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COMPREHENSIVE EVALUATION OF ADIPO-METABOLIC AND INFLAMMATORY RESPONSES TO CONTINUOUS POSITIVE AIRWAY PRESSURE COMBINED WITH STRUCTURED LIFESTYLE MODIFICATION AND PRANAYAMA IN OBESE NON-DIABETIC PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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ABSTRACT

Background: Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder closely associated with obesity, chronic low-grade inflammation, and adipokine dysregulation. Although continuous positive airway pressure (CPAP) effectively alleviates upper airway obstruction and improves sleep-disordered breathing, its effects on obesity-related metabolic abnormalities are often limited. Adjunctive lifestyle interventions and breathing exercises may enhance therapeutic outcomes by improving metabolic homeostasis, inflammatory status, and sleep quality.

Objectives: To evaluate and compare the effects of CPAP alone, CPAP combined with structured lifestyle modification, and CPAP combined with pranayama on polysomnographic parameters, anthropometric indices, adipokines, inflammatory biomarkers, and lipid profile in obese non-diabetic patients with obstructive sleep apnea.

Methods: This prospective interventional study included 61 obese non-diabetic adults with obstructive sleep apnea confirmed by overnight polysomnography. After confirmation of eligibility and obtaining written informed consent, participants were consecutively enrolled and allocated to one of the three intervention groups according to the predefined treatment protocol. Group 1 received CPAP alone (n = 17), Group 2 received CPAP combined with structured lifestyle modification (n = 24), and Group 3 received CPAP combined with pranayama (n = 20).

Anthropometric measurements, polysomnographic indices (apnea-hypopnea index, sleep efficiency, sleep stages, mean oxygen saturation and Epworth Sleepiness Scale), adipokines (leptin, adiponectin and ghrelin), interleukin-6, and lipid profile were assessed before and after the intervention. Data were analyzed using paired Student's *t*-test, one-way ANOVA with appropriate post-hoc comparisons, and Pearson correlation analysis. A p value <0.05 was considered statistically significant.

Results: All three interventions markedly improved polysomnographic, anthropometric, metabolic, inflammatory, and adipokine parameters ($p<0.05$). Significant reductions were observed in apnea-hypopnea index, Epworth Sleepiness Scale scores, leptin, ghrelin, interleukin-6, body mass index, and atherogenic lipid indices, accompanied by significant increases in adiponectin, sleep efficiency, rapid eye movement sleep, and mean nocturnal oxygen saturation. Overall, the CPAP plus structured lifestyle modification group demonstrated the greatest improvements in anthropometric measurements, adipokine profile, inflammatory status, and lipid parameters, whereas the CPAP plus pranayama group showed the most pronounced improvement in apnea-hypopnea index, rapid eye movement sleep, mean oxygen saturation, and selected sleep architecture parameters. Correlation analysis demonstrated significant associations between reductions in apnea-hypopnea index and improvements in sleep efficiency, oxygen saturation, Epworth Sleepiness Scale scores, adipokines, and inflammatory markers.

Conclusion: CPAP therapy significantly improved respiratory function, metabolic profile, inflammatory status and adipokine homeostasis in obese non-diabetic patients with obstructive sleep apnea. The addition of structured lifestyle modification produced the greatest overall improvement in cardiometabolic and anthropometric outcomes, while adjunctive pranayama provided additional benefits in selected polysomnographic and oxygenation parameters. These findings support the integration of structured lifestyle modification with CPAP as a comprehensive management strategy for obesity-associated OSA, while suggesting a complementary role for pranayama in optimizing sleep physiology and nocturnal oxygenation.

KEYWORDS: Obstructive sleep apnea; Continuous positive airway pressure; Lifestyle modification; Pranayama; Obesity; Adipokines; Leptin; Adiponectin; Ghrelin; Interleukin-6; Polysomnography.

INTRODUCTION

Sleep is a basic physiological activity that is crucial for the equilibrium of metabolism, endocrinology, neurocognition, cardiovascular and immunological systems. In regular sleep, various restorative processes control energy balance, hormone production, metabolism, protein synthesis, tissue repair, and immunological function. However, inadequate quantity or quality of sleep interferes with these physiological mechanisms and results in activation of the sympathetic nervous system, hormonal imbalance, oxidative stress and systemic inflammation. There is accumulating evidence that chronic sleep disorders are associated with obesity, hypertension, cardiovascular disease, metabolic dysfunction and increased all-cause mortality, emphasizing the significance of sleep as a significant determinant of general health [1].

Obstructive sleep apnea (OSA) is the most prevalent type of sleep disordered breathing in a wide range of sleep associated illnesses. OSA is characterized by recurrent episodes of total or partial collapse of the upper airway during sleep resulting to intermittent hypoxia recurrent arousals sleep fragmentation and substantial variations in intrathoracic pressure. Such repetitive episodes lead to a cascade of pathophysiological reactions including sympathetic overactivity, oxidative stress, endothelial dysfunction, systemic inflammation and metabolic dysregulation. OSA is, therefore, increasingly considered as a multiorgan illness that impacts not only respiratory physiology but also cardiovascular, metabolic and neurocognitive function [2]. Obesity is a major health problem worldwide due to its increasing prevalence and the hefty load it throws on the health system. It is estimated that around 1 billion persons aged 30–69 years have OSA worldwide, of whom around 425 million have moderate-to-severe illness requiring medical intervention. OSA is quite widespread yet remains greatly underdiagnosed, leading to delays in adequate treatment and an increased risk of long-term consequences. Untreated OSA independently has been related with hypertension, coronary artery disease, heart failure, cardiac arrhythmias, stroke, poor cognitive performance, depression and a loss in quality of life. Daytime sleepiness and reduced attentiveness further decrease work productivity and increase the likelihood of occupational and road traffic accidents and consequently impose a substantial socioeconomic cost on health care systems globally [3]. Obesity is becoming common, dietary habits are changing, physical activity is decreasing and urbanisation is gathering speed. All this has led to a steady increase in the prevalence of OSA during the last two decades in India. But there is a paucity of knowledge regarding sleep problems and absence of professional sleep diagnostic facilities in many places. Consequently, many affected individuals remain undetected until they develop serious cardiometabolic problems. Increased visceral fat, increased body fat percentage, and cranial morphological variance are anthropometric traits that predispose Asian Indians to upper airway blockage at a significantly lower body mass index (BMI) than Western populations. The ethnic characteristics emphasize the significance of early detection and treatment of OSA in the Indian population [4].

Obesity is the most important modifiable predictor among numerous risk factors for OSA and is considered a primary driver of the increasing global prevalence of OSA. Due to the tight association between obesity and chronic non-communicable diseases, the World Health Organization has classified obesity as one of the main public health challenges of the twenty-first century. Excess fat in the tissues of the neck, tongue and throat can constrict the upper airway and make it more likely to collapse and become blocked again during sleep. Central obesity diminishes functional residual capacity and lung volume, adversely affects ventilatory mechanics and increases vulnerability to sleep-disordered breathing. Large prospective studies have consistently shown a direct link between increased BMI and worsening severity of OSA. Reduction of even a small weight can dramatically enhance respiratory function and reduce illness severity [5].

Obesity is today considered not only a mechanical condition but also a chronic inflammatory and endocrine disease. Adipose tissue is an active endocrine organ secreting several bioactive mediators controlling hunger, energy expenditure, vascular function and immunological responses. An imbalance of these mediators results in a pro-inflammatory, metabolically adverse environment that contributes significantly to the etiology of obesity-related OSA and its cardiometabolic consequences. The elucidation of these biological interactions is of increasing importance for the discovery of novel biomarkers and therapeutic targets that could improve disease management and long-term clinical outcomes [5]. The pathophysiological link between obesity and obstructive sleep apnea is not only due to mechanical restriction of the upper airway but also involves significant endocrine, inflammatory and metabolic alterations. In the past two decades, adipose tissue has been identified as a highly active endocrine organ, rather than a passive energy reserve. Adipocytes produce and secrete several biologically active chemicals, called adipokines, and many inflammatory cytokines that affect hunger, energy balance, lipid metabolism, vascular function and immunological responses. Obesity results in excess buildup of adipose tissue, leading to adipocyte hypertrophy and macrophage infiltration, which causes dysregulation of these endocrine mediators and chronic low-grade systemic inflammation. Changes have an important role in the development and progression of obesity-related OSA and its metabolic and cardiovascular consequences [6].

