CONDYTION OF SYMPATICOADRENAL SYSTEM AND PEROXIDE OXIDATION OF LIPIDS AT ELDERLY PATIENTS WITH ISCHEMIC HEART DISEASE AND COMBINANT SUBCLINICAL HYPOTHYROSIS

[1]Amirmuhammadov U. A., [2]Ulmasov Sh.N., [3]Usmanova D. N., [4]Yuldasheva G. T.
[1,2,3,4] Andijan state medical institute

https://doi.org/10.5281/zenodo.7958019

Abstract. *Aim of the research was the study activity of sympaticoadrenal system (SAS) at elderly patients with ischemic heart disease (IHD) and combinant subclinical hypothyrosis (SH) the level of daily excretion of cateholamines (CA) and activity of monoaminoxyase (MAO) in combination with determine activity processes of peroxide oxidation of lipids (POL). Results of examination of 28 patients with IHD and 14 patients with IHD in combination with SH were analyzed. Patients with IHD in combination with SH had the decrease of activity of SAS, which manifested by decrease excretion of CA. The maximum decrease of activity of MAO in patients with IHD and concomitant SH was detected. Also processes of POL were augmented, it was verified by increased level of malonic dialdehyde – final substance of peroxidation. On the base of received results, it could be supposed, that decrease activities of SAS and POL are interrelated inpatient with combined pathology.*

Keywords: *sympaticoadrenal system, cateholamines, monoaminoxyase, ischemic heart disease, subclinical hypothyrosis, peroxide oxidation of lipids.*

Cardiovascular pathology is the most important problem of modern medicine. In all developed countries, the frequency and severity of coronary artery disease in the elderly is progressively increasing, exceeding 50% in the structure of total mortality.

Recent studies have shown that in order to understand the pathogenesis of coronary artery disease in the elderly, further study of the circulatory regulation systems, in particular the sympathetic-adrenal system (SAS), is necessary. To judge the state of tone and reactivity of the SAS allows the study of the excretion of catecholamines (CA), metabolic products of biogenic amines and enzymes involved in their metabolism.

It has been known for more than 30 years about the decrease in the level of thyroid hormones in case of manifestation of trouble in the human body.[4] Subclinical hypothyroidism (SH) is especially common, manifested by the only symptom complex - hypercholesterolemia, which is characterized by refractoriness to statins and other lipid-lowering drugs. [2,9,13,14,15,16] thyroid activity and the highest level of cholesterol. [4,13,16,20] In old age, especially in the presence of other risk factors, these lipid disorders characteristic of hypothyroidism are more pronounced and more difficult to treat and can contribute to the progression of atherosclerosis of the coronary arteries. [7,12,16]

In the metabolism of biogenic amines, the reaction of their oxidative deamination catalyzed by monoamine oxidase (MAO) is of key importance. The results of numerous experiments suggest that under conditions of insufficiency of thyroid hormones, the activity of different types of MAO changes equally. [1,12]

It has been established that ischemia is accompanied by a significant increase in lipid peroxidation (LPO). Activation of lipid peroxidation, especially in the elderly, plays the role of a key link in the mechanism of the cardiotoxic effect of CA on the myocardium. [7,11,17,19] Thus, there is no consensus in the literature on the functional state of the SAS in IHD.

The aim of our research was to determine the functional state of the SAS by the level of CA excretion and by the activity of the key enzyme of oxidative deamination of CA - MAO in combination with determining the degree of activity of lipid peroxidation processes in elderly people with comorbidities.

Materials and methods

We examined 57 male (43.8%) and female (56.1%) patients aged 60 to 75 years. Of these, 42 patients received inpatient treatment for coronary artery disease, stable angina FC II-III. All patients were randomized into three large groups. Group I consisted of 15 patients who underwent inpatient treatment for somatic diseases without changes in the SAS at the age of 60 to 73 years and received appropriate pathogenetic therapy. Group II consisted of 28 patients aged 60 to 75 years with a diagnosis of coronary artery disease, stable angina FC II-III with corresponding complications. Group III consisted of 14 patients with a diagnosis of coronary heart disease, stable angina FC II - III in combination with acquired or subclinical hypothyroidism aged 60-70 years.

Urine and blood sampling for analysis was carried out on the 1st day of admission to the hospital before the start of treatment and on the 8th-10th day after treatment. The daily urinary excretion of free and conjugated forms of CA was studied by the fluorimetric method modified by E.Sh. Matlina 1965[8] The determination of MAO activity in blood serum was carried out according to the colorimetric method of A.V. Balaklevsky 1976[1] To determine the degree of LPO activity, the method of V.B. Gavrilov was used. (1987).[3] The content of lipid peroxidation products was judged by the level in the blood serum of their secondary product, malondialdehyde (MDA), determined by the reaction with thiobarbituric acid.

