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Original Article

The study of the effect of C-PAP therapy in type-II diabetic patients with obesity and obstructive sleep apnea

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ABSTRACT: Type II diabetes mellitus (T2DM) is closely associated with Obstructive sleep apnea (OSA) and obesity. Type 2 diabetes and OSA may be pathophysiologically independent conditions although the joint association with obesity or visceral adiposity. There is a consistent relationship between obesity and OSA, which has been reported in 60-90% of OSA patients. The prevalence of obesity increases with a parallel increase in the prevalence of OSA. Continuous positive airway pressure (CPAP) therapy is an effective choice of treatment for OSA, an overnight test, or titration some patients may reduce apnea events by minimizes airway collapse by CPAP. Several studies showed that the effect of drug treatment with 3 months of C-PAP in patients with type 2 diabetes. In the present study, we include 300 patients in different groups, out of the 100 patients undergoing treatment of CPAP therapy minimum for three months. Blood sugar, HbA_{1c}, and lipid profile were measured and an overnight sleep study was done. The obtained data shows the significant effect of therapy on physiological and biochemical parameters. AHI and BMI were highly significant in group II and Group III when compared to group I. FBS, HbA_{1c}, and Lipid profile parameters also gave significance results (p-value <0.001) in group II and group III when compared with healthy subjects (group I).

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INTRODUCTION

Type II diabetes mellitus (T2DM) is closely associated with obesity and OSA. The parallel rise of both obesity and T2DM epidemics called “DIABESITY” presents an increasing and notable threat to the health of our global population. The relationship between OSA and T2DM is complex and only beginning to be understood [1]. The possible pathophysiology can be, the stimulated insulin receptors phosphorylate itself and several substrates, like members of the IRS family (insulin receptor substrate), thus initiating a signaling event.

The inhibition of downstream signaling of the insulin receptor is a primary mechanism through which inflammatory signaling leads to insulin resistance. Inflammatory signaling pathways activated by metabolic stresses originating from intracellular as well as by extracellular signaling molecules. Insulin resistance is the driving force of hyperglycemia in type-2 diabetes.

Obesity is considered to be a major risk factor for the development of T2DM in adults. Increased BMI and abdominal fat distribution are important risk factors for type II diabetes [2].

BMI = or >30 is obesity, obesity can be subdivided in morbid, super morbid and ultra-morbid obesity by the greater BMI >35 kg m⁻², >50 kg m⁻² and >70kg m⁻² respectively, that shows an association between increase risk of various medical conditions such as cardiovascular disease, stroke with diabetes and OSA [3]. Obesity can be a major risk factor for OSA by the upper airway narrowing during sleep directly or indirectly. For example, promoting enlargement of soft tissue structures within and surrounding the airway [4].

Obstructive sleep apnea (OSA) is a common type of sleep disorder, characterized by repetitive upper airway collapse during sleep resulting in arterial hypoxemia and sleep fragmentation. These pauses in breathing called "apneas" (literally, "without breath"), typically last 20 to 40 seconds [5]. OSA is associated with impaired fasting glucose, glucose intolerance, and type2 diabetes, even after accounting age, sex, waist circumference, and obesity [6]. OSA can be categorized in mild, moderate, and severe according to AHI (apnea - hypo apnea index) between 5-15, 15-30, and >30 events per hour respectively.

Continuous positive airway pressure (CPAP) therapy is an effective choice of treatment for OSA, by face mask is attached to a tube in which a computer-controlled airflow generator generates an airstream at a constant pressure. This pressure is prescribed after overnight titration with CPAP by the patient's physician, an overnight test, or titration some patients may reduce apnea events by minimizes airway collapse by CPAP [7]. Several studies showed that the effect of drug treatment with 3 months of C-PAP in patients with type 2 diabetes, shown significant improvements in insulin resistance [8]. Therefore, the use of CPAP for 3 months would be long enough for any changes in insulin resistance or glycemic control by decreasing the number of apnea-related arousals resulting in sympathetic nervous system activation then improved their insulin resistance.

MATERIALS AND METHODS

Table: 1 showing the comparison of biochemical and physiological parameters between group I, group II and group III subjects.

Parameters	GROUP I		GROUP II		GROUP III		P-value
	Mean	± SD	Mean	± SD	Mean	± SD	
BMI	22.67	1.44	32.81	6.82**	31.5	3.96	<0.001
AHI	4.35	2.81	64.46	15.35**	25.98	7.47	<0.001
FBS	74.95	10.42	166.09	30.30**	118.38	24.57	<0.001
HbA₁C	0.25	0.01	0.74	0.15**	0.5	0.05	<0.001
TC	158.72	20.67	253.94	48.64**	185.12	38.85	<0.001
TG	123.04	18.02	271.48	85.48**	156.34	47.94	<0.001
HDL-C	45.37	7.27	30.43	3.44**	35.75	4.9	<0.001
LDL-C	91.31	25.57	158.28	42.07**	119.86	42.74	<0.001
VLDL-C	24.62	3.53	54.52	16.93**	31.26	9.58	<0.001

