diagnosed each year. Heart failure is the most common reason for hospitalization in the elderly and carries an annual cost of approximately $39 billion. In the Medicare fee-for-service program, heart failure is also the most common reason for re-hospitalization within 30 days of discharge. As the population ages, the incidence of congestive heart failure is rising dramatically; it is estimated that CHF affects about 10 per 1,000 people after age 65.

Cheyne-Stokes Respiration & CHF

Cheyne-Stokes respiration (CSR) is an abnormal respiratory pattern associated with CHF. It is characterized by a crescendo-decrescendo alteration in tidal volume that is separated by periods of apnea or hypopnea. Approximately 45% of patients with CHF and a left ventricular ejection fraction (LVEF) of <40% demonstrate some degree of CSR. Patients with CSR generally experience sleep disruption, arousals and recurrent episodes of nocturnal hypoxemia that often result in marked daytime impairment. The presence of recurrent hypoxia triggers an increase in sympathetic tone through the cyclic release of catecholamines.

The crescendo-decrescendo breathing alterations in CSR compensate for the changing serum partial pressures of oxygen and carbon dioxide that result from sluggish circulation along with timing delays between the pulmonary artery and central and peripheral chemoreceptors. Enhanced sensitivity of peripheral chemoreceptors results in rapid compensatory changes in respiratory drive in response to small changes in serum oxygen and carbon-dioxide (Figure 1). Although the carbon-dioxide level rises and falls in relation to changes in breathing depth and frequency, the mean CO$_2$ level remains below normal. Hypoxia clearly plays a central role in the initiation of CSR as evidenced by the attenuation of periodic breathing following administration of supplemental oxygen. Gottlieb and colleagues studied hemodynamic stress associated with heart failure and concluded that prevention of hypoxia is especially important in this at risk population of patients.
Figure 1. Cheyne-Stokes breathing results from a combination of hypoxia, chemoreceptor up-regulation and sluggish circulation. The crescendo-decrescendo breathing pattern is a result of the circulatory delay. Apnea results from the hypocarbia that occurs during the hyperventilatory phase of breathing. Correction of the hypoxia removes a significant driver of CHR and results in significant reductions in the frequency and duration of events.

**Diagnosing Nocturnal Hypoxemia in CHF**

The diagnosis of mild CSR and associated nocturnal hypoxemia can sometimes prove elusive. Since symptoms are only present during sleep, the pathology may not present during routine physical examination. Patient complaints that may be suggestive of nocturnal hypoxemia may be easily confused with other co-morbid symptoms and therefore, history and physical alone may be inadequate. There is strong evidence that nocturnal oxygen desaturation may be directly correlated to sleep disturbance and CSR in stable CHF patients with treated heart failure and no daytime evidence of hypoxemia.7

Diagnosing nocturnal hypoxemia in known, stable CHF is relatively simple, inexpensive and can be easily performed in the patient’s home. Although complete polysomnography will identify myriad sleep disturbances, the use of a single, overnight pulse oximetry study can serve as an adequate screening test for identifying mild CSR with associated hypoxemia in patients with CHF.8 There is no single definition of clinically significant nocturnal hypoxemia, as severity of desaturation and degree of impairment may be considered patient specific. However, the Medicare coverage policy for nocturnal home oxygen therapy9 provides a reasonable definition:

“An arterial PO2 at or below 55 mm Hg, or an arterial oxygen saturation at or below 88 percent, for at least 5 [cumulative] minutes taken during sleep for a patient who demonstrates an arterial PO2 at or above 56 mm Hg or an arterial oxygen saturation at or above 89 percent while awake.”
**Common Treatment Options**

Oxygen therapy and continuous positive airway pressure (CPAP) are the common treatment options for stable CHF patients with documented sleep disturbances, CSR and hypoxemia. Consideration should always be given to simple and effective interventions such as low-flow nasal oxygen. Many studies have demonstrated the clinical efficacy of low-flow nasal oxygen therapy as an effective treatment for CSR in patients with stable CHF, including studies that compare nocturnal oxygen therapy (NOT) to CPAP.

The beneficial effects of supplemental oxygen on CSR were first described by Pembrey in 1907. He demonstrated that low-flow nasal oxygen reduced or eliminated CSR in patients with CHF. Sasayama and colleagues, in a randomized controlled trial studied the effects of nocturnal oxygen therapy on stable CHF patients with CSR and nocturnal hypoxemia and concluded NOT improves sleep disorder breathing (SDB), left ventricular function and QOL. Shigemitsu, et al. studied the use of NOT in a population of CHF patients diagnosed with central SDB (apnea-hypopnea index \( \geq 20 \)) and hypoxemia. They concluded NOT significantly decreased apnea-hypopnea index (AHI) and suggest that NOT may prevent the progression of CHF in patients with SDB and hypoxemia. Javaheri and colleagues studied a group of stable CHF patients with polysomnographic evidence of periodic breathing and hypoxemia to determine the clinical effects of nasal NOT and concluded that in patients with stable heart failure, nasal NOT significantly improves periodic breathing and virtually eliminates clinically significant oxyhemoglobin desaturation. In a similar study Staniforth and colleagues reported similar outcomes for breathing and arterial saturation in addition to a reduction in urinary catecholamine levels. In a prospective, randomized controlled trial, Krachman and associates compared NOT with CPAP in patients with CHF and CSR and concluded NOT and nCPAP are equally effective in decreasing the AHI in CHF patients with CSR.