Obesity is associated with metabolic dysregulation through numerous adipokines, the most explored of which is leptin. Leptin is a hormone released largely by white adipose tissue that regulates appetite and energy expenditure through hypothalamic signalling pathways, decreasing food intake and increasing satiety. Under normal physiological conditions, circulating leptin levels are correlated with body fat mass and play a role in the maintenance of long-term energy homeostasis. Conversely, obesity is characterized by hyperleptinaemia with leptin resistance, where high levels of circulating leptin do not produce expected physiologic effects. Persistent leptin resistance results in ongoing weight gain, decreased energy expenditure and increasing obesity. Leptin also stimulates the sympathetic nervous system and affects respiratory regulation in addition to its metabolic effects. Experimental and clinical findings suggest that defective leptin signalling may decrease ventilatory responsiveness, increase upper airway collapsibility, and aggravate OSA severity.

Leptin may also have pro-inflammatory effects by boosting cytokine production and endothelial activation and so represents an essential mechanistic link between obesity, systemic inflammation and sleep-disordered breathing [6].
Adiponectin, however, is an adipocyte-derived hormone with potent anti-inflammatory, anti-oxidative and insulin-sensitizing effects. Compared with leptin, circulating levels of adiponectin decrease with increasing obesity. Lower adiponectin levels have been associated with visceral obesity, endothelial dysfunction, and increased cardiovascular risk. Adiponectin activates AMP-activated protein kinase (AMPK) to stimulate glucose uptake, fatty acid oxidation and suppression of inflammatory signal transduction pathways, thereby preserving metabolic homeostasis. In multiple investigations, patients with obesity-related OSA had considerably reduced levels of adiponectin, and the drop was associated with the severity of the condition and intermittent hypoxia. Therefore, the increase in adiponectin levels following effective therapy might be a marker of enhanced adipose tissue function and general metabolic health [6].
Ghrelin, a peptide hormone predominantly generated by the stomach, is another major moderator of energy homeostasis. Ghrelin stimulates hunger, growth hormone release, gastrointestinal motility and energy balance. Changes in circulating ghrelin concentrations have been seen for both sleep restriction and sleep fragmentation, which may lead to increased appetite and calorie consumption. However, the published data regarding the levels of ghrelin in individuals with OSA are varied, due to the differences in the obese status, severity of the disease, dietary variables and treatment modalities. However, the simultaneous evaluation of ghrelin, leptin and adiponectin provides superior insight into hunger regulation and endocrine dysfunction in the setting of obesity-related OSA [2]. In addition to chronic systemic inflammation, adipokine imbalance is another important player in the etiology of obesity-associated OSA. Interleukin-6 (IL-6) is an important indicator of obesity, intermittent hypoxia and metabolic dysfunction among inflammatory mediators. Adipocytes, infiltrating macrophages, endothelial cells, and activated immune cells produce IL-6. Excess adiposity leads to chronic secretion of IL-6, and recurrent intermittent hypoxia further potentiates inflammatory signalling through activation of the hypoxia-inducible factor-1α (HIF-1α) and nuclear factor-kappa B (NF-κB) pathways. Sustained elevation of IL-6 has been linked to endothelial dysfunction, oxidative stress, vascular inflammation, and poor cardiovascular outcomes. Thus, circulating IL-6 is a good predictor of inflammation activity and severity of disease in patients with obesity related OSA [3,6].
In moderate to severe obstructive sleep apnea, the gold standard therapy with continuous positive airway pressure (CPAP) is universally acknowledged. CPAP gives a constant positive pressure to the airway throughout the respiratory cycle, preventing collapse of the upper airway during sleep, eliminating recurring obstructive events and restoring normal breathing. Clinical investigations have indicated that CPAP therapy reduces the apnea hypopnea index (AHI), increases nocturnal oxygen saturation, normalizes sleep architecture and treats excessive daytime sleepiness. Besides the benefits on the respiratory system, CPAP decreases sympathetic nervous system activation, reduces intermittent hypoxia and oxidative stress, resulting in enhanced endothelial function and cardiovascular health. These physiological benefits make CPAP the mainstay of OSA management and increase quality of life for the patients [2].
CPAP has been shown to be beneficial in treating upper airway blockage but its influence on metabolic and inflammatory disorders is less reliable. Several studies have showed that long-term CPAP therapy decreases circulating leptin and IL-6 concentrations and has a minor effect on insulin sensitivity. Other studies, however, have revealed little or no significant changes in adipokine concentrations or metabolic indices despite significant improvement in respiratory function. The disparities in results are probably accounted for by differences in severity of obesity, compliance with treatment, duration of CPAP use and baseline metabolic condition. Importantly, CPAP successfully ameliorates intermittent hypoxia but does not directly address excess adiposity, which remains the primary underlying source of chronic inflammation and metabolic dysfunction in obese persons with OSA [3].
Therefore, systematic weight loss intervention has become an integral feature of modern OSA management. Lifestyle adjustment, including dietary calorie restriction, increased physical activity, and behavioural counselling, can reduce body weight and ameliorate various pathophysiological pathways associated for OSA. Reduction of visceral adiposity improves pulmonary function, respiratory mechanics and upper airway constriction. Simultaneously, weight loss normalizes adipose tissue endocrine function by reducing leptin resistance, increasing adiponectin secretion, and decreasing systemic inflammatory cytokine production. Several clinical studies have demonstrated the importance of even modest weight loss in reducing the severity of OSA and metabolic health. This highlights the need of continuous lifestyle management in the obese patient [1,6].
Emerging evidence suggests that combination CPAP and organized weight loss treatment may provide greater therapeutic benefit than either intervention alone. Weight loss tackles the obesity that causes the chronic inflammation, endocrine dysfunction and metabolic impairment, whereas CPAP quickly resolves the upper airway blockage and intermittent hypoxia. Together, these therapies target the respiratory symptoms and the metabolic basis of obesity-related OSA. Combined therapy was related with larger changes in body weight, waist circumference, inflammatory state, endothelial function and cardiometabolic risk variables compared with CPAP alone. However, there is minimal and frequently conflicting information about the influence of aerobic exercise on adipokine modulation and insulin resistance, and more research is needed [3,6].
Recent breakthroughs in sleep medicine have increasingly recognized OSA as a complex systemic problem rather than just a mechanical disease of the upper airway. The metabolic and cardiovascular consequences are accelerated by the continuous interaction between chronic intermittent hypoxia, oxidative stress, sympathetic overactivity, adipose tissue malfunction and low-grade systemic inflammation. Therefore, evaluation of respiratory measures alone could underestimate the real biological effect of therapeutic therapies. A thorough assessment of endocrine, inflammatory and metabolic indicators [2] is increasingly being realized as a more informative technique to explain illness causes and track therapy response.

Important advances have been made in studying obesity-associated OSA, yet there are significant gaps in knowledge. Previous studies have primarily concentrated on changes of the respiratory indices (AHI, oxygen saturation, etc.). There are relatively few studies that have comprehensively assessed multiple adipokines, inflammatory mediators and metabolic biomarkers after combined CPAP and structured weight-loss intervention. Furthermore, various published studies have recruited mixed populations of diabetic and non-diabetic participants, making it challenging to separate metabolic abnormalities specifically linked with obesity-related OSA from those related to diabetes mellitus. There is a paucity of research about these relationships in obese non-diabetic patients particularly from Indian community. Filling these gaps may increase our understanding of the biological modifications generated by treatment and allow us to identify therapeutically effective biomarkers to track therapeutic response [3,4]. To our knowledge, no previous Indian investigation has assessed polysomnography, adipokines, IL-6, and lipid profile simultaneously after three different CPAP-based therapies in non-diabetic obese OSA patient.

MATERIALS AND METHODS

Study Design and Setting

This prospective interventional study was conducted in the Departments of Biochemistry and Respiratory Medicine at MGM Medical College and Hospital, Kamothe, Navi Mumbai, Maharashtra, India, over an 18-month period [2024 to 2026]. The study was designed to evaluate and compare the effects of three CPAP-based therapeutic strategies—CPAP alone, CPAP combined with structured lifestyle modification, and CPAP combined with pranayama—on polysomnographic parameters, adipo-metabolic and inflammatory biomarkers, and cardiometabolic risk factors in obese non-diabetic patients with obstructive sleep apnea (OSA).

The study protocol was approved by the Institutional Ethics Committee of MGM Medical College and Hospital, Kamothe, Navi Mumbai. Written informed consent was obtained from all participants before enrolment.

Type of Study: The present study was a prospective, non-randomized interventional study.

Study Population: Participants were recruited consecutively from the Departments of Respiratory Medicine and General Medicine after clinical evaluation and overnight attended polysomnography. Individuals fulfilling the predefined inclusion and exclusion criteria were enrolled in the study.

Inclusion Criteria: Adults aged 30–65 years of either sex with obesity (BMI ≥25 kg/m² according to the Asian Indian obesity criteria) and newly diagnosed moderate-to-severe obstructive sleep apnea (Apnea–Hypopnea Index ≥15 events/hour) confirmed by overnight polysomnography were eligible. Only non-diabetic individuals (no previous diagnosis of diabetes mellitus and HbA1c <6.5% according to the American Diabetes Association criteria) who were willing to use CPAP therapy and participate in the assigned intervention programme were included.

