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THE ACTIVITY OF ANTIOXIDANT ENZYMES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN COMBINATION WITH COMORBID OBESITY

Keywords: *chronic obstructive pulmonary disease, obesity, antioxidant defense, enzymes.*

Abstract. Background. *Chronic obstructive pulmonary disease (COPD) is one of the most common diseases in the world, whose mortality continues to increase. The focus of modern medical science and public health is obesity too, because the number of patients are steadily increasing and doubling every three decades.* ***The aim of the study.*** *To study the dependence of the parameters of antioxidative enzymes in the blood in patients with chronic obstructive pulmonary disease, depending on the severity of accompanying obesity.* ***Materials and methods.*** *The study involved 19 patients with COPD without obesity, 48 patients with COPD, combined with obesity grade I, II, III. We determined the content of reduced glutathione levels, level of ceruloplasmin in serum, activity of glutathione peroxidase, glutathione-S-transferase, copper / zinc - superoxide dismutase, catalase activity in the blood.* ***Results.*** *Found that in chronic obstructive pulmonary disease observed decrease in reduced glutathione and activities of copper / zinc superoxide dismutase and catalase in blood with simultaneous increased ceruloplasmin and glutathione peroxidase activities and glutathione-S-transferase levels. These changes are compounded with increasing body mass index and is most observed in the third degree of accompanying obesity.* ***Conclusions.*** *In patients with chronic obstructive pulmonary disease, combined with obesity, there is decompensation of functioning antiradical protection systems, resulting decrease in reduced glutathione and activities of superoxide dismutase and catalase levels, the degree of which depends on the degree of obesity. One form of compensation for breach of antioxidant defense in chronic obstructive pulmonary disease in conjunction with obesity is increasing ceruloplasmin and activities of glutathione peroxidase and glutathione-S-transferase levels, most pronounced in the third-degree obesity.*

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most common diseases in the world, mortality of which continues to increase [1]. The focus of modern medical science and public health is obesity too, because the number of patients with it is are steadily increasing and doubling every three decades [2].

Therefore, finding and studying new factors in the pathogenesis of COPD combined with obesity is one of the important directions in the development of effective treatment. We know that one of these factors is oxidative stress, which is produced as a result of pathogenic concentration of active oxygen metabolites, which are controlled by endogenous antioxidants: catalase (CT), superoxide dismutase (SOD), glutathione, glutathione peroxidase (GPO), vitamin E and others. [3].

A lot of researches are devoted to the study of oxidative stress processes in COPD and obesity, but their results are rather contradictory. However, the activity of antioxidant enzymes for COPD combined with obesity is less explored, depending on the severity of the latter.

The aim of the study

To study the dependence of the parameters of antioxidative enzymes in the blood of patients with chronic obstructive pulmonary disease, depending on the severity of accompanying obesity.

Materials and methods

The study involved 19 patients with COPD without obesity (1st group), 18 patients with COPD, combined with obesity grade I (2nd group), 12 patients with COPD, combined with obesity grade II (3rd group), 12 patients with COPD, combined with obesity grade III (4th group) and 18 healthy persons (5th group). The average age of patients was 53,4 ±

4,7 years. There was significant difference by age and sex composition between groups of patients and healthy individuals. All patients were informed about the study and expressed their consent.

Body mass index (BMI, BMI - body mass index) was determined by the formula: BMI = m/h2, where the m-weight (kg), and h-height (m). Evaluation of body weight and degree of obesity was conducted by the WHO classification (1997): Normal weight - BMI 19-24,9 kg/m2, overweight - BMI 25-29,9 kg/m2, and obesity degree - BMI 30-34 9 kg/m2, second degree - BMI 35-39,9 kg/m2, third degree - BMI e" 40 kg/m2. Diagnosis and stage of COPD according to the established order of the Ministry of Health of Ukraine № 128 of 19.03.2007.