The processing of the results of clinical studies was carried out using Student's tables.

Research results

When studying the daily excretion of CA and DOPA in patients with coronary artery disease upon admission to the clinic, we noted a statistically significant decrease in the excretion of adrenaline (A) by 47.9% ($P<0.001$), which is 1.9 times lower than the values of the control group ($P<0.001$) . In patients with coronary artery disease in combination with hypothyroidism, a significant decrease in the daily excretion of A by 57.7% was also noted, which is 2.36 times lower than the values of the control group and by 16.5%, which is 1.2 times lower in relation to the indicators of group II. ($P<0.001$). Accordingly, the lowest level of total A was registered in group III. [Table 1.]

The daily excretion of norepinephrine (NA) was also significantly reduced in groups II and III. Thus, the content of NA in patients with IHD was 51.5%, which is 1.6 times lower than in the control group ($P<0.01$). In patients with IHD in combination with hypothyroidism, a significant decrease in the daily excretion of NA by 58.8% was also noted, which is 2.4 times lower than the values of the control group ($P<0.001$) and by 14.7%, which is 1.5 times lower according to in relation to indicators of group II ($P<0.001$). Thus, the level of total NA in group III was the lowest. [Table 1.]

The release of dopamine (DA) in this category of patients is also reduced. So the content of DA in patients with coronary artery disease is reduced by 71.0% ($P<0.05$), which is 3.36 times

lower than in the control group (P<0.05). In patients with IHD in combination with hypothyroidism, there was also a significant decrease in daily DA excretion by 71.98%, which is 3.57 times lower than the values of the control group (P<0.01) and by 3.2%, which is 1.06 times lower in relation to indicators of group II (P<0.001). [Table 1.]

The level of DOPA was slightly reduced in group II patients by 18.7%, which is 1.23 times lower than in the control group (P<0.05). In IHD patients with hypothyroidism, the DOPA level was lower than the control level by 29.0% (1.41 times); and in relation to the indicators of patients with CIHD, it is 12.6% lower (1.14 times) (P<0.05). [Tab.1.]

Tab. 1. Indicators of daily excretion of catecholamines (CA) in healthy and IHD patients with hypothyroidism (M ± m)

Groups / Indicators		Healthy (n =15)	Patients with IHD (n=28)	Patients with IHD+ hypothyroidism (n=14)	P1-2	P1-3	P2-3
Adrenalin	Free	4,29±0,33	2,096±0,18	1,56±0,15	0,001	0,001	0,001
	conjugated	3,9±0,35	2,22±0,12	1,92±0,16	0,001	0,001	0,001
	total	8,23±0,326	4,29±0,219	3,48±0,24	0,001	0,001	0,001
Norepinephrine	Free	8,1±0,31	4,6±0,226	3,84±0,21	0,01	0,01	0,001
	conjugated	7,15±0,36	2,3±0,96	2,5±0,24	0,01	0,01	0,001
	total	15,45±0,5	7,5±1,1	6,4±0,3	0,01	0,01	0,001
Dopamine	Free	176,0±9,07	53,6±7,5	50,6±1,8	0,05	0,01	0,001
	conjugated	187,0±7,3	51,7±8,4	51,2±2,21	0,05	0,01	0,001
	total	363,7±13,8	105,3±15,8	101,9 ±3,09	0,05	0,01	0,001
DOPA		41,83±2,17	34,0±0,8	29,7±1,17	0,05	0,05	0,05

As can be seen from the indicators, in patients on admission, the DA/DOPA ratio decreases by 57%, which may indicate inhibition of DA biosynthesis. We also noted an increase in the NA/DA ratio, i.e. possibly stimulated NA biosynthesis. A decrease in the A / NA ratio suggests a possible inhibition of A biosynthesis. In the ratios (Af + Ac) / At; (NAf + NAc)/ NAt ; (DAf + DAc)/DAt did not observe any special deviations from the norm; Obviously, the formation of CA sulfoconjugates in CIHD proceeded as in healthy people.

Studies of MAO activity on the first day of hospital stay revealed a significant decrease in it in patients of group III by 57.1%, which is 2.3 times lower than in the control group (P<0.001)

and 25% (1.3 times) lower indicators of group II. Moderately reduced MAO activity was also observed in group II by 42.8%, which is 1.8 times lower than in the control group (P<0.01). In healthy people, this indicator was 0.07±0.001 units/ext. [Table 2.]

The level of MDA in the serum of patients with CIHD was quite high and exceeded the values of the control group by 69.9% (2.7 times). Accordingly, the level of MDA in the blood serum of patients with IHD in combination with hypothyroidism was reduced in relation to the indicators of group II by 14.8% (1.14 times).

