Correlation between Clinical Parameters, Blood Pressure Dipping, Highly Sensitive CRP Plasma Level and Carotid Intima-Media Thickness in Patients with Obstructive Sleep Apnea

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Abstract

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***Background*:** Mechanisms for linkage between sleep disordered breathing and cardiovascular diseases are not fully determined but surges in sympathetic nerve activity are seen at the end of each apnoeic episode accompanied by large rises in systemic arterial blood pressure.

Material & Methods: The study was conducted on 50 patients complaining of snoring and/ or excessive daytime sleepiness assessed by **Epworth Sleepiness Scale**. All were subjected to sleep study **,** 24hour ambulatory blood pressure monitoring ,carotid duplex scanning and quantitative determination of high sensitivity C- reactive protein

Results*:* Patients having apnea hypopnea index (AHI)≥5 diagnosed as apnea group (group I) and those having AHI less than 5 were diagnosed as snorers (group II).Seventy eight percentage of study population were non nocturnal dippers, 81.3% of group I versus 72.2% of group II with non significant p value (p = 0.494) . Mean diastolic day and night blood pressure, was higher in group I compared to group II with significant p value 0.028 and 0.007 respectively. Mean Carotid intima media thickness (IMT) was significantly higher in group I with p <0.001.

Conclusion: Epworth Sleepiness Scale is good reflector of sleep study data. Mean diastolic day and night blood pressure, mean arterial blood pressure are significantly higher in apnea patients. Increased carotid IMT is associated with higher AHI, lower minimum saturation assessed during the sleep study and higher HS- CRP serum level.

Key words: Obstructive Sleep Apnea

Cardiovascular diseases

CONTENTS

LIST OF ABBREVIATIONS

AASM : American Association of Sleep Medicine
ABPR : Ambulatory blood pressure recording
AHI : Apnea hypopnea index
ARIC : Atherosclerosis Risk in Communities
BMI : Body mass index
BP : Blood pressure
CAC : Coronary artery calcification
CAD : Coronary artery disease
CAI : Central Apnea Index
CPAP : Continuous positive airway pressure
CRT : Cardiac resynchronization therapy
CSA : Central sleep apnea
CSB : Cheyne Stokes Breathing
CVD : Cardiovascular diseases
ESS : Epworth Sleepiness Scale
HS CRP : High sensitivity C – reactive protei*n*
IMT : Intima -media thickness
MSLT : Multiple Sleep latency Test
OSA : Obstructive sleep apnea
OSA : Obstructive sleep apnea
OSAS : Obstructive sleep apnea syndrome
RDI : Respiratory disturbance index
RERA : Respiratory effort-related arousal
SDB : Sleep disordered breathing
Syndrome SAH : Syndrome sleep apnea hyperpnoea
UARS : Upper airway resistance syndrome
WHR : Waist-to-hip ratio

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INTRODUCTION

Sleep-disordered breathing (SDB) briefly means cessation of breathing during sleep at least 5 times per hour. It affects 9 to 24% of the middle-aged and overall 4% of the middle-aged males. Several major epidemiological studies have shown that SDB is not only an independent risk factor for systemic hypertension but it is also associated with cardiovascular complications such as heart failure, stroke, and sudden death.

Obstructive sleep apnea OSA is characterized by repetitive interruption of ventilation during sleep caused by collapse of the pharyngeal airway. An obstructive apnea is a ≥10-second pause in respiration associated with ongoing ventilatory effort. Obstructive hypopneas are decreases in, but not complete cessation of, ventilation, with an associated fall in oxygen saturation or arousal.

Diagnosis of OSA syndrome is accepted when a patient has apnea-hypopnea index (AHI; number of apneas and hypopneas per hour of sleep) more >5 and symptoms of excessive daytime sleepiness

The primary abnormality in patients with OSA is an anatomically small pharyngeal airway resulting from obesity, bone and soft tissue structures, or, in children, tonsils and adenoids.

During wakefulness, this leads to increased airflow resistance and greater intrapharyngeal negative pressure during inspiration.

Mechanoreceptors located primarily in the larynx respond reflexively to this negative pressure and increase the activity of a number of pharyngeal dilator muscles, thereby maintaining airway patency while awake .

However, during sleep, the reflex pharyngeal muscle activity that drives this neuromuscular compensation is reduced or lost, leading to reduced dilator muscle activity and ultimately to pharyngeal narrowing and intermittent complete collapse.

During the subsequent apnea or hypopnea, hypoxia and hypercapnia stimulate ventilatory effort and ultimately arousal from sleep to terminate the apneic event. Thus, an upper airway that requires reflex-driven muscle activation to maintain patency during wakefulness may be vulnerable to collapse during sleep.

Central sleep apnea CSA is characterized by repetitive cessation of ventilation during sleep resulting from loss of ventilatory drive. A central apnea is a ≥10-second pause in ventilation with no associated respiratory effort. Generally, >5 such events per hour are considered abnormal.

CSA syndrome is present when a patient has >5 central apneas per hour of sleep and the associated symptoms of disrupted sleep (frequent arousals) and/or hypersomnolence during the day. Because central apneas also may occur in an individual with obstructive apneas, care must be exercised in deciding that CSA rather than OSA is the principal problem. Although there is no absolute standard in this regard, studies of patients with CSA require that >50% of all events be central, with >80% central events often being required.

Cheyne-Stokes respiration (CSR) generally occurs in patients with heart failure, although it has been described in association with neurological disorders, including neurovascular disorders and dementia. It is characterized by a crescendo-decrescendo pattern of breathing with a central apnea or hypopnea at the nadir of ventilatory effort. In patients with heart failure, CSR is believed to result from a high-gain ventilatory control system (increased hypercapnic responsiveness) combined with a prolonged circulation time. This combination leads to unstable ventilatory control and this particular pattern of periodic breathing.

