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PREVALENCA METABOLIČKOG SINDROMA KOD OBOLELIH OD HRONIČNOG OBSTRUKTIVNOG BRONHITISA

PREVALENCE OF METABOLIC SYNDROME IN PATIENTS SUFFERED FROM CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Sažetak: Uočeno je da postoji povezanost hroničnog obstruktivnog bronhitisa i metaboličkog sindroma, a kao mogući uzrok te povezanosti navodi se sistemska inflamacija koja im je zajednička. Ipak, razlog prave povezanosti ove dve bolesti nije jasno dokazan. Metod: Studijom su obuhvaćena 232 pacijenta obolela od hroničnog obstruktivnog bronhitisa u stabilnoj fazi, bez znakova egzacerbacije i upotrebe kortikosteroidne terapije tri meseca pre uključivanja. Od 232 pacijenta, njih 60 je imalo metabolički sindrom. Za postavljanje dijagnoze metaboličkog sindroma neophodno je bilo ispuniti 3 ili više sledećih kriterijuma: obim struka preko 102cm za muškarce i 88cm za žene, trigliceridi našte 150 mg/dL ili više (≥1.69 mmol/L), vrednosti HDL manje od 40 mg/dL (<1.0 mmol/L) za muškarce i 50 mg/dL (<1.3 mmol/L) za žene, vrednost krvnog pritiska preko 130/85 mmHg, glukoze našte 110 mg/dL ili više (≥6.1 mmol/L). Kriterijumi za postavljanje dijagnoze hroničnog obstruktivnog bronhitisa sledeli su sledeće kriterijume: FEV1<80% i FEV1/FVC<0,7 od predvidjene vrednosti, a kao blaga, umerena i teška obstrukcija smatrane su vrednosti FEV1>80, 50-80 i <50% redom. Rezultati: U ovoj studiji prevalence metaboličkog sindroma u hroničnom obstruktivnom bronhitisu je 25. 9. Oba pola su u istom riziku od oboljevanaj od metaboličkog sindroma. Zaključak: Metabolički sindrom susreće se vrlo često u hroničnom obstruktivnom bronhitisu, stoga bi trebalo razmišljati o skriningu za isti.
Ključne reči: gojaznost, dislipidemija, HOBP, hipertenzija

Summary: There is some evidence that chronic obstructive pulmonary disease (COPD) and metabolic syndrome may be related, perhaps through systemic inflammation, which is common to both. However, the association between these two conditions has not yet been clearly shown. Methods: The study included 232 patients suffering from COPD with no signs of exacerbation and usage of corticosteroid therapy three months prior the examinations. Of the 232 patients, 60 patients had metabolic syndrome. The criteria for the identification of the metabolic syndrome included 3 or more of the following features: waist circumference exceeding 102 cm for men and 88 cm women, fasting triglycerides of 150 mg/dL or more (≥1.69 mmol/L), HDL-C less than 40 mg/dL (<1.0 mmol/L) for men and less than 50 mg/dL (<1.3 mmol/L) for women, blood pressure exceeding 130/85 mm Hg, and fasting plasma glucose levels of 110 mg/dL or more (≥6.1 mmol/L). The criteria for COPD were made by spirometry encompassing the following parameters: FEV1<80% and FEV1/FVC<0.7 of the predicted value. Mild, moderate and severe obstructions were defined as FEV1>80, 50-80 and <50% of the predicted, respectively. Results: The prevalence of metabolic syndrome in COPD patients is 25.9. Both genders are in the same risk of metabolic syndrome. Conclusion: The presence of metabolic syndrome is very frequent in patients with COPD. Hence, this population should be considered for screening for metabolic syndrome.
Key words: obesity, dyslipidemia, COPD, hypertension

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by airflow obstruction that is not fully reversible. Spirometry is the gold standard for diagnosing and monitoring progression of COPD which is defined by irreversible lung function impairment with a reduced FEV1/vital capacity (VC) ratio less than 70% of the predicted. The Global Initiative for chronic obstructive lung disease (GOLD) criteria classify COPD into four stages based primarily on lung function impairments as stage I (FEV1>=80%), II (FEV1 50-79%), III (FEV1 30-50%) and IV (FEV1<30% of the predicted) [1].

In COPD patients, unrelated disorders are relatively under recognized [2]. Those patients have much comorbiditiy like: cardiovascular diseases, osteoporosis, diabetes, and metabolic syndrome, more

commonly than expected by chance. These associations are greater than expected from common aetiological factors, such as smoking, suggesting that these comorbidities may be causally associated with the mechanisms of COPD, probably due to systemic inflammation [3, 4].