PAP therapies, in the forms of CPAP, bi-level and most recently adaptive servo-ventilation (ASV) have been used to treat mild to severe CSR. Studies focused on the effectiveness of these therapies have met with mixed results, although in advanced CSR there is a clear benefit, particularly for treatment with ASV. These mixed outcomes may, at least in part, be attributed to the targeting of therapy to treat symptoms (irregular breathing) rather than the cause (poor oxygenation) of those symptoms.

In a controlled trial, Bradley and colleagues randomized 258 CHF patients with central apnea to receive CPAP or no CPAP and followed them for two years. They concluded that CPAP therapy improved central apnea, nocturnal desaturation and left ventricular ejection fraction. CPAP also lowered norepinephrine levels. However, there was no difference in
mortality in the CPAP and non-CPAP groups. Buckle\textsuperscript{17} and Davies\textsuperscript{18} compared CPAP to room air and sham CPAP (respectively) in controlled randomized trials. Both studies found no difference in AHI, and Buckle found no improvement in nocturnal saturation or sleep efficiency.

Krachman and colleagues\textsuperscript{19} compared oxygen therapy with nasal CPAP on CSR in patients with CHF. Polysomnography was performed on 25 stable CHF patients with 14 identified as having CSR. Those patients identified as having CSR were randomized to a night of oxygen therapy (2 L/min by nasal cannula) and another night on nasal CPAP therapy ($9 \pm 0.3$ cm H\textsubscript{2}O). Nine of the 14 patients completed the study. When compared with baseline measurements, both oxygen and nasal CPAP significantly decreased the AHI (from $44 \pm 9$ to $18 \pm 5$ and $15 \pm 8$ events per hour, respectively; $p < 0.05$), with no significant difference between the two modalities. The mean oxygen saturation increased significantly and to a similar extent with both oxygen and CPAP therapies (from $93 \pm 0.7\%$ to $96 \pm 0.8\%$ and $95 \pm 0.7\%$, respectively; $p < 0.05$). Total sleep time and sleep efficiency decreased only with nasal CPAP therapy (from $324 \pm 20$ to $257 \pm 14$ min, and from $82 \pm 3$ to $72 \pm 2\%$, respectively; $p < 0.05$).

While the data for CPAP in CSR is mixed, there is growing evidence supporting ASV, a form of noninvasive ventilation in the treatment of moderate – severe CSR. A number of recent papers have identified the effectiveness of ASV over CPAP or oxygen therapy alone in treating more severe SDB and CSR in CHF.\textsuperscript{20,21,22}

**Compliance to Therapy**

The best, most effective therapy is of no value if patients fail to adhere to it. Successful, effective treatment of CSR is an issue of practical comfort and convenience for the patient. Buckle\textsuperscript{16} found that most of the CHF/CSR patients treated with CPAP did not tolerate the therapy and they would not have accepted long-term therapy even if it had shown some benefit to them. Indeed, much attention has been given in the sleep literature to the issue of compliance, with data suggesting about 50\% of CPAP users are non-compliant. Although these studies are primarily directed at the treatment of obstructive sleep apnea, they highlight issues such as air leaks, nasal and sinus discomfort, pressure sores and others which drive patients away from adhering to therapy. CHF patients with CSR have the potential to encounter the same obstacles. Low flow oxygen therapy is much more familiar and less intrusive than PAP, particularly when it is administered as a nocturnal only therapy. It is relatively easy for the patient to use and is not associated with the numerous side effects and patient complaints recognized in PAP therapies.
**Step wise approach to therapy**

Like many treatment protocols, an evidenced based approach that starts with the most practical, clinically appropriate, low intensity therapy is ideal for most patients. In a comprehensive review of the treatment of sleep disorders in heart failure, Arzt evaluated eleven studies that reviewed either oxygen therapy or CPAP treatment or compared both and concluded that reduction in AHI was similar in the two therapies, but greater improvement in oxygenation was achieved when low-flow oxygen was the primary treatment.23  Similarly, Naughton concluded that CPAP improves cardiac function but fails to reduce the underlying hypoxemia that triggers CSR.24  A logical approach to treating nocturnal hypoxemia and CSR in stable CHF is to start with low flow (1-4 liters/min) nasal oxygen therapy. CPAP or ASV can be added to the treatment regimen as the frequency and severity of symptoms progress.

**Table 1. Step-wise treatment of Cheyne - Stokes respiration**

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<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<tbody>
<tr>
<td>Low-flow oxygen</td>
<td>X</td>
<td>XX</td>
<td>XX</td>
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<tr>
<td>Adaptive Servo Ventilation</td>
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<td>XX</td>
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**Summary**

Stable CHF patients with no daytime symptoms may have undiagnosed CSR with associated nocturnal hypoxemia. The diagnosis and treatment process is relatively simple and can be employed on an outpatient basis in the patient’s home via overnight pulse oximetry. Patient’s with stable CHF demonstrating nocturnal desaturation may be ideal candidates for early treatment with low flow nasal oxygen therapy. As the disease progresses, additional and more comprehensive therapies, such as ASV may be integrated into the treatment plan.

**References**

2. Ibid
References Cont.


8. Ibid