Exclusion Criteria: Participants with previously diagnosed type 1 or type 2 diabetes mellitus, pregnancy or lactation, chronic kidney or liver disease, heart failure, chronic inflammatory or autoimmune disorders, active infection, malignancy, long-term corticosteroid or immunosuppressive therapy, previous CPAP therapy, history of bariatric surgery, current use of anti-obesity medications, severe psychiatric illness affecting treatment compliance, or inability to complete the follow-up period were excluded.

Sample Size: The sample size was calculated using G*Power software version 3.1, assuming a moderate effect size (0.50), a 95% confidence level, 80% statistical power, and a two-sided significance level of 5%. The minimum required sample size was 54 participants. After accounting for an anticipated dropout rate of 10–15%, a total of 61 obese non-diabetic patients with moderate-to-severe OSA confirmed by overnight polysomnography were enrolled.

Following confirmation of eligibility and written informed consent, participants were consecutively enrolled and allocated to one of three intervention groups according to the predefined intervention protocol. Group 1 received CPAP therapy alone (n = 17), Group 2 received CPAP combined with structured lifestyle modification (n = 24), and Group 3 received CPAP combined with pranayama (n = 20).

Clinical Assessment: At baseline, demographic and clinical information was recorded, including age, sex, medical history, medication history, smoking status, alcohol consumption, height, weight, body mass index (BMI), waist circumference, hip circumference, waist-to-hip ratio, neck circumference, and blood pressure. Anthropometric measurements were repeated at the end of the intervention period.

Diagnosis of Obstructive Sleep Apnea: All participants underwent overnight attended Level-I polysomnography (PSG) in the sleep laboratory. The recorded sleep variables included total sleep time, sleep efficiency, sleep stages (N1, N2, N3, and REM sleep), Apnea–Hypopnea Index (AHI), Oxygen Desaturation Index (ODI), minimum oxygen saturation, mean nocturnal oxygen saturation, and arousal index.

Continuous Positive Airway Pressure (CPAP) Therapy: Participants diagnosed with moderate-to-severe OSA received auto-adjusting continuous positive airway pressure (Auto-CPAP) therapy following pressure titration. Before initiation of therapy, all participants underwent CPAP education, mask fitting, device familiarization, and adherence counselling. Adequate CPAP adherence was defined as device usage for at least 6-8 hours per night on at least 70% of monitored nights.

The intervention period was six months. Participants received their assigned intervention (CPAP alone, CPAP plus structured lifestyle modification, or CPAP plus pranayama) throughout the six-month study period. Anthropometric, polysomnographic, and biochemical assessments were performed at baseline and repeated after completion of the 6-month intervention.

Structured Lifestyle Modification Programme

Participants allocated to the CPAP plus structured lifestyle modification group (Group 2) received individualized dietary counselling and a structured lifestyle intervention throughout the study period. The programme aimed to achieve a mean

weight reduction of approximately 7%, with participants encouraged to lose at least 10% of their baseline body weight where feasible. Dietary intervention included meal replacement with a liquid shake for two meals per day (usually breakfast and lunch), one healthy snack, and a regular evening meal comprising familiar cuisine. Participants were encouraged to consume a diet rich in fruits, vegetables, and other low-energy-density foods. Physical activity recommendations included progressive exercise beginning with regular walking, followed by brisk walking or equivalent aerobic activity. Participants were instructed to achieve at least 175 minutes per week of moderate-intensity physical activity by the sixth month and to gradually increase their daily step count by approximately 250 steps per week until reaching a target of at least 10,000 steps per day. Lifestyle counselling was reinforced during scheduled follow-up visits.

Pranayama Intervention

Participants allocated to the CPAP plus pranayama group (Group 3) received CPAP therapy together with a structured pranayama programme. Participants were instructed to practice pranayama breathing exercises for at least 200 minutes per week throughout the intervention period and were advised to maintain regular practice in addition to CPAP therapy. Smoking cessation counselling was also provided where appropriate. CPAP therapy was recommended for 6–8 hours each night throughout the study period.

General Lifestyle Advice

All participants, irrespective of study group, were encouraged to maintain regular sleep schedules, avoid smoking and alcohol consumption, and comply with CPAP therapy throughout the study period.

Blood Sample Collection

Following an overnight fast of 10–12 hours, approximately 10 mL of venous blood was collected from each participant at baseline (before intervention) and again at the end of the 6-month intervention period. Serum was separated by centrifugation at 3000 rpm for 10 minutes and stored at −80°C until biochemical analysis.

Biochemical Analysis

Serum lipid profile (total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, and VLDL-cholesterol) was measured using commercially available enzymatic reagent kits on a fully automated clinical chemistry analyzer. Serum leptin, adiponectin, ghrelin, and interleukin-6 (IL-6) concentrations were measured using commercially available sandwich enzyme-linked immunosorbent assay (ELISA) kits (Diagnostic Biochem Canada Inc., Canada, CatbNo. CAN-L-4260, E1550Hu, E3091Hu, E009OHu) according to the manufacturer's instructions.

Statistical Analysis

Statistical analysis was performed using SPSS version 24.0. Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data. Categorical variables were presented as frequencies and percentages.

Data normality was assessed using the Shapiro–Wilk test. Comparisons between baseline and post-intervention measurements within each group were performed using the paired Student's *t*-test for normally distributed variables or the Wilcoxon signed-rank test for non-parametric variables. Comparisons among the three intervention groups were performed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test where appropriate. Pearson's correlation analysis was used to evaluate associations between continuous variables. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

Table 1. Comparison of Polysomnography (PSG) and ESS (Epworth Sleepiness Scale) Score in Non-Diabetic Obese with OSA in G1, G2 and G3 groups.

Groups/Variance	Only CPAP (G1)		CPAP + Lifestyle (G2)		CPAP + Pranayama (G3)	
	Baseline	After 6 Months	Baseline	After 6 Months	Baseline	After 6 Months
AHI	42.20 ± 28.41	14.54 ± 4.93**	40.45 ± 35.01	10.84 ± 8.55**	42.75 ± 20.41	6.83 ± 3.16***
SE %	79.97 ± 13.57	84.56 ± 10.14*	82.24 ± 9.11	87.49 ± 7.85**	82.87 ± 4.09	89.75 ± 2.77***
Stage I %	16.66 ± 10.77	10.84 ± 3.36	15.02 ± 10.13	10.23 ± 6.51	14.15 ± 9.55	6.54 ± 2.20*
Stage II %	58.81 ± 11.43	55.40 ± 5.69	56.71 ± 11.25	51.96 ± 5.67	48.61 ± 8.40	51.70 ± 4.66
Stage III %	14.34 ± 10.93	15.64 ± 4.59	11.97 ± 9.23	16.64 ± 6.41	22.82 ± 11.76	19.86 ± 4.59
REM %	10.04 ± 7.00	19.90 ± 3.82*	16.74 ± 10.67	20.95 ± 8.06*	17.23 ± 4.90	22.06 ± 1.68*
SpO_2 %	92.11 ± 2.32	94.44 ± 1.63**	91.64 ± 4.33	94.56 ± 2.26**	91.32 ± 4.62	97.12 ± 1.00**
ESS	13.71 ± 4.75	6.43 ± 2.15***	14.79 ± 5.35	5.07 ± 3.47***	14.25 ± 3.33	4.25 ± 3.14***

Values are expressed as mean ± SD.

***p<0.001 (Very highly significant), **p<0.01 (Highly significant), *p<0.05 (Significant).

AHI: Apnea–Hypopnea Index; SE: Sleep Efficiency; REM: Rapid Eye Movement sleep; SpO_2: Mean Oxygen Saturation; ESS: Epworth Sleepiness Scale.

Table 2. Comparison of Anthropometric Evaluation in Non-Diabetic Obese with OSA in G1, G2 and G3 Groups

Groups/Variance	Only CPAP (G1) Baseline	Only CPAP (G1) After 6 Months	CPAP + Lifestyle (G2) Baseline	CPAP + Lifestyle (G2) After 6 Months	CPAP + Pranayama (G3) Baseline	CPAP + Pranayama (G3) After 6 Months
BMI	31.27 ± 2.75	29.50 ± 2.69***	30.97 ± 5.19	28.42 ± 4.63***	30.61 ± 2.44	27.08 ± 1.65***
Waist Circumference (cm)	112.43 ± 15.06	108.57 ± 13.61***	109.14 ± 11.33	104.57 ± 10.10***	109.25 ± 7.07	103.08 ± 6.46***
Hip Circumference (cm)	116.14 ± 16.16	112.57 ± 14.34***	113.00 ± 8.90	109.07 ± 8.52***	113.67 ± 7.24	107.50 ± 7.85***
W/H Ratio	0.97 ± 0.02	0.96 ± 0.02	0.96 ± 0.02	0.96 ± 0.03	0.96 ± 0.02	0.96 ± 0.04
Neck Circumference (cm)	40.00 ± 1.38	38.93 ± 1.17***	39.46 ± 2.78	38.14 ± 2.55***	39.08 ± 1.31	37.38 ± 1.19***

Values are expressed as mean ± SD.
*** p<0.001 (Very highly significant), ** p<0.01 (Highly significant), * p<0.05 (Significant).

