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COMORBID OBSTRUCTIVE SLEEP APNEA ON PATIENTS WITH METABOLIC SYNDROME AND RESULTS OF THERAPEUTIC INTERVENTIONS

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SUMMARY OF DOCTORAL THESIS

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The thesis can be found at:

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INTRODUCTION

Obstructive Sleep Apnea (OSA) is a sleep disorder characterized by recurrent complete and partial upper airway obstructive events, resulting in intermittent hypoxemia, autonomic fluctuation, and sleep fragmentation. The prevalence of OSA in the community varies widely between studies due to methodological heterogeneity. Intermittent hypoxia with repeated awakenings will create sympathetic nerve stimulation, oxidative stress and systemic inflammation - the source of cardiovascular diseases such as hypertension, atherosclerosis, coronary artery diseases, arrhythmias, metabolic syndrome, type 2 diabetes and stroke.

Metabolic syndrome (MetS) with its component disorders including hypertension, hyperlipidemia, decreased blood HDL-C, increased waist circumference and increased glycemia has been shown to be closely related to OSA. Both of these syndromes are risks for serious cardiovascular events or death for patients.

Effective treatment of OSA will reduce apnea-hypopnea episodes, improve blood oxygen saturation during sleep, reduce asourals and has been shown a positive impact on the control of blood pressure (BP), heart rate, glycemia and lipidemia.

With current conditions in Vietnam, the diagnosis and treatment of OSA has not received adequate attention from the community and the health insurance system, and the cost of diagnosis and treatment is still quite expensive.

In Vietnam, we have not found any studies investigating the prevalence of OSA in people with MetS and evaluating the effectiveness of interventions for OSA people with MetS. Therefore, we have conducted a study on the topic ***"Comorbid obstructive sleep apnea on patients with metabolic syndrome and results of therapetic interventions"*** with the following objectives:

1. *Describe clinical and paraclinical characteristics and results of polygraphy in subjects with metabolic syndrome comorbid with obstructive sleep apnea at Hai Phong Medical University Hospital from February 2019 to February 2023.*
2. *Evaluate clinical and paraclinical characteristics after health education interventions and continuous positive airway pressure ventilation.*

NEW CONTRIBUTIONS OF THE THESIS

This is one of the first research topics on OSA in subjects with MetS in Vietnam, on clinical and paraclinical features, on results after health education interventions and CPAP therapy in patients with comorbid MetS and moderate-to-severe OSA. The research results make an important contribution to improving understanding of OSA, a new health problem that has not received adequate attention from both medical system and the community, contributing to prevention, diagnosis and treatment of OSA, minimize harmful effects of OSA and improve quality of life. The fundamental scientific data presented in the Thesis will be the premise to open further research directions related to OSA in general and OSA within cardiovascular and metabolic diseases in particular.

STRUCTURE OF THE THESIS

The full thesis has 130 pages, including following parts: Introduction: 2 pages; Overview: 33 pages; Subjects and Methods: 24 pages; Results: 33 pages; Discussion: 35 pages; Conclusion and Recommendations: 3 pages. The thesis has 172 references, including 10 documents in Vietnamese and 162 in English. The thesis has 26 tables, 14 charts and 17 figures.

Chapter 1. OVERVIEW

1.1. Overview of Obstructive Sleep Apnea and Metabolic syndrome

Obstructive Sleep Apnea

OSA is a common problem with an estimated prevalence of 2 - 4% in the general population and on a continuous upward trend. With the diagnostic threshold determined to be an AHI index ≥ 5 times/hour, the incidence of OSA ranges from 9 - 38%. In 2018, the ESASIE study found that the prevalence of OSA in Vietnamese adults was 8,5%.

The pathogenesis of OSA related to many factors such as: neuromuscular control, structural abnormalities in the maxillofacial area, overweight/obesity, etc., causing narrowing/collapse of the upper airway during sleep. The mechanism causing airway narrowing can be explained through the Starling resistance model - a model of a rigid tube with a collapsible middle section located in a closed box. This segment corresponds to the human pharynx. Common symptoms of OSA include nighttime symptoms such as snoring, witnessed apnea, nocturia and daytime symptoms

such as excessive sleepiness, fatigue, and mental impairment memory, poor concentration among others.

Metabolic syndrome

MetS is currently a major health problem in the world. The incidence of MetS tends to increase and consistent with the situation of overweight, obesity and type 2 diabetes (T2DM). About 85% of people with type 2 diabetes also have MetS and at higher risk of cardiovascular diseases. In 2017, about 12,2% of the adult population in the United States had T2DM, the prevalence of MetS was estimated at about one-third of the adult population in the United States. Insulin resistance is considered core factor in the pathogenesis of MetS, the cause of this condition is mainly related to the visceral fat of the body.

Association between obstructive sleep apnea and metabolic syndrome

Overweight and obesity have been proven to be the most important risk factors for OSA. At least half of adults with OSA are overweight. In the Wisconsin study, 690 middle-aged adults were followed for 4 years to assess the occurrence of OSA and found that each 10% increase or decrease in weight predicted an increase of 32% or decrease of 26% in AHI respectively. In addition, as age increases, the risk of OSA and MetS increases, and insomnia is also related to both of these syndromes.

Pathogenesis and cause-effect relationship between OSA and MetS

The combination of OSA and MetS has led to the name "syndrome Z" in people with these two syndromes. There was experimental and clinical evidence show that OSA is an independent risk factor for the development and severity of metabolic disorders. Conversely, MetS and its components - especially obesity and insulin resistance/T2DM - may influence the development of OSA. It has been suggested that OSA itself may be also a "metabolic disorder" and be considered a component of MetS.

OSA clearly affects glucose metabolism disorders, insulin resistance, hypertension and lipid metabolism disorders. Intermittent hypoxia in OSA can promote SNS stimulation, HPA axis stimulation and systemic inflammation, which is the source of cardiovascular and metabolic disorders.

1.2. Treatment of OSA in subjects with Metabolic syndrome

Intervention methods for the treatment of OSA

General measures including sleep hygiene, weight loss (if overweight /obese), increased physical activity, postural therapy, avoiding alcohol, tobacco are generally applied to all mild-to-severe OSA. Physical therapy with exercises to increase muscle tone of the oropharynx also contributes to reducing the AHI and has significantly effective in mild-to-moderate OSA.

Continuous Positive Airway Pressure (CPAP) is the preferred treatment option for moderate-to-severe OSA and can be also considered for mild OSA with excessive daytime sleepiness (EDS) or cardiovascular comorbidities. CPAP provides a fixed level of continuous positive pressure, similar to end-expiratory positive pressure, which helps reduce AHI, improve EDS and restless sleep. CPAP will be more effective when combined with weight loss program and increased physical activity.