Metabolic syndrome is a set of risk factors that includes: abdominal obesity, a decreased ability to process glucose (increased blood glucose and/or insulin resistance), atherogenic dyslipidemia (elevated triglycerides levels, small low-density lipoprotein [LDL] particles, low high-density lipoprotein cholesterol [HDL-C] levels, raised blood pressure and prothrombotic and inflammatory states [5]. Patients who have this syndrome have been shown to be at an increased risk of developing cardiovascular disease and/or diabetes type 2. Recently, the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adults Treatment Panel III) (ATP III) have highlighted the importance of the metabolic syndrome and provided guidelines for the screening of this syndrome. The ATP III guidelines define the metabolic syndrome as a new secondary target for cardiovascular risk reduction therapy beyond low-density lipoprotein cholesterol (LDL-C) lowering. According to the ATP III report, the diagnosis of the metabolic syndrome requires 3 or more of the following criteria: waist circumference exceeding 102 cm and 88 cm for men and women, respectively, fasting triglycerides of 150 mg/dL or more (≥1.69 mmol/L), HDL-C less than 40 mg/dL (<1.0 mmol/L) for men and less than 50 mg/dL (<1.3 mmol/L) for women, blood pressure exceeding 130/85 mm Hg, and fasting plasma glucose levels of 110 mg/dL or more (≥6.1 mmol/L) [6].

The root cause of most cases of metabolic syndrome can be traced back to poor eating habits and a sedentary lifestyle. Some cases occur in those already diagnosed with hypertension and in those with poorly controlled diabetes; a few are thought to be linked to genetic factors that are still being researched [6]. On the basis of this, we suspected that patients with COPD would be at risk for the metabolic syndrome since these patients are limited by respiratory symptoms and adopted to a sedentary lifestyle, increasing their risk for weight gain and insulin resistance.

This study was undertaken to evaluate the presence of the metabolic syndrome in COPD patients.

MATERIAL AND METHODS

In a year and a half period, among 232 patients suffering from COPD we revealed 60 patients, who had metabolic syndrome according to the criteria. The diagnosis of COPD was made previously according to the GOLD criteria. Inclusion criteria apart from spirometric findings (FEV1/FVC<0.7, and FEV1<=80% of predicted) were no signs of exacerbation and use of systemic corticosteroid in the preceding 3 months. Among them, 57 were Caucasians and 3 belonged to the Roma population. The NCEP APT III criteria previously described was used for checking the presence of the metabolic syndrome. Individuals also met the criteria for hypertension if they were taking antihypertensive, and diabetes if they used oral hypoglycemic agents or insulin. Body weight, height, and waist circumference were obtained in all participants. Waist circumference was measured by a single observer using an inelastic tape at the midpoint between the lowest rib and the iliac crest. Blood pressure measurements were taken according to the American Heart Association's reco-mmendations. Blood pressure was taken from both arms and the higher measurement was used for te analysis [6, 7]. Participants were asked to fast for 12 hours before blood sampling. We analyzed serum glucose concentration, triglycerides, HDL-C and LDL-C levels and a standard pulmonary function test (spirometry-three consecutive measurement), arterial PaO2 and PaCO2.

Descriptive statistics were used to evaluate baseline characteristics. Data are reported as mean ±SD or proportions and 95% confidence intervals.

Statistical analysis was performed by unpaired t test, chi square test and Fisher exact test. A value of $P < 0.05$ was considered statistically significant.

RESULTS

The pulmonary function tests of the COPD group are presented in Table 1. Mean values for arterial PaO2 and PaCO2 were within normal range.

Baseline characteristics of all participants are given in Table 2. All women were postmenopausal. No woman was on hormone replacement therapy (HRT). Statistically important difference among women and men was found in HDL levels, usage of antihypertensive, hypolipemic and oral hypoglicemic therapy, as well as in obesity ($p<0.05$). Abdominal obesity, elevated blood pressure, and elevated triglycerides were the principal features of the metabolic syndrome observed in this group of COPD patients.

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Table 1. Characteristic of parameters of pulmonary function test and blood gasses

All	Men (n=36)	Women (n =24)	p value
FVC, % predicted	73±16.54	76.43±17.50	0.001
FEV1, % predicted Postbronhodilatator	50.49±15.64	56.04±18.53	0.03
FEV1/FVC, % predicted	61.08±85.14	65.36±17.40	0.09
PaO2, mm Hg	76± 9.1	85±12.1	0.04
PaCO2, mm Hg	41±4	37±3	0.001

FVC indicates forced vital capacity; FEV1, forced expiratory volume in first second;FEV1/FVC, forced expiratory volume in first second /forced vital capacity ratio; PaO2, partial pressure of oxygen; and PaCO2, partial pressure of carbon dioxide. Values are mean ± SD.