Table 3. Comparison of Lipid Profile in Non-Diabetic Obese with OSA in G1, G2 and G3 groups.

Groups	Only CPAP (G1)		CPAP + Lifestyle Change (G2)		CPAP + Pranayama (G3)	
Variance	Baseline	After 6 Months	Baseline	After 6 Months	Baseline	After 6 Months
TCH (mg/dL)	206.40 ± 75.97	180.71 ± 65.01*	175.95 ± 37.03	166.90 ± 24.44*	167.12 ± 30.62	158.00 ± 24.77**
TG (mg/dL)	146.31 ± 60.56	125.09 ± 44.75**	185.53 ± 126.15	146.64 ± 81.16*	116.78 ± 59.12	105.08 ± 46.95*
HDL (mg/dL)	33.13 ± 19.34	40.56 ± 20.63*	32.34 ± 9.65	37.29 ± 7.27*	37.73 ± 15.19	40.33 ± 10.04*
LDL (mg/dL)	151.92 ± 52.17	124.00 ± 45.97*	113.21 ± 37.00	102.77 ± 22.15**	100.53 ± 41.87	93.25 ± 35.08*
VLDL (mg/dL)	29.25 ± 12.06	22.97 ± 6.94**	29.25 ± 13.81	21.50 ± 9.41***	23.18 ± 12.48	19.91 ± 8.89***

Values are expressed as mean ± SD.
***p<0.001 (Very highly significant), **p<0.01 (Highly significant), *p<0.05 (Significant).
TCH: Total Cholesterol; TG: Triglyceride; HDL: High-density Lipoprotein Cholesterol; LDL: Low-density Lipoprotein; VLDL: Very Low-density Lipoprotein.

Table 4. Comparison of Serum Adiponectin, Ghrelin, Leptin & IL-6 levels in Non-Diabetic Obese with OSA in G1, G2 and G3 groups.

Groups	Only CPAP (G1)		CPAP + Lifestyle Change (G2)		CPAP + Pranayama (G3)	
Variance	Baseline	After 6 Months	Baseline	After 6 Months	Baseline	After 6 Months
Leptin (ng/mL)	10.07 ± 4.57	7.41 ± 3.17*	13.12 ± 7.53	9.63 ± 5.03*	14.73 ± 7.26	8.48 ± 4.02***
Adiponectin (mg/L)	5.83 ± 2.38	11.64 ± 4.01***	5.82 ± 3.59	10.12 ± 4.30***	5.98 ± 2.17	10.54 ± 3.36***
Ghrelin (pg/mL)	31.2 ± 5.51	23.4 ± 6.43***	31.4 ± 5.67	20.2 ± 6.44***	31.3 ± 5.33	17.6 ± 7.24***
IL-6 (pg/mL)	5.66 ± 2.40	3.91 ± 1.58***	6.88 ± 3.83	4.25 ± 1.93***	5.08 ± 2.34	3.13 ± 1.06***

Values are expressed as mean ± SD.
***p<0.001 (Very highly significant), **p<0.01 (Highly Significant), *p<0.05 (Significant).

Table 5. Correlation between AHI with Polysomnography and ESS in Non-Diabetic Obese with OSA in G1, G2 and G3 groups.

Group	Polysomnography and ESS	r value
G1. CPAP Group	AHI	1
	Sleep Efficiency %	-0.85**
	Stage I %	-0.41*
	Stage II %	0.25
	Stage III %	-0.19
	REM %	-0.45*
	Mean SpO_2 %	-0.60**
	ESS	0.60*

G2. CPAP + Lifestyle Change Group	AHI	1
	Sleep Efficiency %	-0.61*
	Stage I %	-0.46*
	Stage II %	0.18
	Stage III %	0.40*
	REM %	-0.54*
	Mean SpO_2 %	-0.79**
	ESS	0.76**
G3. CPAP + Pranayama Group	AHI	1
	Sleep Efficiency %	-0.72**
	Stage I %	-0.01
	Stage II %	-0.16
	Stage III %	0.49*
	REM %	-0.59*
	Mean SpO_2 %	-0.81**
	ESS	0.78**

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is highly significant at the 0.01 level (2-tailed).

DISCUSSION

The present study was designed to evaluate the effects of three treatment methods, viz. CPAP alone (G1), CPAP with structured lifestyle modification (G2) and CPAP with pranayama (G3) on polysomnographic parameters and daytime sleepiness in obese non-diabetic patients with moderate-to-severe obstructive sleep apnea (OSA). All 3 therapies resulted in clinically relevant changes in sleep architecture and respiratory metrics at 6 months. However, the highest benefits were continuously shown in the CPAP + Pranayama group (G3) followed by the CPAP + Lifestyle group (G2) whereas CPAP alone (G1) showed lesser but statistically significant improvements. These results show that supplementary non-pharmacological therapies may increase the therapeutic advantages of CPAP by targeting both respiratory irregularities and the underlying physiological alterations associated with obesity-related OSA.

The Apnea–Hypopnea Index (AHI) is the most accepted objective measure of the severity of OSA and is defined as the number of episodes of apnea and hypopnea per hour of sleep. In the present investigation, baseline AHI levels were equivalent between the three groups, indicating comparable illness severity before intervention. After 6 months of treatment, AHI was considerably decreased in all intervention groups (Table 1). Mean AHI decreased from 42.20 ± 28.41 to 14.54 ± 4.93 events/hour, 40.45 ± 35.01 to 10.84 ± 8.55 events/hour and 42.75 ± 20.41 to 6.83 ± 3.16 events/hour in CPAP, CPAP + Lifestyle and CPAP + Pranayama groups respectively. The improvement was most pronounced in G3 ($p < 0.001$).

CPAP mechanically splints the upper airway and prevents recurrent pharyngeal collapse during sleep, which is expected to reduce AHI after CPAP therapy. CPAP keeps the airway open throughout the respiratory cycle, abolishing obstructive respiratory episodes, restoring normal airflow and improving nocturnal oxygenation. This in turn leads to a significant reduction in intermittent hypoxia, recurrent arousals and sleep fragmentation, resulting in enhanced quality of sleep and daily performance. These physiological effects have reinforced the role of CPAP as the gold-standard treatment for moderate-to-severe OSA [2].

The larger improvement seen in the CPAP + Lifestyle group presumably reflects the favourable effects of weight loss on the upper airway mechanics. Lifestyle intervention decreases visceral and upper airway fat deposition, neck circumference and improves respiratory mechanics, therefore decreasing pharyngeal collapsibility during sleep. Weight loss also improves lung sizes and functional residual capacity, with improvement in caudal tension on the upper airway and reduction of airway blockage. These structural changes are in addition to the pneumatic splinting effect of CPAP that may explain the higher reduction in AHI than with CPAP alone [1].

Interestingly, the highest reduction in AHI was in the CPAP + Pranayama group. Pranayama can increase the stability of the upper airway by respiratory muscle strengthening, improvement of diaphragmatic function and optimization of the autonomic nervous system balance. Slow deep breathing stimulates parasympathetic activity and decreases sympathetic overactivity. Respiratory control and ventilatory efficiency are increased. Regular practice of pranayama may also enhance upper airway muscle tone, increase lung expansion and improve oxygen use, all of which may lead to a further reduction in obstructive respiratory episodes beyond the benefit of CPAP alone [7].

Our results are in line with the findings of Carneiro-Barrera et al. [9], who showed that an interdisciplinary weight-loss and lifestyle intervention plus CPAP resulted in significant reduction in the apnea–hypopnea index (AHI), improvement in nocturnal oxygenation, improvement in cardiometabolic health, and sustained remission of obstructive sleep apnea compared with CPAP therapy alone. Similarly, Georgoulis et al. [10] showed in the MIMOSA randomized clinical trial that a Mediterranean diet-based weight loss and lifestyle intervention combined with CPAP produced significantly greater reductions in OSA severity than standard care, emphasizing the significance of targeting obesity as the main pathogenic factor underlying upper airway collapse. Moreover, Georgoulis et al. [11] have established a dose-dependent association between the extent of weight loss and the improvements in OSA severity, whereby the larger the weight loss, the larger the reductions in AHI and the lower the prevalence of severe OSA. Together, these studies confirm our present findings

that multimodality treatment approaches that address both upper-airway blockage and obesity-related pathophysiology result in higher reductions in disease severity than CPAP therapy alone.