Other measures such as surgery, oral appliances or hypoglossal nerve stimulator are also significantly effective in treating OSA.

Interventions to OSA in subjects with MetS not only needs to follow general principles in treating OSA but also pay attention to weight loss, increasing physical activity and treating specific risk factors for MetS such as hypertension, T2DM and dyslipidemia.

Effects of OSA treatment on Metabolic syndrome

In addition to the obvious effectiveness of CPAP on OSA, many studies have proven that maintaining CPAP has effects on components of MetS such as reducing cholesterolemia, triglyceridemia and plasma LDL-C, increasing plasma HDL-C; reducing systolic and diastolic BP. CPAP adherence in patients with moderate to severe OSA is associated with reduced incidence of T2DM and reduced complications of diabetes.

Thus, through the effects on OSA and components of MetS, CPAP shown a positive role in reducing the risk of cardiovascular events in patients with these two syndromes.

Chapter 2. SUBJECTS AND METHODS

2.1. Subjects, location and time of research

The study was conducted on 146 subjects aged 18 years and older, diagnosed with MetS, examined and treated at the Department of respiratory cardiovascular disease and Medical Examination Department, Hai Phong Medical University Hospital in the period from February 2019 to February 2023.

Selection criteria of research subjects

Patients 18 years of age or older, agree to participate in the study, had at least 3 out of 5 diagnostic criteria to determine MetS according to the 2009 consolidated standards (based on adjusted NCEP - ATPIII in 2005, with waist circumference applicable to Asians): (1) Waist circumference > 90 cm for men and > 80 cm for women. (2) Triglyceridemia ≥ 1,7 mmol/l or being treated to reduce triglyceridemia. (3) HDL-C < 1,03 mmol/l for men and < 1,29 mmol/l for women. (4) Systolic BP ≥ 130 mmHg and/or diastolic BP ≥ 85 mmHg or being treated for hypertension. (5) Fasting glycemia ≥ 5,6 mmol/l or being treated for diabetes.

Exclusion criteria

1. Those with combined diseases: asthma, COPD (chronic obstructive pulmonary disease), heart failure; neuromuscular disease, mental disorders, dementia; chronic kidney disease at least stage 4 or malignant diseases.
2. Patients with maxillofacial structural abnormalities (micrognathia, tonsils hypertrophy, short neck,…).
3. Patients with central sleep apnea (determined based on polygraphy results).
4. People suffering from acute illnesses such as fever, muscle pain
5. Pregnancy

2.2. Research methods

Study design: Cross-sectional descriptive and prospective cohort.

Study sampling and sample size

Formula for calculating cross-sectional research sample sizes:

$$n = Z^2_{1-\alpha/2}\frac{p(1-p)}{d^2}$$

Formula for calculating prospective cohort research sample sizes:

$$n = \frac{2C(1-r)}{(ES)^2}$$

With: $C = (z_{\alpha/2} + z_b)^2$ $ES = \frac{\bar{d}}{s}$

The minimum sample size for the cross-sectional design is 93 subjects and for each intervention and control group in the prospective cohort design is 23 subjects. Subjects who have the selection criteria and do not have exclusion criteria, agree and voluntarily participate were selected for the

study until the necessary sample size is sufficient for both objectives. In this study, to have the necessary sample size for 2nd phase, the sample size of the cross-sectional descriptive study was up to 146 subjects.

Research variables and indicators

Demographic and anthropometric variables: age, gender, place of residence, height, weight, BMI, neck circumference, waist circumference.

Variables and indicators of medical history, habits and clinical features of OSA: smoking status, alcohol consumption; history of hypertension, diabetes and dyslipidemia; night symptoms, daytime symptoms of OSA, Epworth score, Pichot score.

Variables, paraclinical indicators and polygraphy results: Fasting glycemia, total cholesterolemia, triglyceridemia, plasma HDL-C and LDL-C; AHI, average SpO2 and SpO2 nadir during sleep.

Variables regarding compliance with interventions and CPAP adverse effects: Number of days of physical activity, duration of physical activity and number of days of oropharyngeal muscle excercise per month; Number of nights using CPAP $\geq$ 4 hours/night per month, duration of CPAP per night and adverse effects of CPAP.

Research equipment

Sample medical history, electronic scale, tapeline for meassurement of weight, height, waist circumference and neck circumference; Alice NightOne polygraph devices (Phillip Respironics, USA) and autoCPAP devices (Phillip Respironics or ResMed, USA).

Data processing

The data collected in the study were processed according to appropriate medical statistical algorithms using SPSS 20.0 software.

Research ethics

This research was carried out with the Biomedical Research Ethics Approval Council No. 3B/HĐĐĐ dated October 12, 2019 of Hai Phong University of Medicine and Pharmacy. The study was conducted with the consent of Hai Phong Medical University Hospital. Research participants were clearly explained the purpose of the research as well as fully explained and advised about the intervention measures before they decided to choose the intervention and voluntarily participate into research. Patient-related information is kept confidential and used for research purposes only.

Chapter 3. RESEARCH RESULTS

Research results showed that, in 146 subjects with MetS participating in the study, the prevalence of OSA was very high (82,9%), of which the frequency of mild OSA was 16,4%, of moderate OSA was 32,9% and the severe OSA was 33,6%.

3.1. Clinical and paraclinical characteristics and polygraph results in subjects with MetS and OSA

Table 3.1. Demographic and anthropometric characteristics of subjects

Characteristics	**Both groups (n = 146)**	**OSA group (n = 121)**	**Non-OSA group (n = 25)**	**p**
Age (years), *mean ± SD*	55,4 ± 10,7	56,7 ± 10,7	49,3 ± 8,5	**<0,001**
Male, *rate (%)* Female, *rate (%)*	67 (45,9) 79 (54,1)	56 (46,3) 65 (53,7)	11 (44,0) 14 (56,0)	0,85
Urban area, *rate (%)* Rural area, *rate (%)*	127 (85,1) 19 (14,9)	106 (87,6) 15 (12,4)	21 (84,0) 4 (16,0)	0,62
BMI (kg/m^2), *mean ± SD*	23,9 ± 1,7	24,3 ± 1,6	22,2 ± 0,6	**<0,001**
Neck circumference (cm), *mean ± SD*	42,4 ± 2,4	42,9 ± 2,3	40,0 ± 1,6	**<0,001**
Waist circumference (cm), *mean ± SD*	90,1 ± 6,7	90,8 ± 6,8	86,5 ± 5,3	**0,004**
Smoking, *rate (%)* Non smoking/stopped smoking, *rate (%)*	39 (26,7) 107 (73,3)	34 (28,1) 87 (79,1)	5 (20,0) 20 (80,0)	0,4
Drinking lot of alcohol/beer, *rate (%)* Non drinking lot of alcohol/beer, *rate (%)*	35 (24,0) 111 (76,0)	28 (23,1) 93 (76,9)	7 (28,0) 18 (72,0)	0,6

Remarks: The average age of the study group was 55,4 years old, the OSA group had average age of 56,7 years old, statistically significantly higher than the non-OSA group.