Unstable ventilatory control can promote obstructive events in an individual with a collapsible pharyngeal airway resulting from diminished upper airway muscle activation at the nadir of the cycling respiration. Thus, both central and obstructive events are commonly seen in these patients.

A recent analysis of data from >6000 adults participating in the **Sleep Heart Health Study** noted that hypopneas accompanied by oxyhemoglobin desaturation of $\geq$ 4% were associated with prevalent cardiovascular disease independently of confounding covariates.

In contrast, no association was observed between cardiovascular disease and hypopneas associated with milder desaturation or arousals.

The mechanisms for the linkage between SDB and cardiovascular diseases are not fully determined but surges in sympathetic nerve activity are seen at the end of each apnoeic episode accompanied by large rises in systemic arterial blood pressure (BP). The increased levels of muscle sympathetic nerve activity are diminished by nasal continuous positive airway pressure (CPAP) therapy.

Numerous studies have found a hypercoagulable state in terms of increased clotting factor and platelet activities, and impaired fibrinolysis in coronary artery disease, ischaemic stroke, and SDB.

Common carotid artery intima-media thickness (IMT) has been shown to correlate with traditional vascular risk factors and may predict the likelihood of

acute coronary events and stroke. Recently, carotid artery IMT has been shown to have positive correlations with the severity of SDB.

Screening of patients for SDB can be accomplished by several different methods, although the sensitivity and specificity of these have not been well documented, particularly in cardiovascular patients, and may be expected to be affected by pretest probability. Some of these options include the **Epworth Sleepiness Scale**, **Berlin questionnaire**, overnight oximetry, and devices combining limited respiratory assessment, ECG, and oximetry

In patients with suspected OSA, a definitive diagnosis often requires spending a night in a sleep laboratory during which multiple physiological variables are continuously recorded (polysomnography). These variables generally include sleep staging using the electroencephalogram, electromyogram, electrooculogram, respiration (flow, effort, oxygen saturation), and snoring. With these signals, disordered breathing, in addition to its effect on sleep and oxygenation, can be precisely quantified.

The importance of the cardiovascular response to sleep has been recognized in the recently revised Sleep Scoring Manual from the **American Association of Sleep Medicine (AASM),** which now includes scoring of a continuous-lead ECG as a recommended component of polysomnography.

There is controversy as to whether disordered breathing during sleep can be adequately assessed using fewer signals recorded in the home. Most of these systems are limited to monitoring the respiratory channels listed above and do not include sleep staging or other non respiratory signals.

Obesity is the single most important cause of OSA. Weight loss can lead to a decrease in AHI, improved sleep efficiency, decreased snoring, and improved oxygenation. The most dramatic results have been reported with surgical weight loss. In addition, apnea often is worse in the supine posture, with some patients having OSA only in that position. For patients with "positional apnea," behavioral techniques aimed at keeping the patient in the lateral posture during sleep (an uncomfortable object sewn into the back of the nightshirt or positional alarms) may offer benefit.

Effective treatment of OSA by CPAP has been shown to markedly and acutely decrease BP and sympathetic traffic during sleep. Chronic effects of CPAP treatment are less clear because of the relative lack of robust longitudinal controlled studies. Many of the early studies had no control group or did not include 24-hour ambulatory BP recording. In an observational study of CPAP-treated versus CPAP intolerant patients, no significant differences were evident

in the development of new cases of hypertension in the treated versus untreated group. In addition, short-term CPAP treatment in patients with well-controlled hypertension did not elicit any BP improvement.

Recent studies have more often been placebo controlled, comparing CPAP with either placebo pills or with sham CPAP. BP reduction is either modest or absent in normotensive subjects but may be more evident in hypertensives. Three studies reporting a fall in BP used subtherapeutic (sham) CPAP in the control arm. The largest of all the studies (118patients) reported a reduction of 3.4/3.3 mm Hg (slightly larger during the day than during the night). In patients taking antihypertensive drugs, the 24-hour mean BP fall was about twice as large (6.7 versus 3.3 mm Hg), and the benefit was greater in patients with more severe OSA. The second study found that both placebo CPAP and real CPAP reduced daytime BP equally well but that only real CPAP lowered the nighttime pressure. The third study found that therapeutic CPAP lowered daytime BP by 10.3/11.2 mm Hg more than subtherapeutic CPAP and nighttime pressure by 12.6/11.4 mm Hg.

However, in another study comparing the effects of CPAP in hypertensives with and without OSA, CPAP lowered the nighttime pressure in those with OSA but had no effect on the daytime pressure.

A randomized placebo-controlled study of 1 month of therapeutic CPAP versus subtherapeutic CPAP on ambulatory BP showed no significant changes in systolic, diastolic, daytime, or nighttime BP

Considered together, these studies suggest that there are moderate and variable effects of CPAP on BP in patients with OSA. Patients with more severe OSA, difficult-to-control hypertension, and better CPAP compliance may have more substantial BP reduction with CPAP.

Despite the effectiveness of CPAP in treating OSA, adherence to therapy continues to be a major problem. This relates primarily to the facial interface (mask) and the pressure required to prevent airway collapse, with some patients finding CPAP intolerable.

When CPAP proves unacceptable, oral appliances should be considered. Most such appliances lead to anterior mandibular repositioning, which acts by pulling the lower jaw (and thus the tongue) forward, thereby enlarging the pharyngeal airway.