Sleep efficiency, a crucial indication of overall sleep quality, is defined as the ratio of time spent asleep to time spent in bed. Patients with OSA experience impaired sleep efficiency due to frequent respiratory episodes causing recurrent cortical arousals and sleep fragmentation. In the present study, sleep efficiency considerably improved following intervention in all treatment groups. Mean sleep efficiency improved from 79.97 ± 13.57% to 84.56 ± 10.14% in G1, from 82.24 ± 9.11% to 87.49 ± 7.85% in G2 and from 82.87 ± 4.09% to 89.75 ± 2.77% in G3, with maximum improvement shown in the CPAP + Pranayama group.

The increase in sleep efficiency during CPAP therapy is mainly due to the absence of recurrent apnea and hypopneas which results in less sleep fragmentation and permits continuous passage through normal sleep stages. Continuous sleep restoration aids in improving sleep continuity and overall sleep quality. Increased nocturnal oxygenation also reduces the frequency of cortical alertness and sympathetic activation thus further enhancing sleep efficiency [11].

Furthermore, lifestyle adjustment may improve sleep efficiency through weight loss, improved metabolic health and better circadian control. Research shows that more exercise can improve sleep depth, reduce sleep latency and enhance overall sleep time. In addition, nutritional modification decreases systemic inflammation and metabolic stress, which have been linked in altered sleep architecture in obese persons [1].

The greater improvement after pranayama may be attributed to its favourable effects on autonomic control and psychological well-being. Controlled breathing exercises lower sympathetic nervous system activity and increase parasympathetic tone, leading to decreased physiological arousal and increased sleep continuity. Pranayama has also been linked to a decreased anxiety, lower release of stress hormones and an increased relaxation before sleep therefore helping to produce more consolidated and restorative sleep [8]. These mechanisms might explain the greatest sleep efficiency in G3 despite similar baseline features.

Our findings are similar to those of Issa FG, et al., who found a considerable improvement in sleep efficiency following successful CPAP therapy [12]. Likewise, the combined therapy of obesity and OSA has been shown to improve respiratory function and sleep architecture more than the standalone treatment options [13]. These findings support the hypothesis that better improvements in total sleep quality are obtained with the combination of treatment of both airway obstruction and the underlying metabolic abnormalities.

Restoration of normal sleep architecture is another essential goal of OSA care apart from the reduction of respiratory episodes. Recurrent upper airway obstruction, intermittent hypoxia and repetitive cortical arousals result in a significant alteration in the physiologic distribution of sleep stages in patients with obstructive sleep apnea. Untreated OSA patients generally have increased light sleep (stage I), decreased slow-wave sleep (stage III), fragmented rapid eye movement (REM) sleep, and poor sleep continuity. Therefore, effective treatment should not only reduce the apnea–hypopnea index, but also regulate sleep-stage distribution to improve restorative sleep and daytime functioning [2].

Stage I sleep is the lightest stage of non-rapid eye movement (NREM) sleep and usually accounts for just 5–10% of total sleep time. Patients with OSA usually spend too much time in Stage I sleep because recurring respiratory episodes regularly disrupt deeper sleep, resulting in frequent cortical arousals and interfering with the development into restorative sleep phases.

All three groups in the present study showed a reduction in Stage I sleep following the intervention. The average Stage I sleep decreased from 16.66 ± 10.77% to 10.84 ± 3.36% in CPAP group, from 15.02 ± 10.13% to 10.23 ± 6.51% in CPAP + Lifestyle group and from 14.15 ± 9.55% to 6.54 ± 2.20% in CPAP + Pranayama group, the greatest significant drop was in G3 ($p<0.05$).

The decrease in Stage I sleep is an indication of enhanced sleep continuity after the cessation of recurrent obstructive respiratory episodes. CPAP keeps the upper airway open, reducing frequent respiratory-related arousals that fragment sleep and push patients back into lighter sleep stages. This results in better consolidated sleep and easier transition into deeper stages of NREM and REM sleep.

The additional improvement shown in the Lifestyle and Pranayama groups could be due to processes other than airway stability alone. Losing weight reduces upper airway collapsibility and reduces respiratory effort during sleep. Regular physical activity promotes synchronization of the circadian rhythm and overall sleep quality. Further, pranayama improves autonomic balance by reducing sympathetic activity and enhancing vagal tone, therefore reducing physiological arousal and allowing further progression into deeper stages of sleep [6,8].

Our findings agree with those of McArdle N et al. who reported that successful CPAP therapy reduced the amount of light sleep due to a reduction in respiratory arousals [14]. Similarly, Carneiro-Barrera et al. [9] demonstrated that the addition of a structured weight-loss and lifestyle intervention to CPAP therapy significantly improved sleep-related outcomes such as nocturnal sleep quality, indices of respiratory disturbance and overall polysomnographic parameters when compared with CPAP therapy alone.

Stage II sleep is a transitional phase between light and deep sleep and comprises around 45-55% of total sleep time. Stage II sleep is not as restorative as slow wave sleep but it is necessary for memory consolidation, motor learning and cardiovascular stability. In the present investigation, only little alterations in Stage II sleep were found following intervention. Mean values ranged from 58.81 ± 11.43% to 55.40 ± 5.69% in G1, 56.71 ± 11.25% to 51.96 ± 5.67% in G2 and 48.61 ± 8.40% to 51.70 ± 4.66% in G3.

The minor alterations that occur in Stage II sleep are physiologically predicted. As the number of respiratory episodes diminishes, sleep becomes more continuous and time spent in fragmented Stage I sleep is transferred to Stage II and deeper restorative periods. However, major alterations after therapy are less likely, as Stage II normally comprises around

50% of total sleep time. Increments in REM sleep and decrements in Stage I sleep should be considered in conjunction with increments in Stage II sleep rather than in isolation [2].

The small rise in G3 may reflect better stabilization of regular sleep cycle while the small decrease in G1 and G2 probably reflects redistribution of sleep toward REM and slow-wave sleep. Mander BA et colleagues made similar conclusions, reporting that CPAP improves overall sleep organization without causing major changes in the duration of Stage II [12].

Stage III sleep, commonly known as slow-wave sleep (SWS) or deep sleep, is the most restorative stage of NREM sleep. This phase is characterized by the highest growth hormone secretion, reduced sympathetic nervous system activity, tissue repair, immunological modulation, and metabolic recovery. Recurrent hypoxia and frequent arousals continually disrupt the preservation of slow-wave sleep in untreated OSA [5].

In the current study Stage III sleep showed modest improvement after intervention. Mean values increased from 14.34 ± 10.93% to 15.64 ± 4.59% in the CPAP group and 11.97 ± 9.23% to 16.64 ± 6.41% in the CPAP + Lifestyle group. The post-treatment value of G3 was significantly greater than the other two groups, but G3 decreased somewhat from 22.82 ± 11.76% to 19.86 ± 4.59%, but it was within the normal physiological range.

The increase in slow-wave sleep after treatment with CPAP is mainly due to the cessation of recurrent respiratory episodes and the return of uninterrupted sleep cycles. Reduction of nocturnal hypoxia reduces sympathetic activity such that long periods of deep rest or restorative sleep are facilitated. Lifestyle management may further improve slow-wave sleep via improvements in metabolic health, reduction in systemic inflammation and increased daily physical activity [6].

The relatively higher baseline Stage III values in G3 probably constrained the extent of additional development due to a ceiling effect. Maintenance of physiologically appropriate slow wave sleep after intervention reflects preserved restorative sleep despite large decreases in respiratory episodes and should not be interpreted as treatment failure.

Similar improvements in slow-wave sleep after CPAP therapy have been observed by Weaver and Grunstein, who have shown that adequate treatment of OSA normalizes sleep architecture [15]. REM sleep is necessary for emotional modulation, cognitive functioning, memory consolidation and neural plasticity. The natural decrease in the tone of the skeletal muscles during REM sleep leads to a more significant collapse of the upper airways and, therefore, OSA often interrupts REM sleep. Consequently, patients with untreated OSA tend to have reduced REM duration and fragmented REM episodes [14].

The present study showed a considerable improvement in REM sleep after intervention. REM sleep rose from 10.04 ± 7.00% to 19.90 ± 3.82% in G1, from 16.74 ± 10.67% to 20.95 ± 8.06% in G2 and from 17.23 ± 4.90% to 22.06 ± 1.68% in G3 ($p<0.05$). This rise is due to normalization of sleep cycling after removal of apnea-induced arousals. CPAP keeps the upper airway open during REM sleep, leading to uninterrupted REM sleep episodes and less sleep fragmentation. Additionally, enhanced oxygenation further improves neuronal recovery and cerebral metabolic activity, which contributes to the correction of REM sleep architecture [14,5].

