The Effects of Nasal Continuous Positive Airway Pressure on Platelet Activation in Obstructive Sleep Apnea Syndrome*

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Objective: A case-controlled study to assess the effects of nasal continuous positive airway pressure (CPAP) on platelet activation in patients with obstructive sleep apnea (OSAS) syndrome. Methods: We recruited 65 patients with suspected OSAS for this study. Blood samples were taken with the patient in the supine position in the morning immediately after polysomnography, and 1 night and 3 months after the start of nasal CPAP therapy to measure an index of platelet activation (IPA+), which reflected both the quantity and quality of platelet activation. Significant OSAS was defined as an apnea-hypopnea index (AHI) of ≥ 10 events per hour.

Results: There were 42 patients with significant OSAS and 23 control subjects with AHI < 10 events per hour. The mean (± SD) age for the OSAS patients was 48 ± 9 years, the mean body mass index was 30.7 ± 4.8, the mean AHI was 47 ± 25 events per hour, the mean arousal index (AI) was 37 ± 23 events per hour, and the mean minimum arterial oxygen saturation was 74 ± 11%. Following multiple linear regression analyses of the clinical and polysomnography parameters, AI was the independent factor that correlated best with the baseline IPA+ (β-coefficient, 0.386; p = 0.006). Following nasal CPAP treatment with a mean objective CPAP compliance of 3.9 ± 1.9 h per night, there was a significant decrease in IPA+ from 15.1 ± 12.2 U (at baseline) to 12.2 ± 5.2 U (p < 0.001) and 9.8 ± 4.3 U (p = 0.005), respectively, after 1 night and 3 months, whereas no significant change was noted among the control subjects. Using univariate analysis of variance to compare the changes in IPA+ between the two groups at 3 months with adjustment for the baseline value, nasal CPAP reduced IPA+ by 5.63 (SE, 1.85), whereas IPA+ increased in control subjects by 1.33 (SE, 1.27) [least-squared mean difference between groups, 3.34; 95% confidence interval, 0.42 to 6.26; p = 0.026].

Conclusions: OSAS, through repeated episodes of arousals, may lead to platelet activation, which can be reduced by nasal CPAP therapy. (CHEST 2004; 125:1768–1775)

Key words: continuous positive airway pressure; platelet activation; sleep-disordered breathing

Abbreviations: AHI = apnea-hypopnea index; AI = arousal index; BMI = body mass index; CPAP = continuous positive airway pressure; EMG = electromyogram; ESS = Epworth sleepiness scale; IPA+ = index of platelet activation; log SaO2 < 90% = logarithm of the percentage of total sleep time with arterial oxygen saturation at < 90%; MCF+ = mean channel fluorescence; OSAS = obstructive sleep apnea syndrome; %+ = CD62 expression percentage; SaO2 = arterial oxygen saturation; SDB = sleep-disordered breathing; TST = total sleep time
There is growing evidence that untreated OSAS is associated with an increased risk of hypertension, myocardial infarction, pulmonary hypertension, and stroke. Several epidemiologic studies have shown an independent association between SDB and hypertension after controlling for confounding factors such as age, body mass index (BMI), sex, alcohol, and smoking. A case-control study has shown that patients with OSAS have increased ambulatory diastolic BP both during the day and night, and increased systolic BP at night. Cross-sectional associations from the baseline examination of the Sleep Heart Health Study cohort have shown modest-to-moderate effects of SDB on various manifestations of cardiovascular diseases, and SDB was more strongly associated with reported stroke and heart failure than with coronary artery disease. In addition, a longitudinal study of > 7 years among otherwise healthy middle-aged men with OSAS has shown an increased incidence of cardiovascular diseases.

Except for the strong association between SDB and hypertension, the mechanisms linking SDB and cardiovascular events have remained unclear. Some of the proposed mechanisms include repeated nocturnal hypoxemia, sympathetic activation, disturbed endothelial function, depressed baroreflex sensitivity, increased vasoconstrictor sensitivity to angiotensin II, insulin resistance, and increased platelet activation and aggregation.