We determined the content of reduced glutathione (RG) levels by titration method of O.V.Travina (1955) as modified I.F. Meshchyshen, I.V. Petrova (1983) modification. The level of ceruloplasmin (CP) in serum was determined by the method of Revina (V.H.Kolb, 1976). The activity of glutathione peroxidase (GP) (EC 1.11.1.9) was examined according to I.F. Meshchyshen (1982) method, the activity of glutathione-S-transferase (GT) (EC 2.5.1.18) – by I.F. Meshchyshen (1987), the activity of copper / zinc - superoxide dismutase (SOD) (EC 1.15.1.11) – according to R.Fried (1975), catalase activity (KT) (EC 1.11.1.6) – by M.A. Koroliuk et al. method (1988). Activation of enzymes was calculated per 1 g of hemoglobin (Hb).

Statistical analysis of the results was made on a personal computer using the software package licensed «Microsoft Excel 2010» (Microsoft) and «Statistica ® 6.0» (StatSoft Inc., USA).

Discussion

Analysis of the data presented in the table shows that in COPD there is a decrease in reduced glutathione levels by 19,3% (p<0,05), activities of copper / zinc superoxide dismutase and catalase (16.7% and 15, 4%, respectively, p<0.05) with a simultaneous increase in serum ceruloplasmin at 23,8% (p<0,05) and activities of glutathione peroxidase and glutathione-S-transferase levels (by 31.2% and 30, 4%, respectively, p<0,05) as compared with those in healthy individuals.

In the presence of accompanying obesity in patients with COPD changes in these parameters were more significant (Table). In particular, for the first-degree obesity RG content and SOD activity and CT decreased as compared with in healthy individuals at 29,5%, 31,4%, 23,1% (p<0,05), for II-degree – by 44,3%, 42,2%, 33,5% (p<0,001), for third-degree – 58%, 53.6%, 48.4%, respectively (p<0,001). The level and activity of CP, GPO and GT significantly (p<0,05) increased respectively by 39.0%, 60.3%, 52.8% (in the second group of patients), at 58.5%, 75.8 %, 68.1% (in

Table

The content of reduced glutathione, ceruloplasmin levels and activity of superoxide dismutase, catalase, glutathione peroxidase and glutathione-S-transferase levels in chronic obstructive pulmonary disease, combined with different degrees of obesity (Mm)

Variable	Groups				
	COPD patients (1st group) n = 19	Patients with COPD, combined with obesity grade I (2nd group) n = 18	Patients with COPD, combined with obesity grade II (3rd group) n = 12	Patients COPD, combined with obesity grade III (4th group) n = 12	Healthy subjects (5th group) n = 18
Reduced glutathione, mkmol/ml	0,71±0,05 *	0,62±0,05 *	0,49±0,05 */**	0,37±0,06 */**/***	0,88±0,04
Ceruloplasmin, mg/l	205,78±13,37 *	231,26±18,68 *	263,5024,60 *	295,4322,31 */**	166,289,71
Superoxide dismutase, un/1 g of Hb per 1 min	2,550,11 *	2,100,10 */**	1,770,12 */**	1,420,12 */**/***	3,06±0,10
Catalase, mmol /g of Hb per 1 min	11,96±0,45 *	10,870,38 *	9,41±0,61 */**	7,290,51 */**/***	14,140,66
Glutathione peroxidase, nmol RG of 1 g Hb per 1 min.	248,15±15,45 *	303,24±24,76 *	332,53±30,96 */**	367,17±38,68 */**	189,19±10,76
Glutathione-S-transferase, nmol RG of 1 g Hb per 1 min.	141,23±9,30 *	165,50±8,10 *	182,00±12,44 */**	238,85±14,15 */**/***	108,28±6,13

Notes. * - degree of reliability of indices concerning the control (p<0,05); ** - degree of reliability of indices between the 2 and 1 groups, 3 and 1 groups, 4 and 1 groups (p<0,05) ; *** - degree of reliability of indices between the 3 and 2 groups, 4 and 2 groups, (p<0,05); **** - degree of reliability of indices between the 4 and 3 groups (p<0,05).

the third group of patients), at 77.7%, 94.1%, 120.6% (in the fourth group of patients).

However, when comparing the data in the first and second groups only indicators of SOD activity ($p < 0,05$) differed significantly in the first and third groups – RG content indicators, activities of SOD, KT, GPO, GT ($p < 0,05$); in the first and fourth groups - RG content indicators, securities activities of SOD, KT, GPO, GT ($p < 0,05$), in the second and fourth groups - indicators of RG content, SOD activity and GT ($p < 0,05$). Differences between parameters in patients with COPD, and combined with the first degree of obesity and in patients with COPD combined with second degree obesity were unreliable ($p > 0,05$).