The average BMI of the study group was 23,9 kg/m^2 (corresponding to the overweight level according to the WHO classification for the Asia-Pacific region). The average BMI of the OSA group was 24,3 kg/m^2, the statistically significant difference than the non-OSA group ($p < 0,001$).

The average neck and waist circumference of the study group were 42,4 cm and 90,1 cm, respectively. These ones of the OSA group were higher than that of the non-OSA group ($p < 0,001$ and $p = 0,004$, respectively).

There was 26,7% of the subjects were smoking and 24% were drinking a lot of alcohol or beer. There was no statistically significant difference in

smoking status and alcohol consumption between two groups.

The ratio of male/female and people living in urban/rural areas was not differ between the OSA and non-OSA groups.

Table 3.2. Clinical characteristics of OSA in subjects with MetS

Characteristics	**Both groups (n = 146)**	**OSA group (n = 121)**	**Non-OSA group (n = 25)**	**p**
sBP (mmHg), *mean ± SD*	141,2 ± 11,8	143,6 ± 10,9	129,8 ± 9,6	**0,001**
dBP (mmHg), *mean ± SD*	86,1 ± 7,4	87,8 ± 4,9	81,9 ± 3,8	**<0,001**
Loud snoring ≥ 3 nights per week, *rate (%)* < 3 nights per week, *rate (%)*	 117 (80,1) 29 (19,9)	 110 (90,9) 11 (9,1)	 7 (28,0) 18 (72,0)	**<0,001**
Observed apnea ≥ 3 nights per week, *rate (%)* < 3 nights per week, *rate (%)*	 49 (33,6) 97 (66,4)	 48 (39,7) 73 (60,3)	 1 (4,0) 24 (96,0)	**0,001**
Nocturia ≥ 3 nights per week, *rate (%)* < 3 nights per week, *rate (%)*	 111 (76,0) 35 (24,0)	 97 (80,2) 24 (19,8)	 14 (56,0) 11 (44,0)	**0,01**
Gasping or choking ≥ 3 nights per week, *rate (%)* < 3 nights per week, *rate (%)*	 86 (58,9) 60 (41,1)	 80 (66,1) 41 (33,9)	 6 (24,0) 19 (76,0)	**<0,001**
Morning headache ≥ 3 days per week, *rate (%)* < 3 days per week, *rate (%)*	 67 (45,9) 79 (51,1)	 64 (52,9) 57 (47,1)	 3 (12,0) 22 (88,0)	**<0,001**
Xerostomia ≥ 3 days per week, *rate (%)* < 3 days per week, *rate (%)*	 58 (39,7) 88 (60,3)	 51 (42,1) 70 (57,9)	 7 (28,0) 18 (72,0)	0,19
Epworth score, *mean ± SD*	12,9 ± 3,2	14,2 ± 1,8	7,0 ± 1,1	**<0,001**
Pichot score, *mean ± SD*	22,3 ± 3,3	23,2 ± 2,9	18,2 ± 1,9	**<0,001**

Remarks: The mean systolic and diastolic BP of the OSA group were 143,6 ± 10,9 mmHg and 87,8 ± 4,9 mmHg, respectively, and were statistically significantly higher than the non-OSA group ($p < 0,001$).

The prevalence of symptoms of loud snoring, observed apnea, nocturia, gasping or choking during sleep and morning headache in the OSA group ranged from 39,7% to 90,9%, statistically significantly higher than the non-OSA group.

The prevalence of xerostomia in the OSA group was 42,1% and was not different from the non-OSA group.

The average of Epworth score and Pichot score of the OSA group are quite high, 14,2 ± 1,8 and 23,2 ± 2,9 points respectively, significantly higher than the group without OSA (p < 0,001).

Table 3.3. Comorbidities in OSA group and non-OSA group

Characteristics	**Both groups (n = 146)**	**OSA group (n = 121)**	**Non-OSA group (n = 25)**	**p**
Hypertention:				
Yes	76 (52,1)	70 (57,9)	6 (24,0)	**0,002**
No	70 (47,9)	51 (42,1)	19 (76,0)	
Type 2 diebetes:				
Yes	35 (24,0)	32 (24,6)	3 (12,0)	0,12
No	111 (76,0)	89 (73,6)	22 (88,0)	
Dyslipidemia:				
Yes	59 (40,4)	54 (44,6)	5 (20,0)	**0,02**
No	87 (59,6)	67 (55,4)	20 (80,0)	

Remarks: The prevalence of hypertension (57,9%), type 2 diabetes (24,6%) and dyslipidemia (44,6%) in the study subjects was quite high.

The prevalence of hypertension and dyslipidemia in OSA group was statistically significantly higher than non-OSA group (p = 0,002 and p = 0,02, respectively). The prevalence of T2DM was not differ between the two groups.

Table 3.4. Paraclinical characteristics of OSA in subjects with MetS

Characteristics	**Both groups (n = 146)**	**OSA group (n = 121)**	**Non-OSA group (n = 25)**	**p**
Fasting glycemia (mmol/l), *mean ± SD*	6,93 ± 1,67	6,89 ± 1,72	7,17 ± 1,37	0,16
Cholesterolemia (mmol/l), *mean ± SD*	5,49 ± 1,41	5,48 ± 1,46	5,58 ± 1,15	0,73
Triglyceridemia (mmol/l), *mean ± SD*	2,67 ± 1,55	2,69 ± 1,48	2,56 ± 1,87	0,38
Plasma LDL-C (mmol/l), *mean ± SD*	3,04 ± 1,21	2,93 ± 1,25	3,16 ± 0,99	0,58
Plasma HDL-C (mmol/l), *mean ± SD*	1,24 ± 0,27	1,23 ± 0,27	1,26 ± 0,25	0,7

Remarks: There was no statistically significant difference in mean fasting glycemia, cholesterolemia, triglyceridemia, plasma LDL-C and plasma HDL-C levels between the OSA group and the non-OSA group.