All the features of the metabolic syndrome were present in the same proportion of COPD men and COPD women Indeed, 58.3% patients had central obesity, hypertension had 85% pts, dyslipidemic were 52%, 37% had diabetes mellitus, 43.3% were smokers, 13.3% non smokers, and 43.4 ex-smokers. Metabolic syndrome had almost 2/3 pts.

Table 2. Characteristics of patients suffered from COPD and metabolic syndrome

	Men	Women	P value
Mean Age	70.03±1.39	61.78±2.13	0.575
BMI, kg/m2	26.95±0.72	26.87±1.25	0.03
Waist circumference	102.62±2.71	93.86±5.06	0.80
Systolic BP	140.55±3.36	138.75±3.74	0.04
Diastolic BP	84.72±1.61	85.83±2.20	0.016
Triglycerides, mmol/L	1.78±0.22	1.77±0.28	0.018
HDL cholesterol, mmol/L	1.07±0.57*	0.87±0.6	p<0.05
LDL cholesterol, mmol/L	2.97 ± 0.74	2.06±0.24	0.441
Fasting glucose, mmol/	6.81±0.49	5.76±1.98	0.03
Bronchodilatators, %	85.5	96.3	0.019
Antihypertensive agents, %	19.4*	8.3	p<0.05
Oral hypolipemic agents, %	41.7*	25	p<0.05
Oral anti diabetic agents, %	58.3*	41.7	p<0.05
Obesity	30.6*	20.8	

Obesity is defined as a BMI ≥ 30 kg/m2.

DISCUSSION

To our knowledge, there are a few reports regarding the metabolic syndrome in COPD patients. Our results suggest that the presence of the metabolic syndrome may be frequent in patients with COPD, especially in older population. In our study, the overall prevalence of the metabolic syndrome COPD patients is 25, 9 (men 15.5, women 10.3). Men smoked 46.78 packs/year and women 31.3. This could be one of explanations for higher prevalence in men because smoking induces systemic inflammation which may cause metabolic syndrome.

Also, this is a group of elderly pts (aged 68.78), with many co-morbid conditions, but 60% of metabolic syndrome is very high, which needs more future investigations.

Interestingly, HDL-C levels were elevated in men with COPD. Tisi et al reported a finding and hypothesized that the increased work of breathing might constitute a chronic exercise stimulus for the respiratory muscles, resulting in an increase in HDL-C levels [8]. Although possible, it is doubtful that respiratory muscles may have such a systemic impact. It has also been suggested that the effects of some drugs, such as β2-agonists, might be responsible for an increased level of HDL-C [9]. However, salbutamol administered at a 0.8 mg daily dosage is not known to interfere with the lipoprotein profile [10]. Inhaled corticosteroids could be responsible for the raised HDL-C levels, although inhaled high-dose budesonide (1600 mcg daily) has no major effect on lipid profile in patients with asthma [11]. Other mechanisms unknown at this time may be responsible for the increased HDL-C levels encountered in COPD patients. In our study men had higher level of HDL-C which could be explained with frequent physical activity. They

walked for more than 30 minutes daily unlike women. Apart from that, it is interesting to emphasize that the features of the metabolic syndrome were encountered in the same proportion between genders.

It is known that oral corticosteroid therapy induces visceral obesity and diabetes and those glucocorticoids can be produced locally by the visceral adipocyte from inactive 11-keto forms through the enzyme 11-hydroxysteroid dehydrogenase type 1 [12]. An increased activity of this enzyme produces a syndrome of central obesity accompanied by diabetes, dyslipidemia, and hypertension. It is important to emphasize that our patients did not use oral corticosteroid in the 3 months prior the evaluation. COPD patients often result in a sedentary lifestyle and physical deconditioning, which could explain the higher prevalence of the metabolic syndrome.

In conclusion, our findings suggest that the features of the metabolic syndrome may be equally frequent in men and women with COPD. These findings provide a potential explanation for the increased risk for cardiovascular disease in these patients. As the prevalence of metabolic syndrome is high, it implies that screening for features of metabolic syndrome is necessary. Screening can prevent and decrease mortality rate of cardiovascular disease as well as of diabetes mellitus and all its consequences.

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