Thus, in COPD there is decompensation of functioning antiradical protection systems, the resulting of which is a decrease in reduced glutathione content and SOD activity and CP levels. One form of the compensation mechanisms for violations of antioxidant defense is improving ceruloplasmin activities in GPO and GT levels. These changes are intensified with increasing body mass index and are the most observed in the third degree of accompanying obesity.

Obviously, a stable oxidative stress in patients with COPD is associated with an increased influence of exogenous oxidants (smoke), increased production of endogenous oxidants due to inflammation / recurrent infection / oxygen therapy, suboptimal sufficiently powerful antioxidant protection and greater generation of oxidants due to a chain reaction. It is known that oxidative stress "conducts" inflammatory response / malfunction of the immune system that causes damage to the lungs. Thus, we can substantiate the oxidant / antioxidant hypothesis development and progression of COPD, including against a background of obesity. Moreover, this hypothesis provides a rationale to explain the pathogenic mechanisms of COPD and choosing the right approach to therapeutic strategy for management of these patients [3].

Taking into consideration the obtained the findings, it should be noted that antioxidants can become a universal part of the medical appointments against a background standard therapeutic regimens of the patients with COPD in combination with obesity.

Conclusions

1. In patients with chronic obstructive pulmonary disease, combined with obesity, there is decompensation of functioning antiradical protection systems, that is shown by the decrease in reduced glutathione and activities of superoxide dismutase and catalase levels, the degree of which depends on the degree of obesity.

2. One of the compensation mechanisms of antioxidant defense disorder in chronic obstructive pulmonary disease in combination with obesity is an increase of ceruloplasmin level and activities of glutathione peroxidase and glutathione-S-transferase levels in the blood, the most pronounced in the third-degree obesity.

Prospects for further research

We will continue research as to effectiveness of drugs use with antioxidant action in chronic obstructive pulmonary disease in combination with obesity - one of the main components of the metabolic syndrome.

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АКТИВНІСТЬ АНТИОКСИДАНТНИХ ФЕРМЕНТІВ ПРИ ХРОНІЧНОМУ ОБСТРУКТИВНОМУ ЗАХВОРЮВАННІ ЛЕГЕНЬ У ПОЄДНАННІ З ОЖИРІННЯМ

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Резюме. При обстеженні 61 хворого та 18 практично здорових осіб встановлено, що при хронічному обструктивному захворюванні легень спостерігається декомпенсація функціонування захисних протирадикальних систем, що проявляється зменшенням вмісту відновленого глутатіону та активностей мідь/цинк-супероксиддисмутази та каталази в крові. Одним із механізмів компенсації порушень антиоксидантного захисту є підвищення рівня церулоплазміну та активностей глутатіонпероксидази та глутатіон-S-трансферази в крові. Зазначені зміни поглиблюються із збільшенням індексу маси тіла і є найбільш вираженими за III ступеня супровідного ожиріння.

Ключові слова: хронічне обструктивне захворювання легень, ожиріння, антиоксидантний захист, ферменти.

АКТИВНОСТЬ АНТИОКСИДАНТНЫХ ФЕРМЕНТОВ ПРИ ХРОНИЧЕСКОМ ОБСТРУКТИВНОМ ЗАБОЛЕВАНИИ ЛЕГКИХ, СОЧЕТАННОМ С ОЖИРЕНИЕМ

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Резюме. При обследовании 61 больного и 18 практически здоровых лиц установлено, что при хроническом обструктивном заболевании легких наблюдается декомпенсация функционирования защитных антирадикальных систем, что проявляется уменьшением содержания восстановленного глутатиона и активностей медь/цинк-супероксиддисмутазы и каталазы в крови. Одним из механизмов компенсации нарушений антиоксидантной защиты является повышение уровня церуллоплазмина и активностей глутатионпероксидазы та глутатионтрансферазы в кровы. Указанные изменения углубляются по мере повышения индекса массы тела и являются наиболее выраженными при III степени сопутствующего ожирения.

Ключевые слова: хроническое обструктивное заболевание легких, ожирение, антиоксидантная защита, ферменты.

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