Table 3.5. Polygraphy results of OSA in subjects with MetS

Characteristics	**Both groups (n = 146)**	**OSA group (n = 121)**	**Non-OSA group (n = 25)**	**p**
AHI (times/hour), *mean ± SD*	27,1 ± 14,8	30,9 ± 13,2	8,4 ± 1,7	
Average SpO2 (%),*mean ± SD*	93,3 ± 1,6	92,8 ± 1,2	95,7 ± 0,6	**< 0,001**
SpO2 nadir (%),*mean ± SD*	85,9 ± 5,7	84,5 ± 5,2	92,7 ± 1,1	**< 0,001**

Remarks: The average AHI of the OSA group was 30,9 times/hour, equivalent to the threshold of severe OSA. The average SpO2 in the study group was 93,3% and the SpO2 nadir was 85,9%. The average SpO2 and SpO2 nadir in the OSA group were statistically significantly lower than in the non-OSA group (both p < 0,001).

Table 3.6. The relationship between OSA and demographic, anthropometric characteristics in subjects with MetS

Characteristics	**OR**	**CI 95%**	**p**
Age group (≥ 50 /< 50 years)	2,4	0,98 – 5,8	0,052
Gendre (Male/ Female)	1,1	0,5 – 2,6	0,8
Location (Urban area/Rural area)	1,3	0,4 – 4,4	0,6
BMI: (Overweight or Obesity/ Underweight or Normal)	54,8	11,9 – 250,3	**< 0,001**
Neck circumference group: (High risk/ Low risk)	20,8	4,7 – 92,7	**< 0,001**
Waist circumference group: (High risk/ Low risk)	3,0	1,2 – 7,8	**0,02**

Remarks: Subjects with MetS and "overweight or obesity" had 54,8 folds higher risk of OSA than subjects with MetS and "underweight or normal weight" (p < 0,001).

People with MetS and neck circumference at "high-risk" (over 43 cm in male and over 41 cm in female) had 20,8 folds higher risk of OSA than people

with MetS and neck circumference at “low-risk” (p < 0,001). Similarly, people with MetS and "large waist circumference" (over 90 cm in male and over 80 cm in female) had 3 folds higher risk of OSA than people with MetS and "small waist circumference" (p = 0,02).

Table 3.7. Associations between OSA and clinical characteristics in subjects with MetS

Characteristics	OR	CI 95%	p
Smoking status: (Smoking/Non smoking or stopped smoking)	1,6	0,5 – 4,5	0,4
Drinking status: (Drinking a lot/Non drinking a lot of alcohol)	0,8	0,3 – 2	0,6
Loud snoring: (≥ 3 nights per week / < 3 nights per week)	25,7	8,8 – 75	**< 0,001**
Observed apnea: (≥ 3 nights per week / < 3 nights per week)	15,8	2,1 – 47,5	**< 0,001**
Nocturia: (≥ 3 nights per week / < 3 nights per week)	3,2	1,3 – 7,9	**0,01**
Gasping or choking: (≥ 3 nights per week / < 3 nights per week)	6,2	2,3 – 16,7	**< 0,001**
Xerostomia: (≥ 3 days per week / < 3 days per week)	1,9	0,7 – 4,8	0,2
Morning headeache: (≥ 3 days per week / < 3 days per week)	8,2	2,3 – 28,9	**< 0,001**

Remarks: People with “snoring ≥ 3 nights per week” or “observed apnea ≥ 3 nights per week” had 25,7 folds and 15,8 folds higher risk of OSA than people without these symptoms (p < 0,001).

People with "gasping or choking ≥ 3 nights per week" or "morning headache ≥ 3 days per week" had 6,2 folds and 8,2 folds higher risk of OSA than people without these symptoms (p < 0,001).

People with "nocturia ≥ 3 nights per week" had 3,2 folds higher risk of OSA than people without nocturia (p = 0,01).

This study found no relationship between OSA and smoking, drinking a lot of alcohol or xerostomia (p > 0,05).

3.2. Clinical and paraclinical results in people with OSA and MetS after three months of health education intervention and CPAP

Table 3.8. Characteristics of the intervention groups at the beginning

Characteristics	**CPAP group (n = 24)**	**Exercise group (n = 23)**	**Non-adherent group (n =26)**	**p**
Age (years), *mean ± SD*	51,4 ± 11,4	55,5 ± 12,8	54,9 ± 9,7	0,4
Male, *rate (%)*	13 (39,4)	10 (30,3)	10 (30,3)	0,5
BMI (kg/m^2), *mean ± SD*	24,4 ± 2,1	24,6 ± 1,3	24,4 ± 1,1	0,9
Waist circumference (cm), *mean ± SD*	92,4 ± 6,4	91,7 ± 6,3	91,7 ± 5,9	0,8
Neck circumference (cm), *mean ± SD*	43,6 ± 1,7	43,6 ± 1,7	44,0 ± 2,3	0,7
Loud snoring ≥ 3 nights per week, *rate* < 3 nights per week, *rate*	 23 1	 22 1	 25 1	0,9
Observed apnea ≥ 3 nights per week, *rate* < 3 nights per week, *rate*	 12 12	 14 9	 12 14	0,6
Nocturia ≥ 3 nights per week, *rate* < 3 nights per week, *rate*	 21 3	 20 3	 21 5	0,8
Gasping or choking ≥ 3 nights per week, *rate* < 3 nights per week, *rate*	 16 8	 19 4	 20 6	0,4
Morning headache ≥ 3 days per week, *rate* < 3 days per week, *rate*	 15 9	 16 7	 17 9	0,9
Xerostomia ≥ 3 days per week, *rate* < 3 days per week, *rate*	 11 13	 15 8	 13 13	0,4
Epworth score, *mean ± SD*	15,0 ± 1,9	14,5 ± 1,6	14,6 ± 1,8	0,6
sBP (mmHg), *mean ± SD*	142,8 ± 9,3	146,3 ± 10,8	143,3 ± 12,1	0,5
dBP (mmHg), *mean ± SD*	90,2 ± 4,4	90,7 ± 4,2	88,1 ± 4,4	0,08
Fassting glycemia (mmol/l), *mean ± SD*	6,25 ± 0,97	6,65 ± 1,32	6,68 ± 1,06	0,3
Cholesterolemia (mmol/l), *mean ± SD*	5,79 ± 1,17	5,30 ± 1,56	4,86 ± 1,23	0,05
Triglyceridemia (mmol/l), *mean ± SD*	3,67 ± 1,88	2,66 ± 1,17	2,64 ± 1,59	0,06
Plasma LDL-C (mmol/l), *mean ± SD*	2,88 ± 1,09	3,06 ± 1,50	2,69 ± 1,04	0,5

Plasma HDL-C (mmol/l), *mean ± SD*	1,24 ± 0,23	1,24 ± 0,24	1,31 ± 0,29	0,5
AHI (times/hour), *mean ± SD*	39,7 ± 12,6	35,9 ± 8,3	32,5 ± 8,7	0,06
Average SpO2 level (%), *mean ± SD*	92,3 ± 0,8	92,4 ± 0,8	92,4 ± 0,8	0,8
SpO2 nadir level (%), *mean ± SD*	80,8 ± 4,4	82,6 ± 3,3	83,1 ± 5,0	0,2

Remarks: There were no statistically significant differences in anthropometric indices, clinical symptoms and paraclinical symptoms between three groups at the beginning of the study.