* Significant at 0.01 (p<0.01) between Group I, Group II and Group III subjects;

** Highly Significant at 0.001 (p<0.001) between Group I, Group II and Group III subject;

NS- Non-Significant

In the present study, we included 300 subjects, in which 100 were healthy individuals (group I), 100 were type II diabetic obese patients suffering from OSA (group II), and 100 types II diabetic obese patients suffering from OSA who were using CPAP therapy (group III). All diabetic patients were taking oral hypoglycemic drugs. Healthy subjects were selected from the individuals who came for a sleep study for another problem, they were of the same age. The written consent of patients was also taken. All ethical measures were taken before and during the study. Biochemical parameters like Fasting Blood Sugar (FBS), Glycosylated hemoglobin (HbA₁c), Total Cholesterol (TC), Triglyceride (TG), High-density lipoprotein cholesterol (HDL-c), Low-density lipoprotein cholesterol (LDL-c), Very low-density lipoprotein cholesterol (VLDL-c), Insulin and Insulin resistance by HOMA-IR were measured. Physical parameters like AHI (Apnea- hypo apnea index by overnight polysomnography and BMI were measured.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS version 21. Demographic and clinical data are reported as mean ± standard deviation (SD). Statistical comparisons between group means were done by the ANOVA.

RESULT

Table 1 showing the comparison of biochemical and physiological parameters between group I, group II and group III subjects. AHI and BMI were highly significant in group II and Group III when compared to group I. FBS, HbA₁C, and Lipid profile parameters also gave significance results (p-value <0.001) in group II and group III when compared with healthy subjects (group I). The level of all parameters was significantly lower in group III when compared to group II.

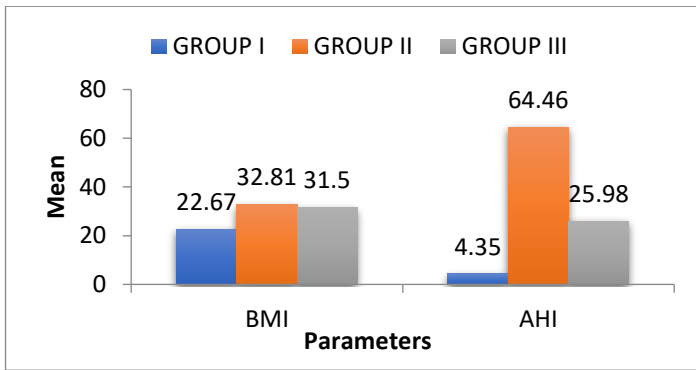


Fig. 1: showing the status of BMI and AHI in group I, group II and group III subjects.

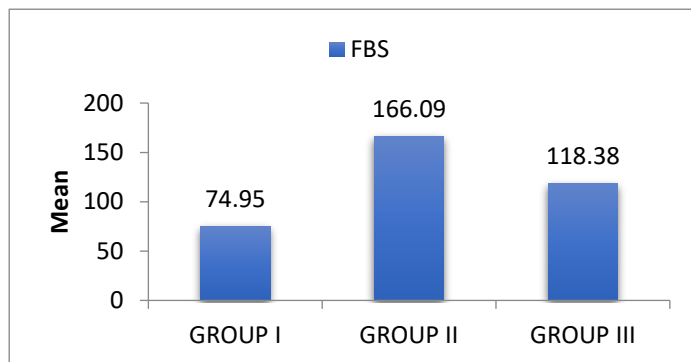


Fig. 2: showing the status of Fasting Blood Sugar in group I, group II and group III subjects.

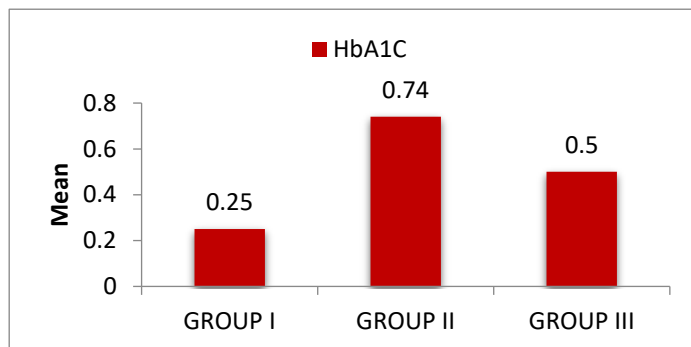


Fig. 3: showing the status of HbA1c in group I, group II and group III subjects.