Lifestyle change can improve REM recovery by enhancing metabolic balance and lowering obesity-related inflammation. The better improvement seen in G3 may also be indicative of the autonomic benefits of pranayama such as lower sympathetic activity, increased vagal tone and reduced psychological stress therefore promoting undisturbed REM sleep [8].

We are in agreement with Malhotra et al. who reported considerable REM rebound on commencement of CPAP therapy [14]. Carneiro-Barrera et al. [9] also showed that CPAP treatment with a structured interdisciplinary weight loss and lifestyle intervention produced significantly better improvements in obstructive sleep apnea severity, nocturnal oxygenation, sleep-related quality of life and overall polysomnographic outcomes compared to CPAP treatment alone, showing the benefit of treating upper airway obstruction and obesity-related pathophysiology simultaneously [9].

Recurrent nocturnal hypoxemia is one of the most important physiologic effects of obstructive sleep apnea, and is the consequence of repeated bouts of upper airway collapse during sleep. Intermittent hypoxia triggers a series of pathogenic processes such as oxidative stress, sympathetic nervous system activation, systemic inflammation, endothelial dysfunction and metabolic impairment, which all have a role in the elevated cardiovascular risk in OSA. Thus, improvement of the nocturnal oxygen saturation after treatment is an essential marker of successful restoration of normal respiratory physiology [2].

In the present investigation, the mean oxygen saturation (SpO_2) improved significantly after 6 months of participation in all three therapy groups. Mean Spo2 improved from 92.11 ± 2.32 % to 94.44 ± 1.63 % in CPAP group (G1), 91.64 ± 4.33 % to 94.56 ± 2.26 % in CPAP + Lifestyle group (G2) and 91.32 ± 4.62 % to 97.12 ± 1.00 % in CPAP + Pranayama group (G3). G3 had the largest improvement ($p<0.01$), implying that adjunctive pranayama improved nocturnal oxygenation beyond the effect of CPAP alone.

The improvement seen with CPAP therapy is mostly due to the maintaining of patency of the upper airway during sleep. CPAP prevents recurrent airway collapse, eliminates periods of apnoea and hypopnoea, restores continuous airflow and dramatically lowers intermittent hypoxia. Thus, arterial oxygen saturation is steadier during sleep and thus reduces oxidative stress, sympathetic activation and endothelial injury. Enhanced oxygen delivery also improves myocardial and cerebral oxygenation and contributes to improved cardiovascular and neuropsychological outcomes [14].

Weight loss and improved respiratory mechanics could explain the increased improvement shown in the Lifestyle Intervention group. Reduced visceral fat and a smaller neck circumference increase the size of the upper airway, increasing lung volume and improving the mobility of the diaphragm. These modifications decrease airway resistance and increase ventilation-perfusion matching, leading to more effective pulmonary gas exchange during sleep [6].

The Pranayama group had the most rise in SpO_2 possibly due to several physiological reasons. Controlled breathing exercises improve diaphragmatic excursion, increase tidal volume and improve alveolar ventilation. It has also been proven that regular pranayama improves the strength of the respiratory muscles, pulmonary compliance and efficiency of

breathing . In addition, slow breathing lowers sympathetic overactivity and improves autonomic balance, consequently enhancing respiratory rhythm and oxygen use. It has also been suggested that the increased release of nitric oxide from the paranasal sinuses during slow nasal breathing improves pulmonary vasodilatation and ventilation-perfusion matching, thus further improving oxygen saturation [16].

The observed results are comparable with those reported by McArdle et al. who demonstrated considerable improvement in nocturnal oxygen saturation following CPAP therapy by reduction of recurrent obstructive respiratory episodes and restoration of upper airway patency [14]. Regular pranayama has also been found to improve pulmonary function, better consumption of oxygen and higher oxygen saturation as per studies on yogic breathing practices, which is in accordance with the findings of the present study [16].

One of the most extensively used subjective measures to identify excessive daytime sleepiness in patients with OSA is the Epworth Sleepiness Scale (ESS). The main reason for daytime sleepiness is the recurrent arousals during the night, sleep fragmentation and insufficient restorative sleep resulting in impaired focus, diminished cognitive performance, lowered work productivity and higher likelihood of occupational and motor vehicle accidents [2].

In the present study, ESS ratings reduced significantly after therapy in all three intervention groups. Mean ESS scores decreased from 13.71 ± 4.75 to 6.43 ± 2.15 in CPAP group, 14.79 ± 5.35 to 5.07 ± 3.47 in CPAP + Lifestyle group and 14.25 ± 3.33 to 4.25 ± 3.14 in CPAP + Pranayama group with highly significant improvement in all groups ($p<0.001$).

The large decrease in daytime sleepiness after CPAP therapy suggests that unbroken sleep is restored and sleep architecture is normalized. Elimination of recurrent respiratory episodes decreases cortical arousals and hence prolongs periods of restorative NREM and REM sleep. Better sleep continuity improves cognitive performance, alertness and daytime functioning, and hence dramatically lowers ESS scores [14].

Further improvement was probably due to lifestyle adjustment that decreased obesity-related fatigue, improved insulin sensitivity and improved total physical fitness. Enhanced physical activity has been demonstrated to have positive effects on sleep quality, modulation of circadian rhythm and psychological well-being, all of which leads to decreased daytime somnolence [6].

The largest reduction in ESS in the Pranayama group can be attributed to its combined physiological and psychological effects. Pranayama regular practice is beneficial in autonomic nervous system balance by enhancing parasympathetic activity and decreasing sympathetic overactivity. It also inhibits the secretion of stress hormones, enhances mental health and induces relaxation before sleep. These effects result in a deeper, more restorative sleep, which in turn leads to increased daytime alertness and lower perceived tiredness [16].

Our results are consistent with the results of Weaver and Grunstein who reported significant improvement in ESS scores after adequate adherence to CPAP [15]. Similarly, Mander BA et al. have shown that enhanced sleep continuity after CPAP therapy leads to significant improvement in daytime performance and quality of life [12].

Here we demonstrate that all three methods of therapy significantly improved objective polysomnographic (PSG) parameters and subjective daytime sleepiness, supporting the effectiveness of CPAP-based treatment in obese non-diabetic OSA patients. Significant reductions in AHI, Stage I sleep and ESS scores, along with increases in sleep efficiency, REM sleep and nocturnal oxygen saturation, imply substantial restoration of normal sleep physiology after six months of intervention.

In all three treatment modalities, the CPAP + Pranayama group showed the best improvement in the majority of polysomnographic variables. The result implies that pranayama may have therapeutic effects in addition to airway stabilization by enhancing respiratory muscle function, autonomic modulation, pulmonary ventilation, and oxygen use. Comparison with CPAP alone showed greater improvement in the CPAP + Lifestyle group, demonstrating the significance of obesity treatment—the most modifiable risk factor for OSA.

Obesity is one of the most important modifiable risk factors for obstructive sleep apnea (OSA) because excess adipose tissue around the neck, belly and upper airway increases pharyngeal collapsibility, decreases lung capacities and promotes repeated upper-airway obstruction during sleep. Thus, anthropometric measures such as body mass index (BMI), waist, hip and neck circumferences are closely connected to development and severity of OSA and are regarded essential treatment targets in the therapy of OSA [2]. In the present investigation, six months of intervention resulted in significant decreases (Table 2) in BMI, waist circumference, hip circumference and neck circumference in all three treatment groups, although the waist-to-hip (W/H) ratio remained almost unaltered. CPAP + Pranayama group showed maximum numerical improvement followed by CPAP + Lifestyle Modification group. CPAP alone also yielded substantial improvement. These results suggest that additional behavioural treatments could add to the metabolic and structural benefits from CPAP therapy [9].

BMI significantly decreased in all intervention groups: G1 from 31.27 ± 2.75 to 29.50 ± 2.69 kg/m2, G2 from 30.97 ± 5.19 to 28.42 ± 4.63 kg/m2 and G3 from 30.61 ± 2.44 to 27.08 ± 1.65 kg/m2. The data show a substantial reduction in overall adiposity after therapy. OSA is connected with obesity, which predisposes to greater fat deposition around the upper airway and thoracoabdominal region, leading to increased airway collapsibility and respiratory effort during sleep. Weight loss improves respiratory mechanics by reducing mechanical loading of the upper airway, increasing functional residual capacity and improving upper airway stability [2]. Current findings are in line with the INTERAPNEA randomized clinical study that shown significant reduction of BMI and improvement of OSA severity after a comprehensive lifestyle intervention comprising dietary modification and physical exercise in obese patients [9]. The decrease in BMI in the CPAP-only group should not be regarded as a direct weight-reducing impact of CPAP. A meta-analysis of randomized trials found a slight rise in body weight with CPAP, not a decrease. The observed reduction in the current study may therefore be due to simultaneous behavioural change, improved daytime functioning or unmeasured lifestyle alteration.