Table 3.9. Clinical characteristics of three groups after interventions

Characteristics	CPAP group (n = 24)	Exercise group (n = 23)	Non-adherent group (n =26)	p
Loud snoring:				**0,003** *
≥ 3 nights per week, *rate*	1	10	25	**0,001** **
< 3 nights per week, *rate*	23	13	1	**0.001** #
Observed apnea:				**0,001** *
≥ 3 nights per week, *rate*	1	11	12	**0,001** **
< 3 nights per week, *rate*	23	12	14	0,9 #
Nocturia:				**0,005** *
≥ 3 nights per week, *rate*	5	14	19	**0,001** **
< 3 nights per week, *rate*	19	9	7	0,3 #
Gasping or choking:				**0,005** *
≥ 3 nights per week, *rate*	5	14	20	**< 0,001****
< 3 nights per week, *rate*	19	9	6	0,2 #
Morning headache				**0,01** *
≥ 3 days per week, *rate*	1	7	18	**< 0,001** **
< 3 days per week, *rate*	23	16	8	**0,007** #
Xerostomia:				**0,02** *
≥ 3 days per week, *rate*	5	12	13	**0,03** **
< 3 days per week, *rate*	19	11	13	0,8 #
sBP (mmHg), *mean ± SD*	137,6 ± 9,3	145,9 ± 10,5	143,2 ± 10,4	**0,02**
dBP (mmHg), *mean ± SD*	87,3 ± 3,9	90,5 ± 4,2	87,7 ± 4,9	**0,03**
Epworth score, *mean ± SD*	9,0 ± 1,6	14,0 ± 1,7	14,8 ± 1,5	**<0,001**
Pichot score, *mean ± SD*	18,3 ± 2,4	23,8 ± 1,1	24,4 ± 1,3	**<0,001**

(*): CPAP group vs Exercise group; (**): CPAP group vs Non-adherent group; (#): Exercise group vs Non-adherent group

Remarks: After three months of intervention, the frequency of loud snoring, observed apnea, nocturia and gasping/choking ≥ 3 nights per week, morning headache and xerostomia ≥ 3 days per week in the "CPAP" group was statistically significantly different than the "exercise" group and the "non-

adherent" group (p < 0,001 to p = 0,03).

The frequency of loud snoring ≥ 3 nights per week and morning headaches ≥ 3 days per week were also significantly different in the "exercise" group compared to the "non-adherent" group (p = 0,001 and p = 0,007). Systolic BP, diastolic BP, Epworth score and Pichot score were significantly different between the three groups. Post-hoc analysis showed that there was a difference in systolic BP and diastolic BP between the "CPAP" group and the "exercise" group (p = 0,02 and p = 0,03, respectively). There was a clear difference in Epworth score and Pichot score between the "CPAP" group and the "exercise" group, between the "CPAP" group and the " non-adherent" group (p < 0,001).

Table 3.10. Paraclinical characteristics and polygraphy results of three groups after interventions

Characteristics	CPAP group (n = 24)	Exercise group (n = 23)	Non-adherent group (n =26)	p
Fassting glycemia (mmol/l), *mean ± SD*	6,05 ± 0,81	6,22 ± 0,98	6,73 ± 1,06	0,1
Cholesterolemia (mmol/l), *mean ± SD*	5,02 ± 0,88	4,97 ± 0,98	5,61 ± 1,23	0,053
Triglyceridemia (mmol/l), *mean ± SD*	2,37 ± 1,22	2,01 ± 0,79	2,28 ± 1,14	0,6
Plasma LDL-C (mmol/l), *mean ± SD*	2,59 ± 0,8	2,79 ± 0,95	3,3 ± 1,07	**0,03**
Plasma HDL-C (mmol/l), *mean ± SD*	1,35 ± 0,29	1,27 ± 0,23	1,29 ± 0,35	0,6
AHI (times/hour), *mean ± SD*	3,7 ± 1,7	35,1 ± 7,8	33,1 ± 8,9	**<0,001**
Average SpO2 level (%), *mean ± SD*	95,3 ± 0,6	93,2 ± 0,8	92,7 ± 0,9	**<0,001**
Minimum SpO2 level (%), *mean ± SD*	95,1 ± 1,0	85,0 ± 3,2	83,5 ± 5,4	**<0,001**

Remarks: After 3 months of intervention, the values of plasma LDL-C, AHI, average SpO2 and SpO2 nadir during sleep were significantly different between the three groups. Post-hoc analysis showed a difference in plasma LDL-C value between the "CPAP" group and the "non-adherent" group (p = 0,03) and a significant difference in mean AHI, average SpO2 and SpO2 nadir values between the "CPAP" group and the "exercise" group, between the "CPAP" group and the "non- adherent" group (p < 0,001).

No difference was found in fasting glycemia, cholesterolemia, triglyceridemia, plasma HDL-C values between the "CPAP" group, the "exercise" group and the "non- adherent" group after 3 months of intervention.

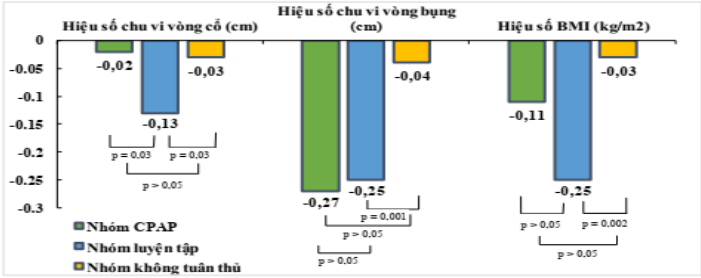

Figure 3.1. Differente changes in anthropometric indices between intervention groups after three months

Remarks: The average of neck circumference in the "exercise" group decreased by 0,13 cm after 3 months and was statistically different than the "CPAP" group and the "non-adherent" group (p = 0,03). No difference in neck circumference difference was found between the “CPAP” group and the “non- adherent” group.

The average of waist circumference decreased by 0,27 cm in the "CPAP" group and 0,25 cm in the "exercise" group after 3 months and was significantly different than the "non-adherent" group (p = 0,001). There was no difference in waist circumference difference in the “CPAP” group and the “exercise” group.

The "exercise” group had the BMI average decrease of 0,25 kg/m^2 after 3 months and was statistically different from the "non-adherent" group (p = 0,002). There was no difference in BMI change after 3 months of intervention in the "CPAP" group compared to the other two groups.

