Cardiac Rhythm Disturbances in the Obstructive Sleep Apnea Syndrome*

Effects of Nasal Continuous Positive Airway Pressure Therapy

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Study objectives: A high incidence of nocturnal cardiac rhythm disturbances among patients with obstructive sleep apnea (OSA) syndrome has been described in some reports, but not in others. We wished to examine the prevalence of significant cardiac rhythm disturbance in patients with established moderate to severe OSA syndrome and, in particular, to assess the impact of nasal continuous positive airway pressure (nCPAP) therapy.

Design and setting: A prospective study of consecutive eligible patients in a dedicated sleep disorders unit of a university teaching hospital.

Measurements and results: Holter monitoring was performed for 18 h in 45 patients with previously diagnosed OSA syndrome (mean [SD] apnea/hypopnea frequency [AHI] of 50 [23]/h) and repeated within 2 to 3 days after institution of nCPAP therapy. Investigators were blinded to the patients’ treatments during data analysis. Thirty-five patients were found to have some cardiac rhythm disturbance, but only 8 had pathologically significant disturbances (ventricular tachycardia or fibrillation, complex ventricular ectopy, new-onset supraventricular tachycardia other than sinus tachycardia, pauses of > 2 s, and second- or third-degree heart block). Significant rhythm disturbances occurred only during the nighttime, and there was a significant correlation between OSA severity and the severity of rhythm disturbance (p = 0.04, r = 0.301). No significant correlation was found between OSA severity and any other anthropometric parameter measured. nCPAP therapy resulted in abolition of rhythm disturbance in seven of these eight patients; the eighth patient was found to have coexisting severe aortic valve disease requiring valve replacement.

Conclusion: The data indicate that OSA syndrome predisposes to clinically significant cardiac rhythm disturbances that can be successfully controlled by nCPAP therapy.

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Key words: arrhythmia; CPAP; sleep apnea

Abbreviations: AHI = apnea/hypopnea frequency; BMI = body mass index; nCPAP = nasal continuous positive airway pressure; OSA = obstructive sleep apnea; OSAS = obstructive sleep apnea syndrome

Nocturnal cardiac rhythm disturbances have been reported to be common in patients with obstructive sleep apnea (OSA) syndrome (OSAS) but also in control subjects.1–5 Indeed, rhythm disturbances such as bradycardia with or without alternating tachycardia6–9 have been regarded as a typical feature of OSAS.10 However, the incidence of pathologically significant rhythm disturbances, such as heart block, supraventricular tachycardia, and ventricular arrhythmia, is less clear-cut.4,11–14 The incidence of pathologically significant rhythm disturbances assumes particular clinical significance in view of the reported increase in cardiovascular morbidity and mortality among patients with OSAS,15–18 and the potential impact of nasal continuous positive airway pressure (nCPAP) therapy on these disturbances.15

Using an ambulatory ECG monitor before and after institution of nCPAP therapy, we prospectively examined the prevalence of cardiac rhythm disturbances in a group of consecutive patients with previously diagnosed OSAS. The principal study aim was to establish the frequency of pathologically significant cardiac rhythm disturbances in the group and, in particular, to determine the effect of nCPAP on these disturbances.

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Materials and Methods

The study included 45 consecutive patients (41 men, 4 women) with previously diagnosed moderate to severe OSAS (diagnosed by standard overnight polysomnography) who were being evaluated in the hospital for nCPAP therapy. Prior to institution of nCPAP, 18-h, four-lead, two-channel ambulatory ECG recordings were performed (from 6:00 PM to 12:00 AM the next morning) on each patient using a Holter monitor (Tracker 2 Holter Monitor; Reynolds Medical; Hertford, UK) with concurrent overnight oximetry using a digital oximeter (model 3700e; Ohmeda; Essex, UK). The ambulatory monitors were fitted to the patients by experienced staff. Each patient’s identity was kept anonymous by means of a seven-digit code number, and Holter tapes bore no evidence of the patients’ identities or date of study. nCPAP therapy was titrated on the following night using an nCPAP titrating device (Autoset nCPAP Titrating Device; ResMed; Sydney, Australia). All patients underwent repeat 18-h ECG and oximetry while in the hospital within 1 to 2 nights of instituting nCPAP therapy (ie, within 2 to 3 nights of the initial Holter studies).