In all groups, waist circumference was lowered, with the largest reduction seen in the G3 group. Waist circumference is a proxy metric for visceral adiposity which is more metabolically active than subcutaneous fat and is highly related with insulin resistance, chronic inflammation and cardiovascular disease. Increased belly fat decreases lung capacity and diaphragmatic excursion, hence increasing upper-airway collapsibility during sleep [5].
Weight loss decreases visceral fat mass, decreases free fatty acid release and improves respiratory mechanics by increasing lung expansion and caudal traction on the pharyngeal airway. These processes minimize the likelihood of upper airway collapse during sleep and are involved in the reduction of OSA severity [6]. The reduction observed in the present study is in line with earlier studies which have shown that lifestyle modification significantly reduces waist circumference and improves cardiometabolic health in obese persons with OSA [9].
All intervention groups showed significant decreases in hip circumference, indicating a widespread reduction in body fat mass. But the waist-hip ratio did not change appreciably. This is biologically predicted because waist and hip circumferences fell similarly. Although the anthropometric measurements were drastically lowered, the estimated ratio did not alter significantly when the numerator and denominator of a ratio were reduced by similar amounts [18].

The absence of a substantial change in the waist-to-hip ratio should not be interpreted as a failure of therapy but rather suggests that fat loss happened proportionately in the central and peripheral body compartments. In the present investigation, only waist circumference appears to be a more sensitive indication of change in intervention associated obesity than waist-to-hip ratio [18]. Neck circumference was highly significantly reduced in all treatment groups from 40.00 ± 1.38 to 38.93 ± 1.17 cm in G1, from 39.46 ± 2.78 to 38.14 ± 2.55 cm in G2 and 39.08 ± 1.31 to 37.38 ± 1.19 cm in G3. Excess fat accumulation in the cervical area causes restriction of the upper airway and greater pharyngeal collapsibility during sleep, and neck circumference is one of the greatest anthropometric predictors of OSA. [2] By reducing the fat in the neck, the external pressure on the upper airway is reduced, the diameter of the airway is increased and the resistance to airflow is decreased. Weight loss also increases lung volume and increases longitudinal traction on the pharyngeal airway, reducing airway collapsibility and increasing nighttime breathing [5]. Hence, the considerable reduction in neck circumference observed in this study may have contributed to the significant drop in AHI and improvement in sleep architecture following intervention. Neck circumference has also been previously found to be independently linked with the severity of OSA and to decrease after successful obesity control [5,6].
The current investigation indicated that the total lipid profile was significantly improved after six months of intervention in obese non-diabetic patients with obstructive sleep apnea (OSA). (table 3) Total cholesterol (TCH), triglycerides (TG), low density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) decreased significantly and high-density lipoprotein cholesterol (HDL-C) increased significantly in all three treatment groups. In CPAP therapy alone, favourable lipid changes were observed. However, the change was greater in patients receiving CPAP therapy along with lifestyle modification and CPAP therapy along with pranayama, suggesting that adjunctive interventions provide further cardiometabolic benefits beyond correction of upper airway obstruction.
Obese patients with OSA are frequently dyslipidaemia and this is an essential contribution to the etiology of atherosclerotic cardiovascular disease. Recurrent intermittent hypoxia and sleep fragmentation contribute to increased sympathetic nervous system activity, oxidative stress, and chronic low-grade inflammation, resulting in altered hepatic lipid metabolism and increased circulating atherogenic lipoproteins. Hypoxia activates hypoxia-inducible factor-1α (HIF-1α) and promotes hepatic lipogenesis via sterol regulatory element-binding protein-1c (SREBP-1c) and suppresses fatty acid β-oxidation. Sympathetic activation causes accelerated lipolysis of adipose tissue and overloading the circulation with free fatty acids (FFA). These free fatty acids are delivered to the liver, where they drive the hepatic synthesis of triglycerides and the overproduction of VLDL particles. VLDL is subsequently gradually digested, leading to increased LDL concentrations and decreased HDL by enhanced cholesteryl ester transfer protein (CETP)-mediated lipid exchange, culminating in the typical atherogenic lipid profile found in OSA [2].
The overall decrease in total cholesterol seen in this study implies an improvement of the global lipid balance after treatment. CPAP therapy decreases intermittent hypoxia and sympathetic overactivity, leading to stabilization of hepatic cholesterol synthesis and reduction in oxidative modification of circulating lipoproteins. Lifestyle change further improves decrease of cholesterol through food improvement, weight loss and increased physical activity Pranayama might indirectly enhance lipid metabolism by decreased neuroendocrine stress, better autonomic balance and decreased systemic inflammation. The combined mechanisms explain the gradual decrease in total cholesterol of the total intervention groups, with the best improvement of the combination intervention groups [5,6].
Similar substantial decreases in triglycerides and VLDL cholesterol suggest enhanced hepatic lipid metabolism and reduced supply of free fatty acids to the liver. Weight loss reduces the bulk of visceral adipose tissue and hence reduces adipocyte lipolysis and the flux of circulatory free fatty acids. Exercise enhances lipoprotein lipase activity in skeletal muscle, resulting in higher plasma triglyceride clearance and improved fatty acid oxidation. In addition, Pranayama may improve triglyceride metabolism lowering sympathetic activity and circulating cortisol levels, which influence hepatic lipid production. CPAP restoration of nocturnal oxygenation also suppresses hypoxia-induced hepatic lipogenesis, suggesting another mechanism for decreasing triglyceride and VLDL levels [16].
Another key finding was a large decrease in LDL cholesterol and a considerable increase in HDL cholesterol following the intervention. High LDL contributes significantly to endothelial dysfunction and the production of atherosclerotic plaque, whereas HDL contains anti-inflammatory, antioxidant and reverse cholesterol transport activities that are protective against cardiovascular disease. Therefore, an improvement in these measures suggests a reduction in future cardiovascular risk. CPAP therapy decreases oxidative stress, which minimizes the oxidation of LDL. This also contributes to the normalization of lipoprotein metabolism owing to enhanced insulin sensitivity and decreased generation

of inflammatory cytokines. Lifestyle adjustment promotes expression of LDL receptors and hepatic clearance of circulating LDL particles. higher physical exercise and weight loss also promote HDL synthesis via higher production of apolipoprotein A-I and enhanced reverse cholesterol transport. potentially, the enhancement of the autonomic function, due to pranayama, may potentially reduce the catecholamine induced lipid mobilization and increase the endothelial nitric oxide bioavailability resulting to a more favourable lipid metabolism [19].

The observed results are in agreement with the results of Mokhlesi et al. who found that the successful treatment of obesity linked OSA improves dyslipidaemia through reductions in intermittent hypoxia, inflammation and insulin resistance [13]. Also, Drager et al. showed that CPAP therapy reduced oxidative stress and improved endothelial function, which contributes to the normalization of lipid metabolism and decrease of cardiovascular risk [20]. Furthermore, Blüher demonstrated that lifestyle adjustment to lower visceral adiposity led to restoration of adipokine balance, suppression of chronic inflammation and improvement of hepatic lipid management with beneficial alterations in circulating lipoproteins [6].

Importantly, combination therapies typically resulted in better lipid responses than CPAP alone, while all treatment groups improved. These data indicate that CPAP corrects the respiratory irregularities responsible for intermittent hypoxia, but supplementary therapies are needed to correct the metabolic derangements associated with obesity. Lifestyle change has direct effect on energy balance, body composition and insulin sensitivity, pranayama enhances autonomic modulation, reduces sympathetic overdrive and decreases physiological stress. The combination of these synergistic mechanisms leads to a more complete improvement in lipid metabolism than airway stabilization alone.

The concomitant improvement of total cholesterol, triglycerides, LDL-C, VLDL-C and HDL-C is from a clinical point of view a demonstration of a significant reduction of the total atherogenic load. Dyslipidaemia is a significant mediator of the relationship between OSA and coronary artery disease, stroke and metabolic syndrome. Thus, early correction of lipid abnormalities by integrated care may lower long-term cardiovascular risk even in obese patients without overt diabetes mellitus. Thus, the current data indicate a multidisciplinary therapy approach involving CPAP in combination with lifestyle management or pranayama to enhance respiratory and cardiometabolic outcomes in obese persons with OSA.

One of the most notable findings of the present study is that successful treatment of obstructive sleep apnea resulted not only in considerable improvement in the polysomnographic parameters but also in the normalization of adipokine secretion and systemic inflammation. After 6 months of intervention, the quantities of leptin, ghrelin and IL-6 were significantly reduced, however adiponectin was significantly elevated in all 3 treatment groups (table 4). These biochemical benefits were observed in parallel to reduced AHI, better oxygen saturation, normalization of sleep architecture and reduced daytime drowsiness. The CPAP plus pranayama group of the 3 intervention groups showed the best overall improvement, showing that a better restoration of metabolic balance is achieved by correcting the airway blockage and modulating the autonomic function.