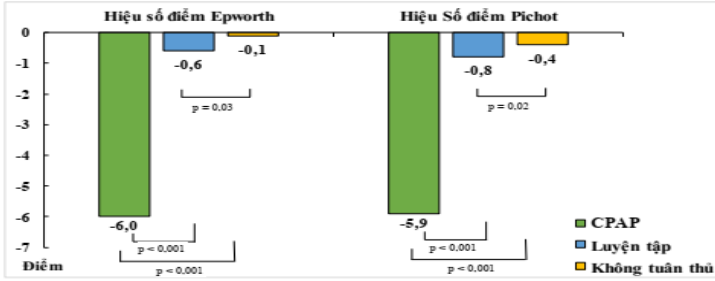

Figure 3.2. Differente changes in Epworth score and Pichot score between intervention groups after three months

Remarks: After 3 months, the "CPAP" group had the Epworth score average

decreased by 6 points, the Pichot score average decreased by 5,9 points. There was a statistically significant difference compared to the "exercise" group" and "non-adherent" group (all p < 0,001).

The Epworth score average and Pichot score average of the "exercise" group decreased by 0,6 points and 0,8 points respectively after 3 months. There was a statistically significant difference compared to the "non-adherent" group (p = 0,03 and p = 0,02 respectively).

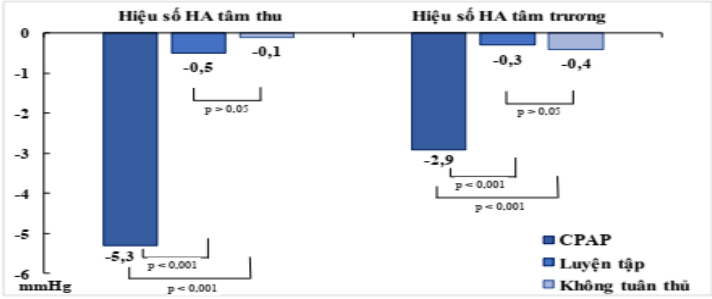

Figure 3.3. Differente changes in blood pressures between intervention groups after three months

Remarks: After 3 months, the "CPAP" group had the systolic BP average decrease of 5,3 mmHg, the diastolic BP average decrease of 2,9 mmHg, a statistically significant difference compared to "exercise" group and "non-adherent" group (all p < 0,001). There was no difference in systolic BP and diastolic BP change between the "exercise" group and the "non-adherent" group.

Table 3.11. Differente changes in paraclinical characteristics between intervention groups after three months

Difference (T3 -T0)	**CPAP group (n = 24)** *Mean ± SD*	**Exercise group (n = 23)** *Mean ± SD*	**Non-adherent group (n =26)** *Mean ± SD*	**p**
Fassting glycemia difference (mmol/l)	-0,19 ± 0,59	-0,43 ± 1,11	0,05 ± 1,28	0,4 * 0,4 ** 0,2 #
Cholesterolemia difference (mmol/l)	-0,77 ± 0,84	-0,32 ± 0,84	0,75 ± 1,43	0,08 * **< 0,001** ** **0,003** #

Triglyceridemia difference (mmol/l)	-1,29 ± 1,21	-0,65 ± 0,83	-0,36 ± 1,64	**0,04** * **0,03** ** 0,4 #
Plasma LDL-C difference (mmol/l)	-0,29 ± 0,96	-0,06 ± 0,75	0,95 ± 1,51	0,4 * **0,001** ** **0,005** #
Plasma HDL-C difference (mmol/l)	0,11 ± 0,3	0,03 ± 0,24	-0,03 ± 0,32	0,08 * 0,1 ** 0,4 #
AHI difference (times/hour)	-36,1 ± 12,3	-0,8 ± 1,5	0,7 ± 1,3	**< 0,001** * **< 0,001** ** **0,01** #
SpO2 nadir levels difference (%)	14,3 ± 4,2	2,4 ± 1,4	0,5 ± 1,3	**< 0,001** * **< 0,001** ** **< 0,001** #

(*): CPAP group vs Exercise group; (**): CPAP group vs Non-adherent group; (#): Exercise group vs Non-adherent group

Remarks: After 3 months of interventions, the "CPAP" group had the cholesterolemia average decrease of 0,77 mmol/l and the LDL-C average decrease of 0,29 mmol/l; the "exercise" group had the average of cholesterolemia decrease of 0,32 mmol/l and the average of LDL-C decrease of 0,06 mmol/l, there was a significant difference compared to the change in the "non-adherent" group ($p < 0,001$ to $p = 0,005$). There was no difference in the change of cholesterolemia average and LDL-C concentrations between the "CPAP" group and the "exercise" group.

The average of triglyceridemia decreased by 1,29 mmol/l in the “CPAP” group. There was a significant difference compared to the changes in the other two groups ($p = 0,03$ and $p = 0,04$). There was no difference in the average of triglyceridemia change between the “exercise” group and the “non-adherent” group.

The average AHI decreased significantly in the “CPAP” group (36,1 times/hour) compared to the other two groups ($p < 0,001$) and decreased significantly in the “exercise” group compared to “non-adherent” group ($p = 0,01$). The SpO2 nadir levels increased significantly in the “CPAP” group (14,3%) compared to the other two groups ($p < 0,001$) and increased significantly in the “exercise” group compared to the “non-adherent” group ($p <0,001$).

Chapter 4. DISSCUSSIONS

4.1. Clinical and paraclinical characteristics and polygraph results in people with MetS and OSA

Our study involved 146 cases of MetS, including 121 subjects with OSA (accounting for 82,9%) and 25 subjects without OSA. Among 121 subjects with OSA, there were 24 subjects with mild OSA (16,4%), 48 subjects with moderate OSA (32,9%) and 49 subjects with severe OSA (33,6%). The relationship between MetS and OSA is a two-way relationship in which overweight and obesity are common risk factors. In general, the incidence of OSA in subjects with MetS and conversely, the incidence of MetS in subjects with OSA are significantly higher than in the general population, of which moderate-to-severe OSA accounts for the majority. With these results, we believe that screening for OSA in high-risk subjects in general and in people with MetS is very important, from which we can provide counseling, support and intervention measures. Treatement is necessary in cases of moderate-to-severe OSA to minimize the risk of future cardiovascular-metabolic events.

