Proteinuria in Patients with Sleep Apnea

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Background. Proteinuria severe enough to be in the nephrotic range has been noted on occasion in patients with obstructive sleep apnea (OSA), but it is not known what factors are related to the severity of proteinuria in these patients. This study was conducted to determine if the severity of proteinuria is related to the number of apneas.

Methods. The level of proteinuria was determined by the dipstick method in 407 patients in whom OSA had been diagnosed. The apnea-hypopnea index (AHI) was calculated in each patient after all-night polysomnography. Sleep apnea was defined as the presence of at least 30 apneas during a 6- to 8-hour monitoring period and an AHI greater than 15.

Results. The apnea-hypopnea index in patients without proteinuria was similar to that of patients with 1+ to 3+ proteinuria. However, the AHI was significantly greater in the 9 patients with 4+ proteinuria.

Conclusions. While severe proteinuria in OSA occurs in patients with a higher rate of sleep apneas, the lesser degree of proteinuria cannot be explained by AHI alone. Other factors that determine the severity of the disease, such as hypoxemia, merit further investigation.

Key words. Sleep apnea syndromes; proteinuria; polysomnography; apnea-hypopnea index. (*J Fam Pract 1995; 40:139-141*)

Obstructive sleep apnea (OSA) syndrome is characterized by intermittent cessation (apnea) and reduction (hypopnea) in airflow that occurs during sleep, plus hypersomnolence, snoring, and disturbed sleep. OAS is usually seen in obese patients.[1,2] This syndrome is fairly common and is estimated to affect between 1% and 4% of the general population.[3]

Proteinuria occurs in some patients with OSA and at times may be severe enough to be in the nephrotic range.[4-8] The relation of proteinuria to the severity of OSA has not been defined. The purpose of this study was to determine the relation between the severity of proteinuria and the number of apneas and hypopneas found during polysomnography.

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Methods

The study included 407 consecutive patients in whom OSA was diagnosed at the Georgia Sleep Center at the Medical College of Georgia in Augusta. All patients were over 18 years of age and had an apnea-hypopnea index (AHI) of more than 15 per hour. AHI is the combined number of apneas and hypopneas per hour of sleep. Patients known to have diabetes mellitus, renal disease, pyuria, hematuria, or central sleep apnea were excluded. Each patient had a 6- to 8-hour polysomnographic recording of electroencephalogram, electromyogram, electro-oculogram, electrocardiogram, oronasal airflow, chest and abdominal wall movements, and oxygen saturation. AHI was calculated.

Apnea was defined as cessation of airflow for at least 10 seconds, and hypopnea was defined as ≥50% reduction in airflow associated with oxygen desaturation of at least 4%. Apneas were classified as obstructive if the chest and the abdominal wall movements continued during the apneic and hypopneic episodes.

Just before undergoing polysomnography, each patient had a urinalysis performed using the dipstick method

(Ames, Multistix, Miles Laboratory, Inc, Elkhart, Ind). The presence of proteinuria was expressed on a scale of 0 to 4+, with 0 representing absence, t representing trace, 1+=≥30 mg/dL, 2+=≥100 mg/dL, 3+=≥300 mg/dL and 4+=≥2000 mg/dL. The patients were divided into six groups based on the level of proteinuria. The data were analyzed using the SPSS program and expressed as mean ± standard deviation (SD). The significant level was set at $P=\leq.05$.

Results

Complete data were available for 407 patients. All these patients had an AHI of more than 15. There was no evidence of proteinuria in 115 (28%) patients (group 1) and only trace proteinuria was found in 157 (39%) patients (group 2). In the remaining 135 patients, proteinuria was 1+ in 84 (group 3), 2+ in 32 (group 4), 3+ in 10 (group 5) and 4+ in 9 (group 6) patients. The results of AHI in each group are shown in the Figure.

The AHI was significantly higher in patients with 4+ proteinuria (group 6) as compared with those in all other groups. However, the AHI was similar among patients with milder degrees of proteinuria or no proteinuria (groups 1 through 5).