Platelets are derived from megakaryocytes, each of which sheds several thousand platelets directly into the circulation in the marrow sinuses. When platelets are activated by adenosine diphosphate, thrombin, or collagen, they contract to become spherical and extend pseudopodia, which adhere to the subendothelium and other platelets. On activation, platelet granules discharge their contents, which encourages further platelet aggregation and fibrin formation. Interplatelet aggregation is dependent on fibrinogen binding to platelet glycoproteins. It is possible that OSAS may lead to cardiovascular events through platelet activation followed by platelet aggregation.

This study examines the effects of OSAS and its treatment with nasal continuous positive airway pressure (CPAP) treatment on platelet activation in a group of OSAS patients compared to a group of control subjects without significant OSAS.

**Materials and Methods**

For this study, we screened 100 consecutive Chinese patients who had been referred to the Respiratory Clinic at the Prince of Wales Hospital with snoring and/or other symptoms suggestive of OSAS over a period of 4 months. The study was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong, and appropriate informed consent was obtained from the subjects.

**Sleep Study**

Significant OSAS was arbitrarily defined as an apnea-hypopnea index (AHI) of ≥ 10 events per hour of sleep as shown by overnight polysomnography (Alice 4; Healthdyne; Atlanta, GA) plus self-reported sleepiness. Subjective sleepiness was evaluated by the Epworth sleepiness scale (ESS), a questionnaire that is specific to symptoms of daytime sleepiness, and the subjects were asked to score the likelihood of falling asleep in eight different situations with different levels of stimulation, adding up to a total score of 0 to 24.

Overnight polysomnography recorded EEG, electrooculogram, submental electromyogram (EMG), bilateral anterior tibial EMG, ECG, chest and abdominal wall movement by inductance plethysmography, airflow by a nasal pressure transducer (PTAF 2; Pro-Tech, Woodinville, WA) and supplemented by an oronasal thermistor, and finger pulse oximetry, as in our previous study. Sleep stages were scored according to the standard criteria of Rechtschaffen and Kales. Apnea was defined as the cessation of airflow for > 10 s, and hypopnea was defined as a reduction of airflow of ≥ 50% for 10 s plus an oxygen desaturation of > 3% or an arousal. An arousal was scored if there was an abrupt shift in EEG frequency to α or θ of ≥ 3 Hz or > 16 Hz, following at least 10 s of sleep, and if arising during rapid eye movement sleep, there must be a rise in EMG tone.

Following the confirmation of significant OSAS from the overnight diagnostic sleep study, each patient was interviewed by the physician on duty and was offered a trial of nasal CPAP treatment. Each patient was given a CPAP education program by a respiratory nurse and then was given a short trial of CPAP therapy with an auto-titrating device (AutoSet; Resmed; Sydney, Australia) for approximately 30 min for acclimatization in the afternoon. Attended CPAP titration was performed with the auto-titrating device on the second night of the study in our hospital. The CPAP pressure for each patient was set at the minimum pressure needed to abolish snoring, obstructive respiratory events, and airflow limitation for 95% of the night, as determined by the results of the overnight CPAP titration study. Previous studies have shown that automatic CPAP titration is as effective as manual titration in correcting the obstructive respiratory events and arousal frequency, and in improving oxygenation. All patients were subsequently prescribed CPAP therapy using a device (Horizon LT 8001; De Vilius; Somerset, PA) with a time counter recording machine run time. Patients were readmitted to the hospital at 3 months after the commencement of CPAP treatment, so that our research staff could check their objective CPAP compliance and take blood to assess their progress.

Subjects with an AHI of < 10 events per hour of sleep on polysomnography served as the control subjects for this study. They were readmitted to the hospital at 3 months for a progress assessment of the levels of the index of platelet activation (IPA*).

**Platelet Activation Measurement**

Whole-blood flow cytometry is a powerful laboratory technique for assessing platelet activation and function. Platelets are analyzed in the presence of leukocytes and erythrocytes, and only small quantities of blood are required per tube. To minimize platelet activation during blood collection, blood samples were obtained, with the patient in the supine position, from an antecubital vein with a 20-gauge butterfly needle using a light
tourniquet in the morning immediately after polysomnography, and the first 2 mL blood was discarded. Blood tests were repeated the morning after the CPAP titration study for those patients with significant OSAS and at 3 months after an overnight stay as inpatients for the two groups.