Table 3.2 shown that the average systolic and diastolic BP values of the OSA group were 143,6 mmHg and 87,8 mmHg, respectively, both statistically significantly higher than the non-OSA group with $p = 0,001$ and $p < 0,001$ respectively. This study also recorded that 57,9% of cases with OSA were diagnosed with hypertension, significantly higher than the rate of hypertension in the non-OSA group ($p = 0,002$) (table 3.3). Increased systolic and/or diastolic BP is one of the five criterias to diagnose MetS, and also a very common consequence in OSA patients. OSA characterized by repeated episodes of apnea or hypopnea during sleep, causes numerous arousals, sleep fragmentation and repeated intermittent hypoxemia, which leads to sympathetic nervous system, oxidative stress, systemic inflammation, vascular endothelial damage. These are all the sources of cardiovascular and metabolic disorders, typically hypertension. Currently, OSA is mentioned as a common and treatable cause of hypertension.

Our study noted that nighttime and daytime symptoms in OSA patients are very diverse. Loud snoring, nocturia, gasping or choking during sleep and morning headaches were found at high rates in the OSA group (90,9%; 80,2%; 66,1% and 52,9%, respectively). This study found that 39,7% of OSA patients had observed apnea and 42,1% had xerostomia. Observed apnea is a very suggestive and specific symptom for OSA.

Among the daytime symptoms of OSA, excessive daytime sleepiness (EDS) is the most common signs. EDS assessed through the Epworth score with eight questions. Epworth score > 10 points is classified as having EDS. Our study found that the average of Epworth score of the OSA group was 14.2 ± 1.8 points, statistically significantly higher than the non-OSA group ($p < 0,001$). Other common symptom in OSA patients is fatigue and poor concentration. In this study, we used the Pichot scale to evaluate participants' fatigue and recorded the average Pichot score of the OSA group was 23,2 ± 2,9 points, statistically significantly higher than the non-OSA group ($p < 0,001$).

Table 3.4 shown that the average of fasting glycemia, cholesterolemia, triglyceridemia, plasma HDL-C and plasma LDL-C concentrations of the OSA group were 6,89 ± 1,72; 5,48 ± 1,46; 2,69 ± 1,48; 1,23 ± 0,27 and 2,93 ± 1,25 mmol/l. There was not statistically difference compared to the non-OSA group.

The results of polygraphy in our study shown that the average of AHI of the OSA group was 30,9 ± 13,2 times/hour, equivalent to the threshold of severe OSA. In general, the average of AHI in MetS patients comorbid OSA in the world is very different, possibly related to differences in age, gender, race and body mass index but they were all at high level. The average SpO2 levels during sleep in the OSA group was 92,8 ± 1,2%, statistically significantly lower than the non-OSA group ($p < 0,001$). The SpO2 nadir during sleep in the OSA group was 85,9%, statistically significantly lower than the non-OSA group ($p < 0,001$). This result is consistent with the literature on the characteristics and consequences of OSA. Intermittent and repeated reduction in SpO2 during sleep is the main cause of sympathetic nerve stimulation, activation of the RAS, oxidative stress and vascular endothelial damage. The consequences of this condition are atherosclerosis, insulin resistance, hypertension, arrhythmias, dyslipidemia, hyperglycemia and stroke.

The relationship between OSA and demographic, anthropometric characteristics shown in table 3.6 showed that people with MetS and "overweight or obesity" had 54,8 folds higher risk of OSA than those with MetS and “underweight or normalweight” ($p < 0,001$). People with MetS and neck circumference at “high-risk” had 20,8 folds higher risk of OSA than people with MS neck circumference at “low-risk” ($p<0,001$). Similarly, people with "large waist circumference” had 3 folds higher risk of OSA than people with "small waist circumference" ($p = 0,02$). Overweight and obesity

cause fat accumulation in the oropharynx, increasing the volume of soft tissue around the upper airway, significantly contributing to the collapse of the upper airway during sleep. With these results, we found that anthropometric characteristics (including BMI, neck circumference, waist circumference) are very important in suggesting the risk of OSA in people with MetS and is easy to apply in clinical practice.

Table 3.7 showed that people with "snoring ≥ 3 nights per week" had 25,7 folds higher risk of OSA than people without this symptom ($p < 0,001$). Snoring is a sound produced by the vibration of soft tissues when the upper airway narrows during sleep. Research results showed that people with "observed apnea ≥ 3 nights per week" had 15,8 folds higher risk of OSA than people without this symptom ($p < 0,001$); People with MetS and "nocturia ≥ 3 nights per week" had 3,2 folds higher risk of OSA than people without this symptom ($p = 0,01$). Similarly, people with MS and "gasping or choking ≥ 3 nights per week" or "morning headaches ≥ 3 days per week" had 6,2 folds and 8,2 folds higher risk of OSA, respectively than people without these symptoms ($p < 0,001$).

4.2. Clinical and paraclinical results in people with OSA and MetS after three months of health education intervention and CPAP

In current study, from 146 subjects underwent polygraphy and participated in the cross-sectional study, 97 patients with moderate-to-severe OSA were recorded. All of these patients are guided and advised on lifestyle changes and exercise, with CPAP treatment. At the end of the second phase study, we recorded 24 cases in the "CPAP" group, 23 cases did not choose CPAP but complied with lifestyle change and exercise intervention were included in the "exercise" group. There were 26 cases who participated and completed the study period but did not choose CPAP and did not comply with the intervention, becoming the "non-adherent" control group in this study. After 3 months of intervention, there were differences in some clinical and paraclinical characteristics between three groups, specifically:

Regarding clinical features, the results in table 3.9 showed the frequency of loud snoring, observed apnea, nocturia and gasping or choking during sleep ≥ 3 nights per week, morning headaches and xerostomia ≥ 3 days per week in the "CPAP" group was statistically different from the "practice" group and the "non-adherent" group ($p < 0,001$ to $p = 0,03$). The "exercise"

group had frequency of loud snoring ≥ 3 nights per week and morning headaches ≥ 3 days per week is also statistically different from the "non-adherent" group (p = 0,001 and p = 0,007 respectively). This result showed that after three months of CPAP intervention and exercise and lifestyle changes in moderate-to-severe OSA cases, there were signs of positive changes in the clinical symptoms of OSA.

Oneway-ANOVA test comparing the mean values of systolic and diastolic BP, Epworth score and Pichot score between the three groups showed that there were statistically significant differences in these indices between the study groups. Post-hoc analysis showed that there was a significant difference in systolic BP and diastolic BP between the “CPAP” group and the “exercise” group (p = 0,02 and p = 0,03 respectively) and there was a significant difference in Epworth score between the “CPAP” group and the “execise” group, between the “CPAP” group and the “non-adherent” group (p < 0,001). This result showed that CPAP not only changes common clinical manifestations of OSA but also positively changes the BP of people with MetS in this study.