For a more detailed analysis of the SAS activity, the ratio coefficients proposed by T.D. Bolshakova (1976) for each CA to its predecessor. [Table 2.]

Tab. 2. Activity of monoamine oxidase (MAO) and content of malondialdehyde (MDA) in healthy and IHD patients with hypothyroidism

№	Groups	MAO (ed/ecst.)	MDA (nmol/ml)
I	Healthy (n =15)	0,07±0,001	3,12±0,63
II	Patients with IHD (n=28)	0,04±0,001	8,42±2,4
III	Patients with IHD + hypothyroidism (n=14)	0,03±0,002	9,67±0,65
	P_{1-2}	P<0,01	P<0,001
	P_{1-3}	P<0,001	P<0,001
	P_{2-3}	P<0,005	P<0,005

The discussion of the results. As is known, SAS is of great interest in the pathogenesis of IHD, since the CA secreted by it play a primary role in the regulation of the activity of the cardiovascular system [6]. At the present stage, the state of the SAS has been carefully studied in patients with various diseases of the cardiovascular system [4].

In the literature, there are separate works concerning the metabolism of CA in patients with coronary artery disease. Along with data on an increase in their concentration in the blood plasma of patients with IHD, there is evidence of a decrease in the excretion of CA, and there is information about the absence of changes in the metabolism of CA in IHD [6,10,18,20].

Studies have shown that hypoxia is accompanied by pronounced changes in the entire hormonal balance. Along with hypersympathicotonia, hypercortisolemia, changes in insulin levels are observed, and with prolonged exposure to hypoxia, the level of thyroid hormones, growth hormone, ACTH decreases.

Clinical observations made it possible to establish a direct relationship between the development of atherosclerosis, coronary heart disease, and impaired functional state of the thyroid gland [2]. A high incidence of coronary artery disease in patients with reduced thyroid function has been noted by many authors [4,13,15]. Numerous studies in goitre-endemic areas have established that atherosclerotic lesions develop faster in hypofunctional forms of goiter than in normal thyroid function [16].

The results of the data obtained showed a statistically significant decrease in CA excretion in daily urine in patients with coronary artery disease, with the most pronounced decrease noted for dopamine, which is consistent with the data of other authors. In patients with CIHD, there was a decrease in the ratio of DA/DOPA, an increase in the ratio of A/NA. In addition, our results showed a sharp decrease in the daily excretion of A in patients with IHD in combination with

hypothyroidism, which is 1.3 times lower in relation to the group of patients with IHD (P<0.001) and 2.37 times lower in relation to the control group. (P<0.001) . The same picture is observed in relation to NA. Thus, the content of NA in patients with IHD in combination with hypothyroidism is 1.1 times lower in relation to the group of patients with IHD (P<0.001) and 2.3 times lower in relation to the control group (P<0.01).

The data obtained by us show the effect of mutual influence of the SAS and thyroid function, which is characterized by the mutual reinforcement of their function, which makes it possible to speak about the synergism of the function of the SAS and the thyroid gland in comorbid pathological conditions.

As is known, in IHD there is an increase in lipid peroxidation [7]. The intensity of lipid peroxidation reflects the degree of metabolic disorders in the body [1]. The results obtained indicate an increase in the activity of lipid peroxidation processes in IHD. And in conditions of combined pathology, the maximum intensification of lipid peroxidation gives us reason to assume that the functional activity of the SAS and the processes of lipid peroxidation are also interconnected, and violations of one of these systems affect the function of the other. According to Khuzhamberdiev M.A. (1985) found that in coronary artery disease, as a result of increased lipid peroxidation, the activity of the catalytic properties of MAO decreases [12]. The reason for the decrease in MAO activity in patients with IHD can be associated with the activation of LPO, which leads to qualitative changes in the catalytic properties of the enzyme.

The question of the role of MAO in CA exchange is much more complicated. The results of numerous experiments give grounds to assume that under conditions of insufficiency of thyroid hormones, the activity of different types of MAO changes equally. It is generally accepted that MAO activity is increased in hypothyroidism, although there are numerous facts contradicting them. There are very few works devoted to the simultaneous study of the daily excretion of CA and the content of A and NA in blood serum with the determination of MAO activity, and all available data are contradictory.

Conclusions. 1. A comprehensive examination of IHD patients with subclinical hypothyroidism showed significant disorders of the sympathetic-adrenal system, namely: a decrease in the levels of adrenaline, noradrenaline, dopamine, DOPA, which indicates the inhibition of the activity of the sympathetic-adrenal system in the elderly.