The preparation of whole-blood samples for flow cytometry analysis has been described in detail elsewhere. In brief, blood was collected into acid-citrate-dextrose tubes. The blood sample was immediately processed by adding 50 μL of blood into 1 mL of 2% formaldehyde in a phosphate-buffered saline solution. The flow cytometer was calibrated using beads that were 2 to 10 μm in diameter, and settings were optimized by logarithmic signal amplification in forward and side-light scatter channels, as well as the fluorescence channels.

CD62 (ie, P-selectin; Caltag Laboratories; Burlingame, CA) is a platelet α-granule protein that is expressed on the platelet surface following activation. Two flow cytometric CD62 monoclonal antibody-binding parameters were used to determine thrombin-induced platelet activation, as follows: the quantity of platelet activation, as measured by the P-selectin (CD62) expression percentage (%); and the quality of platelet activation, as assessed by the mean fluorescence of CD62-positive platelets, expressed in arbitrary units of mean channel fluorescence (MCF+). The % reflected the proportion of activated cells in the total platelet population without registering the activation level of individual cells and allowed a quantitative but not a qualitative measurement of activated cells in the total platelet population. In contrast, MCF+ provided a parameter of the activation of an average platelet by measuring the mean epitope density of CD62 molecules on the platelet surface and reflected the quality of individual platelet activation. The IPA+ was expressed as MCF+ × f, whereas f = ?/100 and represented the fraction of CD62-positive cells in the total platelet population. Thus, IPA+ reflected an integrated amount of CD-62 expressed in the subpopulation of positive cells, and measured both the quality and quantity of platelet activation. In healthy persons, < 1% of platelets express CD62, and the IPA+ is < 1.0. In clinical situations associated with increased platelet activations, for example, in patients with pacemakers, the percentage of CD62 platelets is in the range of 10 to 20%, while IPA+ is in the range of 5 to 15.

Patients who were receiving therapy with aspirin, or any nonsteroidal anti-inflammatory agent or systemic steroid within 2 weeks prior to the study, those who had recently experienced myocardial infarction or stroke, those who had unstable angina, those who had a coagulation or platelet disorder, and those with clinical features of any active infection were excluded from the study.

**Statistical Analysis**

All data are presented as the mean ± SD, unless otherwise stated. Correlations between polysomnography parameters and IPA+ were performed with Pearson correlation analysis. Multiple linear regression analysis was performed for factors with p < 0.1 on Pearson correlation to look for independent association with the baseline IPA+. Comparisons between subjects with and without significant OSAS with regard to changes in IPA+ from baseline to 3 months were conducted by analysis of variance with adjustment for the baseline value. A p value of < 0.05 was considered to indicate statistically significant differences between the groups. Data analysis was performed with a commercially available statistical analysis software package (SPSS, version 10.0 for Windows; SPSS Inc; Chicago, IL).

**Results**

Of the 100 consecutive patients who were screened, 35 were excluded from the study as they were receiving aspirin (10 patients), other nonsteroidal anti-inflammatory agents as analgesia (9 patients), or had refused blood tests (16 patients). There were altogether 42 patients (32 men) with significant OSAS and 23 control subjects (12 men) who met the inclusion criteria. There were 5 current smokers (21.7%) in the control group and 10 current smokers (23.8%) in the OSAS group, but none smoked within our smoke-free hospital environment. The mean age, BMI, and neck circumference for the OSAS patients were 48 ± 9 years, 30.7 ± 4.8, and 40.3 ± 3.3 cm, respectively. Polysomnography of the OSAS group showed an AHI of 47 ± 25 events per hour, an arousal index (AI) of 37 ± 23 events per hour, and a minimum arterial oxygen saturation (SaO2) of 74 ± 11%. A comparison of the OSAS patients and the control subjects with regard to demographics, and hematologic and polysomnography parameters is shown in Table 1. The two groups were similar in age, BMI, and total sleep time (TST), but there were remarkable differences in neck circumference and other polysomnography parameters.

Correlations between several polysomnography parameters vs baseline IPA+ level are shown in Table 2. Since the percentage of TST with SaO2 at < 90% did not follow a normal distribution, the logarithm of percentage of TST with SaO2 at < 90% (log SaO2 < 90%) was used in the Pearson correlation analysis. The AHI, AI, ESS score, and log SaO2 < 90% had significant positive correlation with the baseline IPA+.