These findings support the paradigm that obstructive sleep apnea should not be considered anymore as a disorder of upper airway obstruction but rather as a systemic inflammatory and metabolic disease characterized by adipose tissue dysfunction, autonomic imbalance, oxidative stress and endothelial damage. Recurrent intermittent hypoxia leads to secretion of pro-inflammatory cytokines and changes in adipokine production through activation of hypoxia-inducible factor-1α (HIF-1α), nuclear factor-kappa B (NF-κB) and oxidative stress pathways. This leads to leptin resistance, a decrease in adiponectin synthesis and dysregulation of appetite regulating hormones, all of which cause obesity, insulin resistance and cardiovascular disease [2].

Leptin is a hormone produced by adipocytes that regulates hunger and energy expenditure through hypothalamic centres that influence satiety. However, a characteristic of obesity is leptin resistance, in which circulating leptin levels are high despite diminished responsiveness of the hypothalamus. This anomaly is exacerbated by the intermittent hypoxia, oxidative stress and persistent sympathetic activation of obstructive sleep apnea [21].

Serum leptin was significantly decreased after intervention in all the three groups in the present investigation (table 3) with the maximum reduction seen in the CPAP + Pranayama group (14.73 ± 7.26 to 8.48 ± 4.02 ng/mL; $p<0.001$). Leptin reduction after treatment is likely due to disappearance of intermittent hypoxia, reduced sympathetic overactivity and recovery of hypothalamic leptin sensitivity after CPAP therapy. Lifestyle modification reduces the quantity of adipose tissue which reduces the leptin secretion while pranayama reduces sympathetic activity and hypothalamic-pituitary-adrenal axis activation and thus reduces neuroendocrine stimulation of adipocytes [21].

These results are in accordance with the study of Janmohammadi et al. [22], who showed in a systematic review and meta-analysis that obstructive sleep apnea is associated with a significant dysregulation of adipocytokines, including elevated leptin levels, a marker of adipose tissue dysfunction and chronic low-grade inflammation. Additionally, Carneiro-Barrera et al. [9] showed that CPAP therapy combined with structured weight loss and lifestyle intervention significantly improved cardiometabolic health and obesity-associated metabolic abnormalities compared to CPAP therapy alone, supporting the restoration of adipokine homeostasis using multimodal treatment strategies. Adiponectin is one of the major anti-inflammatory and insulin sensitizing adipokines. Lower levels of adiponectin have been strongly linked with obesity, insulin resistance, endothelial dysfunction and cardiovascular disease [6].

Adiponectin increased significantly in all intervention groups in the present study from about 5.8 mg/l at baseline to >10 mg/l after therapy ($p<0.001$). Such improvement indicates recovery of the adipose tissue endocrine function after correction of the intermittent hypoxia and systemic inflammation. CPAP reduces the production of oxidative stress and inflammatory cytokines. Weight loss prevents macrophages' recruitment into adipose tissue and restores adipocytes' function. Increased insulin sensitivity leads to activation of AMPK and PPAR-γ pathways resulting in increased

adiponectin production. Pranayama may enhance autonomic balance which may further increase adiponectin secretion by reduction of chronic stress and cortisol levels [6].

Our findings are consistent with those of Blüher who demonstrated that higher adipose tissue health is linked with greater adiponectin production and decreased cardiometabolic risk [6]. Similar findings were reported by Janmohammadi et al. [22] who demonstrated that obstructive sleep apnea is characterized by a profound dysregulation of adipocytokines, including increased pro-inflammatory mediators and altered adipokine profiles, supporting the role of adipose tissue dysfunction in OSA pathophysiology. Ghrelin is an important regulator of appetite and is an orexigenic (appetite-stimulating) hormone produced mainly by gastric endocrine cells. Sleep loss and fragmentation increase circulating ghrelin, which promotes excessive food intake and weight gain. In the present investigation, we observed a consistent decline in the ghrelin concentrations after interventions with the maximum reduction in the CPAP + Pranayama group (31.3 ± 5.33 to 17.6 ± 7.24 pg/mL; $p<0.001$). The recovery of normal sleep architecture during CPAP likely normalised the hypothalamic regulation of appetite by decreasing ghrelin secretion. Lifestyle modification improved energy balance and pranayama decreased sympathetic activity and psychological stress, which are involved in hypothalamic circuits controlling appetite [6].

The results were in agreement with the findings of Ciriello J et al [23] who demonstrated the relationship between sleep deprivation and obstructive sleep apnea with the disruption of appetite-regulating hormones with increased ghrelin and altered leptin signalling which resulted in increased appetite, obesity and metabolic dysfunction. The existing data on the role of ghrelin in OSA are conflicting. A recent meta-analysis found no statistically significant difference in circulating ghrelin levels between persons with OSA and controls, and no significant pooled change after CPAP therapy. Therefore, the large reduction found in the present study may reflect the combined effect of improved sleep continuity, weight-related changes and additional behavioural intervention and needs to be confirmed in larger controlled trials [24].

Interleukin-6 (IL-6) is an important pro-inflammatory cytokine which is important in linking obesity, OSA and cardiovascular disease. Recurrent intermittent hypoxia activates the NF-κB signal pathway in adipose tissue and vascular endothelium and stimulates IL-6 release to maintain chronic systemic inflammation [24]. The present study demonstrated a significant reduction in the concentration of IL-6 in all the intervention groups, with maximum reduction being observed in the CPAP + Pranayama group (5.08 ± 2.34 to 3.13 ± 1.06 pg/mL; $p<0.001$). CPAP restores nocturnal oxygenation and decreases hypoxia-mediated inflammatory signalling. Elevated adiponectin also inhibits macrophage activation and NF-κB signalling, and suppresses IL-6 production. Lifestyle change reduces inflammation of fat tissue. Pranayama activates the vagally mediated cholinergic anti-inflammatory pathway, and also reduces the production of cytokines [25]. Our results are consistent with the observations of Lavie et al, who found that successful treatment of OSA reduces oxidative stress and systemic inflammation by correcting intermittent hypoxia [25].

Correlation analysis revealed a substantial negative correlation between AHI and sleep efficiency, between AHI and REM sleep and between AHI and mean oxygen saturation. Therefore, increased sleep fragmentation and nocturnal hypoxaemia are associated with increased severity of OSA. However, there was a significant positive association between AHI and ESS, suggesting that the increased severity of respiratory disruption was directly related to excessive daytime drowsiness. These results are consistent with other polysomnography studies indicating that AHI is the main determinant of nocturnal oxygen desaturation, sleep fragmentation and poor daytime function [23,24]. The strongest inverse association (table 5) was found between AHI and mean SpO_2 (as high as $r = -0.81$), underlining nocturnal hypoxaemia as the main physiological consequence of repeated upper airway obstruction. Likewise, strong negative associations between AHI and sleep efficiency suggest that respiratory episodes repeatedly disrupt normal sleep continuity and the subject is unable to reach the restorative stages of sleep. Positive correlations between AHI and ESS further support that improvement in respiratory physiology translates immediately to improved daytime alertness and quality of life [23,24].

CONCLUSIONS

This prospective interventional study demonstrates that CPAP treatment significantly improves polysomnographic parameters, daytime sleepiness, anthropometric indices, lipid profile, adipokine dysregulation, and systemic inflammation in obese non-diabetic patients with moderate-to-severe obstructive sleep apnea (OSA). Of the three therapeutic approaches, the addition of structured lifestyle modification resulted in the greatest improvement in overall cardiometabolic health, with greater reductions in body mass index, central obesity, dyslipidemia, leptin, ghrelin, and interleukin-6, as well as increased adiponectin levels. In contrast, adjunctive pranayama was linked to better improvements in apnea-hypopnea index, sleep efficiency, rapid eye movement sleep, nocturnal oxygen saturation, and selected sleep architecture parameters, suggesting complementary physiological benefits beyond airway stabilization.

The present study's key strength and novelty lie in its comprehensive and integrated evaluation of polysomnographic outcomes along with adipokines (leptin, adiponectin and ghrelin), inflammatory status (IL-6), and lipid profile across three CPAP based therapeutic strategies in obese non-diabetic Indian patients with OSA. The study presents a multidimensional assessment of the intricate relationships between sleep physiology, adipose tissue biology, systemic inflammation and cardiometabolic dysfunction, providing important evidence towards biomarker-guided comprehensive management of obesity-associated OSA. This work differs from previous studies that primarily investigated respiratory outcomes or weight loss alone.

LIMITATIONS TO THE STUDY

The present study was conducted in a single tertiary care center with a relatively small sample size and a short duration of follow-up, which may affect the generalizability and long-term implications of the results. These findings need to be

confirmed in future multicentre randomized controlled studies with larger sample sizes, longer follow-up and more comprehensive assessment of biomarkers.

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CONFLICT OF INTEREST
The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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