2. In IHD with subclinical hypothyroidism in the elderly, there is a pronounced decrease in the activity of monoamine oxidase, which indicates a change in its catalytic properties.

3. IHD in the elderly in combination with subclinical hypothyroidism is accompanied by a significant intensification of lipid peroxidation processes, which contributes to the development of oxidative stress and a sharp decrease in antioxidant protection.

REFERENCES

1. Балаклевский А.И. Колориметрический способ определения активности моноаминоксидазы в сыворотке крови. // Лабораторное дело. 1976. №3. С. 151-153.
2. Bennet J.M., Steyn A.T. The heart and hypothyroidism. S. Afr. Clin. Endocrin. 1983.: 63(5).: 564-565.
3. Гаврилов В.Б., Гаврилова А.Р., Мажуль А.М. Анализ методов определения продуктов перекисного окисления липидов в сыворотке крови по тесту с тиобарбитуровой кислотой. // Вопросы медицинской химии. 1987. Т. 33. №1. С. 118-122.

4. Дубик В.Т., Ливергант Ю.Э., Капустина Л.В., Власикова Е.К., Шапоренко А.И. Тиреотропно-тиреоидная активность крови с различными проявлениями ишемической болезни сердца. // Врачебное дело. 1984. №9. С. 85-87.
5. Какумиё М.Ш. Распространенность ИБС у лиц факторами риска её развития. // Клиническая медицина. 2001. №7. С. 25-28.
6. Киселёва З.М. Сердце и катехоламины с позиции адаптационно-трофической функции симпатико-адреналовой системы. // Кардиология. 1988. Т. 28. №8. С. 10-14
7. Ланкин В.З. и др. Перекиси липидов и атеросклероз. Ферментативная детоксикация перекисей липидов в крови больных ишемической болезнью сердца, обусловленной атеросклерозом коронарных артерий. // Кардиология. 1979. Т. 19. №6. С. 71-76.
8. Матлина Э.Ш., Рахманова Т.Б. Методы исследования некоторых систем гуморальной регуляции. М.: Наука, 1967: С. 136-143.
9. Мельниченко Г., Фадеев В. Субклинический гипотиреоз: проблемы лечения. // Врач. 2002. С. 41-44.
10. Оганов Р.Г. Симпатико-адреналовая система и ишемическая болезнь сердца. // Кардиология. 1979. Т. 19. №3. С. 10-18.
11. Polidori M.C., Cherubini A., Stahl W. et al. Plasma carotinoid and malondialdehyde levels in ischemic stroke patients. Relation ship to early outcome: Free Radic Res 2002; 36: 265-268.
12. Сайдуллаев Т., Хужамбердиев М. А., Максумова З.А., Горкин В.З. Дисфункция щитовидной железы и нарушения дезаминирования азотистых соединений при атеросклерозе в эксперименте. // Проблемы эндокринологии. 1985. Т. 31. С. 57-59.
13. Сыч Ю.П., Калашников В.Ю., Сыркин А.Л., Мельниченко Г.А. Нарушения функционального состояния сердечно-сосудистой системы при субклиническом гипотиреозе. // Клиническая медицина. 2003. №11. С. 4-9.
14. Терещенко И.В. Патогенез, диагностика и лечение субклинического гипотиреоза. // Клиническая медицина . 2000. №9. С. 8-13.
15. Tereshchenko I.V., Tsepelev V.V., Ivanova E.S. Subclinical hypothyroidism in patients with ischemic heart disease. Cardiology. 1993.: 33(1).: 45-47.
16. Турсунов С.Ю., Махмудов Б., Далимов Х., Ягудаев А.М., Хусаинов К.Д. Особенности течения ишемической болезни сердца при гипофункции щитовидной железы. // Кардиология. 1979. Т. 19. №3. С. 28-33.
17. Урумбаев Р.К., Титеева Г.Р., Бояркина О.В., Рыжикова Е.А., Мамаева С. Характеристика перекисного окисления липидов у здоровых лиц и больных атеросклерозом. // Центрально-Азиатский медицинский журнал. 2003. Т. 9. №1. 16-19.
18. Хужамбердиев М. А., Аскаров Б. и др. К вопросу диагностики болезней сердечно-сосудистой системы. Международная конференция по ишемическим болезням сердца. Андижан, 1998: С 12.
19. Хужамбердиев М. А.Активация процессов перекисного окисления липидов при хронической ишемической болезни сердца. Бюлл. эксп. биол. мед., 1985, т. 100, № 9, с. 285-286.
20. Шеек А.Б. Современные представления о патогенезе хронической недостаточности кровообращения, обусловленной ишемической болезнью сердца. // Медицинский журнал Узбекистана. 2004. №1-2. С. 189-192.