Impact of prooxidant-antioxidant imbalance on the biological age and the rate of aging in arterial hypertension with type 2 diabetes mellitus

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Purpose: to study the state of oxidative-antioxidative balance and its influence on the biological age (BA) and the features of aging in patients with a comorbid course of arterial hypertension (AH) and type 2 diabetes mellitus (T2DM).

Materials and methods. In 96 patients with II stage AH and T2DM and 40 patients with isolated II stage AH (IAH), a BA, rate of aging (according to the method of V. P. Voytenko et al.) and oxidative stress (OS) indexes (activity of glutathione peroxidase, serum levels of sulfhydryl groups, malonic dialdehyde, 8-hydroxy-2-deoxyguanosine) were investigated.

Results. In IAH patients, physiological aging (PhA) was detected in 12.5 %, delayed type of aging (DTA) – in 55.0 %, accelerated type of aging (ATA) – in 32.5 %. In AH and T2DM, PhA was in 9.4 %, DTA – in 31.3 %, ATA – in 59.4 % of patients. Only 5 patients (12.5 %) with IAH and 3 patients (3.13 %) with AH and T2DM had no signs of OS. The patients with ATA in comorbid pathology were characterized by a significant activation of oxidative and stimulation of antioxidant systems compared to those with DTA, which was less common among IAH patients. The presence of correlations between the antioxidant system indicators and age parameters characterizing the degree of aging was found.

Conclusions. OS, which is one of the significant factors resulting in premature aging, was more enhanced in AH and T2DM than in IAH. OS manifestations were more significant in ATA regardless of nosology, but were more pronounced in AH and T2DM. Therefore, OS evaluation together with age-related characteristics can be used both to assess an organism state and as an integral indicator characterizing the effectiveness of therapeutic and preventive measures.

Вплив прооксидантно-антиоксидантного дисбалансу на біологічний вік і темпи старіння при артеріальній гіпертензії та цукровому діабеті 2 типу

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Мета роботи – вивчити стан оксидантно-антиоксидантного балансу та його вплив на біологічний вік (БВ) та особливості старіння у хворих на артеріальну гіпертензію (АГ) із супутнім перебігом цукрового діабету 2 типу (ЦД2Т).

Матеріали та методи. У 96 пацієнтів з АГ II ступеня та ЦД2Т і 40 пацієнтів з ізольованою АГ (ІАГ) II ступеня досліджували біологічний вік, темпи старіння (за методом В. П. Войтенка та співавт.) і показники оксидативного стресу (ОС): активність глутатіонпероксидази, рівні сульфгідрильних груп, малонового діальдегіду, 8-гідрокси-2-деоксигуанозину в сироватці крові.

Результати. При ІАГ фізіологічне старіння (ФС) виявили у 12,5 % пацієнтів, уповільнений тип старіння (УТС) – у 55,0 %, прискорений тип старіння (ПТС) – у 32,5 %. При АГ та ЦД2Т: ФС – у 9,4 %, УТС – у 31,3 %, ПТС – у 59,4 % хворих. Тільки в 5 (12,5 %) пацієнтів з ІАГ і 3 (3,13 %) пацієнтів з АГ і ЦД2Т не виявили ознаки ОС. Наявність ПТС при коморбідній патології характеризувалась вірогідною активацією оксидантної та стимуляцією антиоксидантної системи порівняно з особами з УТС, що не так характерно для пацієнтів з ІАГ. Встановили кореляційні зв'язки між показниками антиоксидантної системи й віковими показниками, що характеризують ступінь старіння.

Висновки. Оксидативний стрес, який є одним зі значущих чинників, що призводять до передчасного старіння, при АГ і ЦД2Т був вираженішим, ніж при ІАГ. Прояви ОС були значущі при ПТС незалежно від нозології, але при АГ і ЦД2Т виражені більше. Тому дослідження оксидативного стресу разом із віковими характеристиками можна використовувати і для оцінювання стану організму, і як інтегральний показник, що характеризує ефективність лікувально-профілактичних заходів.

Влияние прооксидантно-антиоксидантного дисбаланса на биологический возраст и темпы старения при артериальной гипертензии и сахарном диабете 2 типа

В. Д. Немцова

Цель работы – изучить состояние окислительно-антиоксидантного баланса и его влияние на биологический возраст (БВ) и особенности старения у пациентов с артериальной гипертензией (АГ) и сахарным диабетом 2 типа (СД2Т).

Материалы и методы. У пациентов с АГ II стадии в сочетании с СД2Т и 40 пациентов с изолированной АГ (ИАГ) II стадии исследовали БВ, темпы старения (по методу В. П. Войтенко и соавт.) и показатели оксидативного стресса (ОС): активность глутатионпероксидазы, уровни сульфгидрильных групп, малонового диальдегида, 8-гидрокси-2-деоксигуанозина в сыворотке крови.

Результаты. При ИАГ физиологическое старение (ФС) установлено у 12,5 %, замедленный тип старения (ЗТС) – у 55,0 %, ускоренный тип старения (УТС) – у 32,5 %. При АГ и СД2Т: ФС – у 9,4 %, ЗТС – у 31,3 %, УТС – у 59,4 % пациентов. Только у 5 (12,5 %) пациентов с ИАГ и 3 (3,13 %) пациентов с АГ и СД2Т не установили признаки ОС. Наличие УТС при коморбидной патологии характеризовалось значительной активацией окислительной и стимуляцией антиоксидантной систем по сравнению с таковыми при ЗТС, что не столь характерно для пациентов с ИАГ. Установлены корреляционные связи между показателями антиоксидантной системы и возрастными параметрами, характеризующими степень старения.