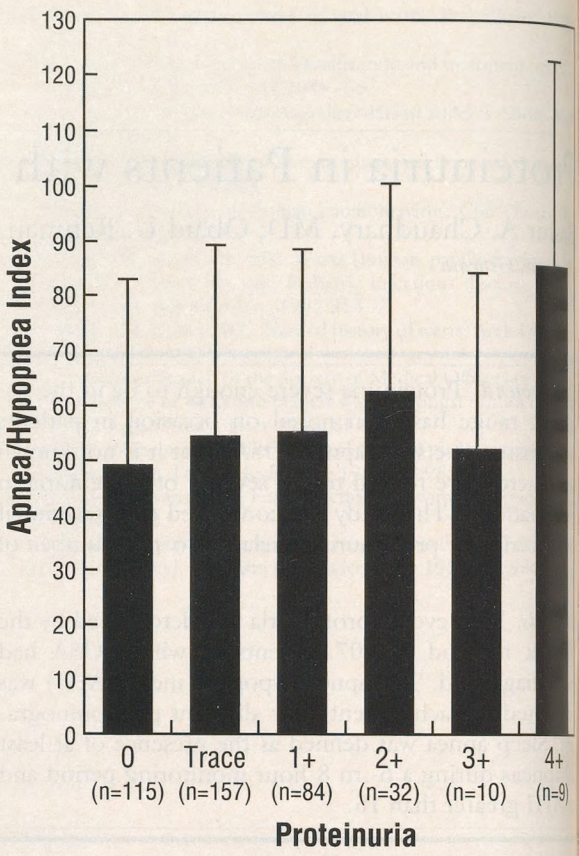

Figure. Proteinuria and apnea-hypopnea index in patients with obstructive sleep apnea (N = 407). The apnea-hypopnea index refers to the combined number of apneas and hypopneas per hour of sleep.

Discussion

The results of this study suggest that patients with obstructive sleep apnea who have 4+ proteinuria have a significantly higher AHI than do patients with no proteinuria or a lesser degree of proteinuria. The AHI, however, is not different among patients with 1+ to 3+ proteinuria as compared with patients without proteinuria.

The use of a semiquantitative method (dipstick) for the measurement of urinary protein is a limitation of our study. The dipstick method detects protein concentrations of ≥30 mg/dL with certainty. Although the correlations between color change and actual protein concentration are only approximate, the comparison of the dipstick method with quantitative methods shows a high degree of agreement.[9]

The occurrence of proteinuria in patients with OSA has been fairly well established.[4–8] The causative factors that determine the severity of proteinuria, however, have not been defined. We had expected to find a linear correlation between the severity of proteinuria and the apnea index. Our failure to find this correlation in patients with OSA who had 1+ to 3+ proteinuria suggests that factors other than apnea index may be involved. There are many potential factors that can contribute to the severity of OSA symptoms in patients, including the number of apneas, obesity, and hypoxemia. It is likely that many of these factors are interrelated.

The impact of obesity on proteinuria is controversial. In 1923, Preble[10] reported a 40% incidence of proteinuria in 1000 obese patients, but it is not clear whether these patients had other diseases causing proteinuria. Goldszer et al,[11] who found proteinuria in only 4 of 257 obese patients, questioned the relation between obesity and proteinuria. We compared the proteinuria in obese patients who had sleep apnea with the proteinuria in obese patients who did not.[6] The protein excretion in the patients with OSA (94 ± 31.8 mg/minute) was approximately three times higher than that in the obese patients without OSA (29.3 ± 9.5 mg/minute). This study suggested that proteinuria in obese patients usually occurs in patients who have sleep apnea. Moreover, we have observed that many patients gain significant amounts of weight just before they come for medical evaluation. This weight gain probably is chiefly due to fluid accumulation

secondary to cor pulmonale and right-sided heart failure. This increase in fluid weight that is thought to contribute to proteinuria may be occurring at the same time that proteinuria worsens as a result of progressive worsening of sleep apnea or hypoxemia.

Nocturnal hypoxemia occurs commonly in patients with OSA and may play a role in the development of proteinuria. Hypoxemia can reduce renal blood flow,[12] which in turn can cause proteinuria.[13] It seems logical to assume that patients with more severe OSA will experience a greater degree of nocturnal oxygen desaturation. In addition to the number of apneas, however, there are many other factors that determine nocturnal oxygen desaturation, such as the duration of apneas, oxygen saturation level prior to apneas, and obesity.[14] Further studies are needed to determine whether hypoxemia plays an etiologic role in the development of proteinuria.

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