ECG tapes were each interpreted at 60 times normal speed, on two separate occasions, by experienced medical staff who were trained in the interpretation of the recordings (J.A.H and P.O.R.), and who were blinded to the patients’ identities and treatment status but not to the underlying diagnosis of OSAS. The interpreting system used was a Reynolds Medical Pathfinder 4 (Reynolds Medical). All deviations from normal sinus rhythm were recorded. In addition to measures of OSAS severity, mean and lowest percentage of oxygen desaturation (taken from the initial diagnostic polysomnography records), each patient had height, weight, and body mass index (BMI) recorded. In addition, fasting blood glucose and lipids analyses were performed, and all patients by experienced staff. Each patient’s identity was kept anonymous by means of a seven-digit code number, and Holter tapes bore no evidence of the patients’ identities or date of study. The ambulatory monitors were fitted to the patients by experienced staff. Each patient’s identity was kept anonymous by means of a seven-digit code number, and Holter tapes bore no evidence of the patients’ identities or date of study.

For the purposes of the present study, rhythm disturbances considered pathologically significant included ventricular tachycardia or fibrillation, complex ventricular ectopy (including salvos of three beats or more, recurrent bigeminy, or polygemeny), new-onset supraventricular tachycardia other than sinus tachycardia, pauses of > 2 s, and second- or third-degree atrioventricular block. Second- or third-degree atrioventricular block was defined as intermittent or persistent loss of association between P waves and QRS complexes seen on the ECG. Other rhythm disturbances, recorded but not deemed significant, included isolated dropped beats, asymptomatic sinus bradycardia or tachycardia, and isolated atrial or ventricular premature systoles.

Statistical analysis was performed using a commercial statistics package (SPSS 9.0.0, SPSS; Chicago, IL). The hospital ethics committee approved the study, and informed consent was obtained from each patient.

Results

Anthropometric and clinical details are given in Table 1. The study population included a broad spectrum of OSAS severity, although most patients had severe disorders. The mean fasting cholesterol was just above the upper limit of normal for our laboratory (5.8 mmol/L), indicating a high incidence of hypercholesterolemia in the study population. Following tape analysis, the patients were classified into three groups: group 0, those with no rhythm disturbances; group 2, those with significant rhythm disturbances; and group 1, those with other rhythm disturbances based on the criteria given above.

Of the 45 patients who underwent ambulatory ECG monitoring prior to commencement of nCPAP therapy, 35 patients (78%) were noted to have some nocturnal rhythm disturbance. However, of these, only 8 patients (18%) demonstrated rhythm disturbances that were pathologically significant; details of these dysrhythmias before and after CPAP therapy are provided in Table 2. Table 2 does not include other rhythm disturbances, present in all of these patients, which were considered not pathologically significant, as described above. Recurring sinus pauses during sleep were the most common dysrhythmia (six patients), lasting 10 s. One patient also developed an episode of variable second-degree atrioventricular block lasting 4.5 min, and one patient developed two salvos of three ventricular ectopic beats. One patient developed intermittent ventricular bigeminy with sinus bradycardia for prolonged periods (≥ 20 min) during sleep; this patient had marked ventricular ectopy in the intervening periods and also suffered pauses of 3 s. All of these rhythm disturbances occurred between the hours of 11:00 PM and 7:00 AM, and no significant rhythm disturbances were noted in patients 1 to 7 outside of these hours. Significant rhythm disturbance persisted in only one patient after institution of nCPAP.

A Pearson correlation matrix analysis was performed with the statistical software package in which the grading of dysrhythmia (0, 1, or 2) was related to

<p>| Table 1—Anthropometric and Clinical Details of the Study Population (n = 45)* |</p>
<table>
<thead>
<tr>
<th>Variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>50 (13.1)</td>
</tr>
<tr>
<td>AHI, per h</td>
<td>50 (23.3)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>32.7 (6.0)</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>132 (14.8)</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>80 (16.7)</td>
</tr>
<tr>
<td>Fasting total cholesterol, mmol/L</td>
<td>5.9 (1.1)</td>
</tr>
<tr>
<td>Fasting serum glucose, mmol/L</td>
<td>5.7 (0.65)</td>
</tr>
<tr>
<td>Peak expiratory flow rate, % predicted</td>
<td>101 (20)</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td>97 (18)</td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>98 (16)</td>
</tr>
</tbody>
</table>

*Data are presented as mean (SD).
a range of anthropometric and other variables; namely, apnea/hypopnea frequency (AHI), mean oxygen saturation during sleep, age, BMI, systolic and diastolic BP levels, and fasting lipid and glucose levels. Only AHI levels showed a significant relationship with the presence of arrhythmias (p = 0.04; Table 3).