Following multiple linear regression analyses of the clinical and polysomnography parameters (ie,

### Table 1—Comparison of Clinical, Laboratory, and Plethysmography Features*

<table>
<thead>
<tr>
<th>Variables</th>
<th>OSAS (n = 42)</th>
<th>Control Subjects (n = 23)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>47.7 ± 9.4</td>
<td>49.1 ± 12.4</td>
<td>0.63</td>
</tr>
<tr>
<td>BMI</td>
<td>30.7 ± 4.8</td>
<td>28.8 ± 3.0</td>
<td>0.10</td>
</tr>
<tr>
<td>Neck circumference, cm</td>
<td>40.3 ± 3.3</td>
<td>38.5 ± 3.1</td>
<td>0.04</td>
</tr>
<tr>
<td>AI</td>
<td>37 ± 23</td>
<td>16 ± 6</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>AHI</td>
<td>47 ± 25</td>
<td>6 ± 3</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>SaO2, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>74 ± 11</td>
<td>88 ± 5</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Mean</td>
<td>92 ± 4</td>
<td>90 ± 2</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>TST, h</td>
<td>6.7 ± 1.0</td>
<td>6.4 ± 1.8</td>
<td>0.68</td>
</tr>
<tr>
<td>TST with SaO2 &lt; 90%, %</td>
<td>24.2 ± 29.0</td>
<td>3.5 ± 6.6</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>ESS at baseline</td>
<td>11.7 ± 5.9</td>
<td>9.8 ± 5.2</td>
<td>0.23</td>
</tr>
<tr>
<td>IPA+ at baseline</td>
<td>15.1 ± 12.2</td>
<td>10.9 ± 3.4</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*Values given as mean ± SD, unless otherwise indicated.
Table 2—Correlation Between Clinical and Plethysmography Parameters vs Baseline IPA+

<table>
<thead>
<tr>
<th>Variables</th>
<th>r Value</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI</td>
<td>0.300</td>
<td>0.022*</td>
</tr>
<tr>
<td>AI</td>
<td>0.321</td>
<td>0.014*</td>
</tr>
<tr>
<td>SaO₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>-0.246</td>
<td>0.065</td>
</tr>
<tr>
<td>Mean</td>
<td>-0.203</td>
<td>0.133</td>
</tr>
<tr>
<td>Log SaO₂ &lt; 90%†</td>
<td>0.326</td>
<td>0.022*</td>
</tr>
<tr>
<td>BMI</td>
<td>0.215</td>
<td>0.129</td>
</tr>
<tr>
<td>CPAP compliance, h/night</td>
<td>-0.201</td>
<td>0.270</td>
</tr>
<tr>
<td>Age</td>
<td>-0.112</td>
<td>0.401</td>
</tr>
<tr>
<td>ESS</td>
<td>0.319</td>
<td>0.015*</td>
</tr>
</tbody>
</table>

*Of statistical significance.
†Log SaO₂ < 90 was used in the analysis since percentage of TST with SaO₂ < 90% did not follow normal distribution.

AHI, AI, minimum SaO₂, ESS score, and log SaO₂ < 90% using the baseline IPA+ as the dependent variable (F = 8.210; adjusted r² = 0.131), AI was the independent factor that correlated best with the baseline IPA+ (β-coefficient, 0.386; 95% confidence interval, 0.053 to 0.302; p = 0.006), whereas AHI (p = 0.286), log SaO₂ < 90% (p = 0.352), minimum SaO₂ (p = 0.353), and ESS score (p = 0.196) were not.