Regarding paraclinical characteristics, when comparing the average value of blood biochemical indices (fasting glycemia, cholesterolemia, triglyceridemia, LDL-C, HDL-C) and the results of polygraphy (AHI, average SpO2 and SpO2 nadir levels) among the three groups, our study recorded differences in plasma LDL-C values, AHI, average SpO2 and SpO2 nadir levels during sleep among the three groups (table 3.10). Post-hoc analysis showed a difference in mean LDL-C values between the “CPAP” group and the “non-adherent” group (p = 0,03) and a significant difference in AHI values, average SpO2 and SpO2 nadir levels between the “CPAP” group and the “exercise” group, between the “CPAP” group and the “non-adherent” group (p < 0,001).

About the differences in changes in anthropometric indicators, chart 3.1 showed that in the "exercise" group, the average of neck circumference decreased by 0,13 cm, the average of waist circumference decreased by 0,25 cm, and BMI average decreased of 0,25 kg/m^2 after three months of the study. There was a statistically significant difference compared to the change in these indicators in the "non-adherent" group (p = 0,03; p = 0,001 and p = 0,002 respectively). The “exercise” group also had a statistically significant difference in neck circumference compared to the “CPAP” group (p = 0,03). This result showed that, although the cases participating in our cohort study

mainly had a weight in the mildly overweight range (the average BMI of the three groups was 24,4 – 24,6 kg/m^2), with weight change is not much after three months, but if maintained regularly and actively lifestyle interventions including physical activity and pharyngeal muscle exercise can also reduce anthropometric indices associated with central obesity - a high risk factor in the common pathogenesis of both OSA and MetS. These results proved the positive effect of pharyngeal muscle strengthening exercises on upper airway stenosis.

Differences observed in blood pressure changes, chart 3.2 showed that after three months of intervention, the average of systolic BP in the "CPAP" group decreased by 5,3 mmHg and the average of diastolic BP decreased by 2,9 mmHg, the remaining two groups were not seen significant changes in these indicators. The difference in systolic and diastolic BP change between the "CPAP" group compared to the "exercise" group and the "non-adherent" group was statistically significant ($p < 0,001$). In the medical literature, there have also been many publications documenting the BP-reducing effect of CPAP therapy. However, some studies did not find any difference in BP after CPAP ventilation. BP reduction effectiveness may be related to the severity of OSA, the duration of CPAP ventilation and patient compliance.

Our study did not observe a significant change in systolic and diastolic BP in the "exercise" group after three months. This can be explained because the lifestyle intervention measures applied in the study mainly focused on physical activity and increasing oropharyngeal muscle strength, with a short follow-up period.

Regarding changes in paraclinical characteristics and polygraphy results, the study noted that cholesterolemia, triglyceridemia and plasma LDL-C concentrations in the "CPAP" group decreased with statistical significance compared to the "non-adherent" group; the “exercise” group had statistically significantly greater reductions in cholesterolemia and plasma LDL-C concentrations than the “non-adherent” group. These results continue to strengthen the conclusion about the effectiveness of CPAP and health education interventions on lipidemia levels, in which CPAP still shows superiority. We expect that with a longer study period and better coordination between CPAP intervention and lifestyle changes, other blood biochemical indicators of MetS will be improved.

Comparing the effectiveness of intervention measures on polygraphy

indices after three months of follow-up, our results showed that the average AHI decreased significantly in the "CPAP" group (- 36,1 times /hour), decreased slightly in the “exercise” group (- 0,8 times/hour) and increased in the “non-adherent” group (0,7 times/hour). The study also found that the SpO2 nadir during sleep increased significantly in the "CPAP" group (increased by 14,3%) compared to the "exercise" group (increased by 2,4%) and the "non-adherent" group (increased by 0,5%).

CONCLUSION

1. Clinical and paraclinical characteristics and polygraph results in people with MetS and OSA

The frequency of OSA in people with MetS in this study was 82,9%.

Prevalence of loud snoring, observed apnea, nocturia, gasping or choking and morning headaches in people with MetS and OSA were high, from 52,9% to 90,9%.

The average of Epworth score and Pichot score of the OSA group were 14,2 ± 1,8 and 23,2 ± 2,9 points, respectively. The mean systolic BP and diastolic BP of the OSA group were 143,6 ± 10,9 mmHg and 86,9 ± 7,2 mmHg, respectively. The average AHI of the OSA group was 30,9 times/hour. The mean values of SpO2 nadir and average SpO2 during sleep in the OSA group were 84,5 ± 5,2 % and 92,8 ± 1,2 %, respectively.

Overweight and obesity, neck circumference, waist circumference and symptoms of loud snoring, observed apnea, nocturia, gasping or choking and morning headaches were statistically significantly related to OSA in people with MetS.

2. After three months of health education intervention and CPAP in patient groups with moderate-to-severe OSA and MetS

CPAP reduces prevalence of common clinical manifestations in OSA patients, including loud snoring, observed apnea, nocturia, gasping or choking, morning headaches, xerostomia, Epworth score and Pichot score. The average AHI decreased by 36,1 times/hour, the average SpO2 and SpO2 nadir values both increased, reaching > 95%.

CPAP improves some components of MetS, including waist

circumference reduced by 0,27 cm; systolic BP decreased by 5,3 mmHg; diastolic BP decreased by 2,9 mmHg and triglyceridemia concentration decreased by 1,29 mmol/l.

Health education intervention reduces prevalence of loud snoring, morning headaches, Epworth score and Pichot score in OSA patients. Average AHI decreased by 0,8 times/hour, SpO2 nadir levels increased by 2,4%.

Health education intervention improves one component of MetS, which was a reduction in waist circumference of 0,25 cm.

RECOMMENDATIONS

1. It is necessary and profitable to screen for OSA in patients with metabolic syndrome.

2. More studies are needed with larger sample sizes and longer cohort follow-up periods to evaluate the effectiveness of CPAP combined with health education interventions in reducing the component indexes of metabolic syndrome, cardiovascular events and mortality, to improve adherence to CPAP (when there are indication) and the quality of life in people with comorbid MetS and OSA.

PUBLISHED SCIENTIFIC WORKS RELATED TO THE THESIS

1. Nguyen Thi Hong Lien, Duong Quy Sy, Pham Van Linh (2023), "Clinical features, laboratory and polygraphic results in identifing comorbid obstructive sleep apnea on patients with metabolic syndrome diagnosed and followed up at Haiphong University hospital", *Vietnam Medical Journal*, Volume 529, August, special issue, pp. 194-201.

2. Nguyen Thi Hong Lien, Duong Quy Sy, Pham Van Linh (2023), "Results of continuous positive airway pressure ventilation, combined habit change intervention and oropharyngeal muscle exercise in patients with comorbid metabolic syndrome and obstructive sleep apnea", *Vietnam Medical Journal*, Volume 529, August, special issue, pp. 392-400.