**Discussion**

The present findings indicate that cardiac rhythm disturbances are common during sleep among patients with OSAS, but they are largely abolished following the institution of nCPAP therapy. The exclusive nocturnal nature of the rhythm disturbances in these patients contrasts with the more common pattern of rhythm disturbances in patients with cardiac disease, where rhythm disturbances are less frequent during sleep than during wakefulness. An interesting finding of the present study is that severity of OSA was greater in patients with rhythm disturbances compared with those without (Table 3). This finding contrasts with other reports that have failed to show a relationship between the presence of rhythm disturbances and severity of OSA. Potential mechanisms for these rhythm disturbances in patients with OSAS include the recurrent episodes of hypoxemia and arousal that are typical features of apnea and which are also associated with increased sympathetic activity and heightened adrenergic response.

The clinical significance of the rhythm disturbances observed in the present study is unclear, particularly because the majority of the rhythm disturbances found in our subjects were relatively mild. There is only limited and inconclusive evidence in the literature linking dysrhythmias in OSAS patients with excess mortality rates, although many units treating patients with respiratory sleep disorders have anecdotal evidence of unexpected sudden deaths during sleep occurring among their patient population with OSAS. A systematic review by Wright and colleagues challenged the significance of OSAS as a risk factor for cardiovascular disease. Whereas the present study did not use a randomized controlled design, the strong suppressant effect of nCPAP on the observed cardiac rhythm disturbances strongly supports a causal relationship between OSAS and at least one form of cardiovascular morbidity. However, further studies are required to establish the pathologic significance of the present findings.

A number of previous reports have examined the relationship of OSAS to cardiac rhythm disturbances and myocardial ischemia and the impact of nCPAP therapy. Two reports have demonstrated a high prevalence (58% and 48%, respectively) of cardiac rhythm disturbance, significantly higher than nonapneic snorers, among large populations of patients with OSA. However, other studies have reported a much lower prevalence of rhythm disturbances that was not significantly different from that of nonapneic snorers. The con-

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**Table 2—Details of Nocturnal Pathologic Dysrhythmias and Impact of nCPAP Therapy**

<table>
<thead>
<tr>
<th>Patient</th>
<th>No.</th>
<th>Age, yr</th>
<th>AH1, h</th>
<th>Before nCPAP</th>
<th>After nCPAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>54</td>
<td></td>
<td>Multiple sinus pauses: 5/h &gt; 2 s; 10/h of 3 to 5.5 s, and 1/h of 10-s duration</td>
<td>No pathologic dysrhythmia</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>48</td>
<td></td>
<td>3 sinus pauses/h, lasting 2 to 3 s</td>
<td>No pathologic dysrhythmia</td>
</tr>
<tr>
<td>3</td>
<td>42</td>
<td>68</td>
<td></td>
<td>Frequent ventricular extrasystoles, 2 salvos of 3 PVCs</td>
<td>No pathologic dysrhythmia</td>
</tr>
<tr>
<td>4</td>
<td>44</td>
<td>109</td>
<td></td>
<td>2 sinus pauses/h, lasting 2.5 to 3 s</td>
<td>No pathologic dysrhythmia</td>
</tr>
<tr>
<td>5</td>
<td>51</td>
<td>55</td>
<td></td>
<td>2 sinus pauses/h, lasting 2.5 to 3 s</td>
<td>No pathologic dysrhythmia</td>
</tr>
<tr>
<td>6</td>
<td>69</td>
<td>21</td>
<td></td>
<td>8 sinus pauses of 2- to 3-s duration</td>
<td>No pathologic dysrhythmia</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>53</td>
<td></td>
<td>1 episode of second-degree atrioventricular block, lasting 4.5 min; 1 sinus pause of 4 s</td>
<td>No pathologic dysrhythmia</td>
</tr>
<tr>
<td>8</td>
<td>41</td>
<td>80</td>
<td></td>
<td>Intermittent ventricular bigeminy; 5 sinus pauses of 2- to 3-s duration</td>
<td>Intermittent ventricular bigeminy; 1 salvo of 5 PVCs; 10 sinus pauses, 2- to 4.5-s duration</td>
</tr>
</tbody>
</table>

*PVC = premature ventricular contraction.