After overnight CPAP titration, there was a reduction of the baseline IPA+ from 15.1 ± 12.2 to 12.2 ± 5.2 (p < 0.001). Following 3 months of nasal CPAP treatment for the OSAS patients, there was a further decrease of IPA+ to 9.8 ± 4.3 U (p = 0.005) compared to the level found after CPAP titration. Among the control subjects, there was no significant change in the IPA+ between baseline and 3 months (10.9 ± 3.4 and 12.2 ± 7.5 U, respectively; p = 0.307). Using univariate analysis of variance to compare the changes in IPA+ between the OSAS group and the control subjects at 3 months with adjustment for the baseline value, nasal CPAP reduced IPA+ by 5.63 (SE, 1.85), whereas control subjects increased IPA+ by 1.33 (SE, 1.27) [least-squared mean difference between groups, 3.34; 95% confidence interval, 0.42 to 6.26; p = 0.026]. Figure 1 shows the IPA+ data points of the two groups at baseline (Fig 1, top) and at 3 months (Fig 1, bottom). In addition, the baseline ESS score in the OSAS group fell from 11.7 ± 6.0 to 5.8 ± 4.3 at 3 months (p < 0.001). The CPAP level was 11.7 ± 2.3 cm H₂O, while the objective CPAP compliance was 3.9 ± 1.9 h per night over the study period of 3 months. There was, however, no correlation between the change in IPA+ and the objective CPAP compliance (r = 0.158; p = 0.38). On further subgroup analysis, there was no clear-cut minimum duration of CPAP compliance that was associated with a more significant reduction of IPA+.

**DISCUSSION**

This study has shown that the IPA+ had positive correlations with several indexes of severity of OSAS (the baseline AHI, AI, and log SaO₂ < 90%), and AI was the independent factor that correlated best with the baseline IPA+. In addition, overnight nasal CPAP treatment resulted in a significant reduction in the IPA+, with a further reduction over a treatment period of 3 months. An example of a histogram showing the change in platelet activation in a patient with OSAS before and 3 months after nasal CPAP treatment is shown in Figure 2.

Despite the potential role of platelet activation and aggregation in the pathogenesis of cardiovascular diseases in SDB, there are surprisingly few publications, all limited by relatively small sample sizes, addressing this issue. Bokinsky et al previously observed a higher degree of platelet activation in six untreated OSAS patients (AHI, 87 ± 23 events per hour) compared to five control subjects (AHI unknown) during sleep, and there was marked reduction in platelet activation and aggregation following 1 night of nasal CPAP treatment. No relationships could be established among the level of platelet activation, platelet aggregation, and the frequency of apneas or the nadir in oxygen saturation values, but this might be due to the small number of patients enrolled in their study.

Eisensehr et al reported significant positive correlations between the AHI and a number of variables (ie, 9:00 PM platelet activation, 9:00 PM and 6:00 AM systolic and diastolic BP, and 6:00 AM epinephrine level), mainly in OSAS patients (seven patients) with an AHI of ≥ 50 events per hour, whereas the 9:00 PM platelet activation also correlated with the 6:00 AM epinephrine level. Multiple regression analysis defined morning epinephrine level and AHI as independent factors for the increased night-time platelet activation. Their results suggest that increased sympathetic activity (as reflected by raised plasma epinephrine levels) and associated platelet activation may play a role in the pathogenesis of cardiovascular events in patients with OSAS.

Geiser et al noted an increased level of platelet activation during sleep (ie, at 4:00 AM) in 12 untreated OSAS patients (AHI, > 10 events per hour) compared to 6 healthy volunteers (AHI, 5 ± 2.9 events per hour [on AutoSet diagnostic mode]) serving as control subjects, but, after 1 night of CPAP therapy, there was only a trend to reduced levels of platelet activation at 4:00 AM.

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Our study is the only study with sufficient sample size for a more meaningful interpretation of data. A sample size of 42 (Power Analysis and Sample Size for Windows software, PASS 2000; NCSS; Kaysville, UT), achieved 80% power to detect a difference of 5.0 between the null hypothesis mean of 15.1 and the alternative hypothesis mean of 9.8, with a known SD of 12.2 and a significance level ($\alpha$) of 0.05 using a two-sided, one-sample $t$ test. The power was probably underestimated because an SD of 12.2 was assumed in both the pretreatment group and the posttreatment group.