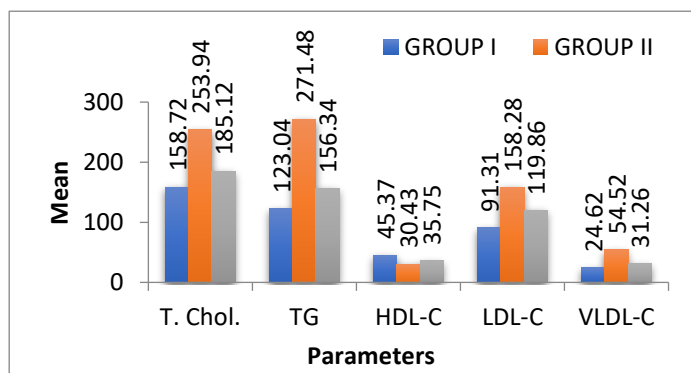


Fig. 4: showing the status of lipid profile in group I, group II and group III subjects.

DISCUSSION

Obesity provides a common pathophysiological mechanism for both OSA and the metabolic syndrome like glucose intolerance, dyslipidemia, hypertension, systemic inflammation all are the significant risk factors for atherosclerosis [9]. On the other hand, type 2 diabetes and OSA may be pathophysiologically independent conditions with joint association with obesity or visceral adiposity [10,11]. Like the common association with obesity, both OSA and T2DM have been independently implicated in contributing to greater morbidity and mortality of the cardiovascular disease. Sleep disorder breathing is pathologically related to impaired glucose homeostasis and the CPAP can be an important therapeutic approach for diabetic patients with SDB [12]. Adriana et al. found that evidence for support a potential role of OSA in the development of insulin resistance, increase diabetic risk, and altered glycemic control in patients with T2DM [13]. A previous study by Nikolaos et al., Showed that both fasting blood glucose and HbA1c exhibited a significant correlation with AHI [14]. The intermittent hypoxemia associated with OSA has been shown to produce surges of sympathetic activation, whereas arousals during sleep can induce bursts of cortisol release in normal humans. Our study supports a previous study finding done by Tamura et al., they found that obstructive sleep apnea and sleep-related hypoxia are associated with higher HbA1c concentrations, irrespective of glycaemic status (normal glucose tolerance, impaired glucose tolerance, or overt diabetes mellitus) [15]. Our findings are also similar to previous reports showing that similar impairments in glycaemic status in obstructive sleep apnea patients with or without diabetes [16]. Hassaballa et al. reported a significant decrease in the HbA1c after at least 3 months of CPAP therapy in a group of obese type 2 diabetics, but their findings were based on a retrospective chart review [17].

Obesity is associated with anatomic alterations that predispose to upper airway obstruction during sleep. These alterations may accrue from adiposity around the pharynx and torso as follows. Increases in neck circumference and fat deposited around the upper airway in obesity might narrow the upper airway with increased upper airway collapsibility, and especially central obesity has been associated with reductions in lung volume also, which leads to a loss of caudal traction on the upper airway, cause greater severity of Obstructive sleep apnea. Thus, obesity imposes mechanical loads on both the upper airway and respiratory system that predispose to upper airway narrowing, collapse, and airflow obstruction during sleep [18]. In the present study, the patterns of lipid profile parameters in type-2 diabetic subjects were also measured and we observed that mean values of TC, TG, HDL-c, and LDL-c were found significantly higher in group II and group III as compared to healthy subjects (group I). The results show the higher value of lipid profile in group II in comparison to group III. OSA, even in patients without obesity, may cause hypertension, systemic inflammation, and insulin resistance. The high prevalence of OSA in patients with type 2 diabetes renders these patients susceptible to complications from both diseases and places them at high risk of atherosclerosis and cardiovascular disease [19]. Diabetic patients with OSA may experience worsening of their glucose control, which improves when the OSA is appropriately treated [20].

The effect of C-PAP in OSA patients cannot be forgotten, for that, we have included the diabetic obese patients with OSA who are using the C-PAP therapy for or more than three months (Group-III). The level of physiological parameters like AHI and BMI along with biochemical parameters like FBS, HbA1c, Lipid Profile, Insulin resistance were lower in these patients when compared with Diabetic obese patients with OSA (group II) who was not using any C-PAP therapy. But the level of all these parameters was significantly elevated when compared to healthy subjects (group I). So that we can say the C-PAP is directly or indirectly reduce the severity of OSA along with T2DM and obesity. A study of Drager et al., showed that the significant improvement in carotid intima-media thickness, suggesting a potential role for C-PAP therapy in reversing endothelial damage due to obstructive sleep apnea and the metabolic syndrome [21].

In conclusion, there is a high prevalence of obesity and Sleep Disorder Breathing (SDB) in diabetic patients. The results of our study support the hypothesis that the treatment of significant SDB in patients with impaired glucose tolerance, or impaired fasting glucose levels, might prevent or delay progression to diabetes. Evaluating this hypothesis could have significant implications for reducing cardiovascular risk in a large number of patients with SDB, obesity, and insulin resistance. Our results suggest that the treatment of SDB by C-PAP in these patients will have an important therapeutic benefit. The degree of HbA1c reduction that we observed with the treatment of SDB could have important implications for the development of diabetic complications. Even more provocatively, the efficacy of CPAP treatment of SDB in improving glucose homeostasis suggests an important pathophysiological role for SDB in producing or worsening, impaired glucose homeostasis.

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