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**Table 3—AHI per Hour Related to the Pressure or Absence of Cardiac Dysrhythmias**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients, No.</th>
<th>AHI, h</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dysrhythmias (group 0)</td>
<td>10</td>
<td>38</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Nonsignificant dysrhythmias (group 1)</td>
<td>27</td>
<td>52</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Significant dysrhythmias (group 2)</td>
<td>6</td>
<td>61</td>
<td>26</td>
<td></td>
</tr>
</tbody>
</table>

*Difference in AHI between groups is significant (p = 0.04, by Pearson correlation analysis). See text for details of dysrhythmia classification.
control populations for these studies have generally consisted of patients undergoing sleep studies for suspected OSA, but who were found not to have a significant OSAS. Thus, it is difficult to draw confident conclusions concerning a potential relationship between OSA and cardiac rhythm disturbance because such control populations could not be considered as normal subjects.

Several reports have examined the impact of nCPAP on rhythm disturbances and ischemia among patients with OSAS, and all have demonstrated objective benefit. However, only two previous reports have evaluated the impact of nCPAP on cardiac rhythm disturbances, both of which examined OSAS patients with heart block. The present report represents the first prospective study of the impact of nCPAP on pathologic rhythm disturbances among consecutive patients with established OSAS.

We recognize the limitations of our study design related to the lack of a matched control group and also to the lack of a randomized, placebo-controlled follow-up of the impact of nCPAP therapy on patients with cardiac rhythm disturbances. These limitations, although similar to those in previous reports, prevent us from drawing firm conclusions on the relative incidence of nocturnal cardiac rhythm disturbances in our patients with OSAS, compared with normal subjects of similar age. However, we strongly doubt that these limitations biased our findings or conclusions for several reasons: first, all patients had baseline and follow-up studies performed within 3 nights, and no therapeutic intervention was instituted other than nCPAP. Second, the magnitude of the treatment effect, where seven of eight patients with significant nocturnal cardiac rhythm disturbances resolved their nocturnal cardiac rhythm disturbance with nCPAP, strongly supports the view that nCPAP therapy had a beneficial impact on these dysrhythmias. The one patient whose rhythm disturbances did not resolve with nCPAP therapy had obvious primary cardiac pathology to account for his dysrhythmias. Finally, the seven patients whose dysrhythmias resolved with nCPAP demonstrated rhythm disturbances almost exclusively during sleep. Previous reports have indicated that cardiac rhythm disturbances are generally more frequent during waking hours. All of the above considerations strongly support the view that the cardiac rhythm disturbances observed were a consequence of the patients' OSAS.

The continuous ECG recording provided by the Holter monitor raises the possibility of using this device to detect episodes of myocardial ischemia during sleep, as described in previous reports of patients with OSAS. Whereas continuous ST-segment monitoring was not directly part of the present protocol, we did assess the potential usefulness of the Holter monitor to detect myocardial ischemia. However, we found the Holter monitor to be unsatisfactory and unreliable in this regard. Two patients with known ischemic heart disease did not show evidence of nocturnal ST-segment changes, despite both having severe OSAS, whereas three patients who did show episodes of nocturnal ST-segment depression > 1 mm were not found to have evidence of significant heart disease on further cardiac investigation. However, we must stress that the present study was not designed to identify myocardial ischemia in patients with OSAS, and our comments in this regard are relevant only to the suitability of the Holter monitor to detect occult myocardial ischemia. The two-channel ECG recording provided by this device would not be sufficient to fully assess the possibility of myocardial ischemia, and the device is primarily designed for assessing cardiac rhythm disturbances.

The finding that nCPAP effectively controls cardiac rhythm disturbances implies that routine cardiac monitoring is not indicated in patients with OSAS treated with nCPAP. However, this conclusion does not apply to those patients who fail to tolerate nCPAP therapy. Furthermore, compliance data indicate that patients receiving continuous home nCPAP therapy use their device for an average of only 5 h per night. These findings raise the possibility of continuing adverse cardiac consequences for patients with OSAS during the hours of sleep when the patients are not using their nCPAP devices. Further studies will be required to assess the cardiovascular morbidity and mortality rates of untreated and undertreated patients with OSAS.

We conclude that cardiac rhythm disturbances during sleep are common in patients with OSAS, that they correlate with OSA severity, and that they are effectively treated by nCPAP therapy.

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