There are several potential mechanisms linking SDB and cardiovascular diseases such as stroke. Although epidemiologic studies can only establish an association rather than a causal role between SDB and hypertension, high levels of AHI –14–16 and sleep time at $\geq 90\%$ oxygen saturation15,16 were associated with greater odds of hypertension in a dose-response fashion, independent of confounding factors such as age, sex, BMI, and other modifiable risk factors. Experimental studies with the rat model40 and canine model$^{14}$ have shown that obstructive SDB can lead to the development of sustained hypertension. Peripheral resistance may increase as a result of recurrent arousals terminating the obstructive respiratory events and activating the sympathetic nervous system.20

In addition to hypertension and sympathetic activation, other potential mechanisms linking SDB and ischemic stroke include increased platelet activation and platelet aggregation,26,38 with possible effects of adrenergic stimulation on platelet function.$^{20,42-44}$ Interestingly, ischemic stroke often occurs during sleep or in the early morning hours,$^{45,46}$ and platelets from healthy subjects have shown enhanced aggregability between 6:00 AM and 9:00 AM.$^{47}$

While we have shown that platelet activation was significantly reduced following 1 night and 3 months of nasal CPAP treatment, other investigators$^{49}$ have...
reported that 6 months of CPAP therapy could reduce platelet aggregation in 17 consecutive male OSAS patients both at 12:00 AM and at 6:00 AM. In addition, platelet aggregability during sleep in the 15 control subjects resembled that found in patients with OSAS during CPAP therapy. The results of the study suggest that OSAS may contribute to platelet dysfunction, while long-term CPAP therapy may reduce platelet aggregability.48 Furthermore, our results suggest that OSAS, through repeated episodes of arousals and nocturnal hypoxia, may lead to platelet activation. Hypoxia that is related to apneic/hypopneic events may result in chemoreflex activation with consequent increases in sympathetic vasoconstrictor traffic to peripheral blood vessels,49,50 whereas arousals are well-known to be associated with increased sympathetic activity.20,51 Catecholamine surge may activate platelets and trigger a hypercoagulable state, increasing the risk of overt thrombosis in patients with atherosclerotic disease.38,43-45,52 Nasal CPAP therapy has beneficial effects in abolishing both hypoxia and arousals related to obstructive respiratory events and sympathetic activation.53

There are several limitations to this study. Although we had a control group for comparison to patients with significant OSAS, there was no placebo control for the treatment effects of nasal CPAP therapy. Further research, preferably with a randomized placebo-controlled design, is needed to demonstrate more convincingly the effects of nasal CPAP therapy on platelet activation. Our control group consisted of some subjects with trivial SDB and might not represent perfectly healthy control subjects, but our measurement of airflow with the nasal pressure transducer54 separated the control subjects from those with significant OSAS more reliably. We did not measure platelet aggregation in our study as current techniques for measuring platelet aggregation only reflect changes in vitro, whereas platelet activation refers to activities in vivo.34

It is difficult to judge the clinical significance of the magnitude of decrease in platelet activation after nasal CPAP therapy as no direct comparative study has been performed against conventional antiplatelet agents in the setting of OSAS. In a crossover study of platelet activation while receiving treatment with aspirin (100 to 300 mg/d), clopidogrel (75 mg/d), and both for 4 weeks after ischemic stroke, Grau et al55 have shown that the antiplatelet agents alone or in combination could reduce CD62 platelets down to between 2.3% and 3.3% (median), a level that is not significantly different from that of their healthy control subjects (median, 2.3%). While the main indication for CPAP treatment in OSAS patients is to relieve disabling symptoms, especially daytime sleepiness,7,8 even a modest reduction in platelet activation with nasal CPAP therapy should be regarded as a bonus benefit, especially with the growing evidence of cardiovascular consequences9-19 related to OSAS.

In summary, this study has shown a positive and independent correlation between the baseline AI and the IPA+. In addition, nasal CPAP treatment overnight has resulted in a significant reduction in the IPA+ over a treatment period of 3 months. The results suggest that OSAS, through repeated episodes of arousals, may lead to platelet activation and that nasal CPAP therapy may possibly confer some cardioprotective effects through the reduction of platelet activation.

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REFERENCES

8 George CF. Reduction in motor vehicle collisions following treatment of sleep apnoea with nasal CPAP. Thorax 2001; 56:508–512
21 Imadojemu VA, Gleeson K, Quraishi SA, et al. Impaired vasodilator responses in obstructive sleep apnea are improved with continuous positive airway pressure therapy. Am J Respir Crit Care Med 2002; 165:950–953
30 Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Los Angeles, CA: Brain Information Service, Brain Information Institute, University of California, 1968
is increased during sleep in patients with obstructive sleep apnea syndrome. Respiration 2002; 69:229–234