Выводы. При АГ и СД2Т отмечен более выраженный, чем при ИАГ оксидативный стресс, который является одним из значимых факторов, приводящих к преждевременному старению. Проявления ОС были более значимы при УТС, независимо от нозологии, но при АГ и СД2Т выражены в большей степени. Таким образом, определение ОС в сочетании с возрастными характеристиками может быть использовано и для оценки состояния организма, и как интегральный показатель, характеризующий эффективность лечебно-профилактических мероприятий.

The growth of elderly and senile population has characterized the world demographic situation changes in recent decades, as a result of which the aging process is increasingly becoming the subject of numerous medical and social studies. At present, Ukraine experiences a challenging medical and demographic situation characterized by a decline in fertility, an increase in all-cause mortality, which, combined with the increasing number of elderly and senile age persons, is a rather powerful argument for activating research in the field of aging demography.

The chronological (calendar) age does not give a proper idea of the body's age-related damage degree and cannot serve as a reliable criterion for determining the life expectancy. Individuals of the same sex and age based on birthdate have varying degrees of age-related disorders in organs and systems of the body, various genetic determinants, pathological processes occurring in the body, have experienced a varying degree of lifetime exposure to environmental damaging factors influence [1,2].

Therefore, at present, the concept of biological age (BA) is used as one of the diagnostic criteria for aging, which is an integral indicator of the human health status, reflecting the reserve potential of the organism. By assessing the deviation of the BA from the proper biological age (PBA) – the population standard of aging, it can be judged whether the body aging is physiological, or it is delayed, or premature [1,3,4]. Although it is impossible to influence the calendar age, BA is a variable value and depends on many factors.

Premature aging promotes the early development of age-related pathology – ischemic heart disease, arterial hypertension (AH), cancer, type 2 diabetes mellitus (T2DM), and the onset of diseases accelerates the rate of human aging [5].

Certain factors, the so-called predictors of premature aging, including, according to modern concepts, oxidative stress (OS) contribute to the pathological (premature) type of aging [5,6]. Today, the theory of OS is considered one of the most popular theories, explaining not only aging, but also the initiation, as well as the progression of many diseases in modern humans, namely cardiovascular diseases, diabetes mellitus (DM). Recently, OS is being actively studied in order to better understand the protective mechanisms and the interaction between oxidative damage and the aging process [7]. The cause of OS is known to be the prooxidant and antioxidant misbalance. Antioxidant levels and providing a good protection by antioxidant systems are very important for preventing OS [6].

Numerous studies have shown that one of the most important indicators of aging is the blood pressure level, which is included in all formulas for BA calculating. Thus, in patients with hypertension, an accelerated rate of aging (ARA) was mainly observed [8]. On the other hand, the same mechanisms that pay the important role in DM pathogenesis are characteristic of age involution (endothelial dysfunction, inflammation, OS etc.) [5,6]. The incidence of DM is known

to have a clear tendency to increase with age due to patients with type 2 of the disease. With a general increase in the life expectancy of people, the number of patients with T2DM grows from year to year, thus determining the social significance of the problem [9]. Back in 1975, T. Furukawa et al., using a battery of 12 tests, after performing a comparative assessment of the aging rate in healthy people and patients with AH and DM, showed that both types of pathology accelerate the course of age-related processes [8].

However, currently available studies on the human aging mechanisms, focused on the latter assessment in individuals with multiple organ pathologies, contains insufficient data on the specific contribution of various diseases to these processes [1,8,10]. The existence of age-related features of the healthy and sick organism reactivity suggests the existence of an interaction between an age-related pathology and aging as a general biological process. Identification of such mechanisms would permit individualizing and optimizing the tactics of geroprophylactic therapy in patients with various pathologies.

Aim

Thus, the purpose of the research was to study the state of oxidative-antioxidative balance and its influence on the biological age and the features of aging in patients with the comorbid course of arterial hypertension and type 2 diabetes mellitus.

Materials and methods

The study included 96 patients (39 males and 57 females), the mean age – 62.66 ± 4.2 years, with stage II AH (disease duration of 10.2 ± 3.7 years, mean systolic blood pressure – 141.05 ± 11.34 mm Hg, diastolic blood pressure – 84.05 ± 5.59 mm Hg) and T2DM (disease duration of 4.1 ± 2.4 years, mean fasting glucose level – 8.46 ± 0.53 mmol/l, mean glycosylated hemoglobin – 7.62 ± 0.23 %). As a comparison group, the study included 40 sex- and age-matched (mean age of 60.59 ± 2.37 years) patients with isolated stage II AH. The control group consisted of 22 sex- and age-matched volunteers (mean age 58.3 ± 1.96 years, 10 males and 12 females) to the examined patients and without cardiovascular diseases and endocrinopathies.

For the patients selection, the AH diagnostic criteria, agreed with the ESC/ERS Guidelines for the diagnosis and treatment of AH (2013) were applied [11]. The diagnosis of T2DM was established in compliance with the International Recommendations of the American Diabetes Association and the European Association for the Study of Diabetes [12].

Along with the dietary recommendations, all patients received basic therapy in accordance with International and National guidelines for the management of patients with the related pathology [11,12]. So, stable antihypertensive therapy was received by all the patients for at least 6 months prior to inclusion into the study with individually-selected

doses using angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ACEI/ARB), diuretics (indapamide); some patients received calcium antagonists (amlodipine or lercanidipine). As antidiabetic therapy, patients with T2DM received metformin at individually-selected doses ranging from 1,000 to 2,000 mg per day, and 3 patients (3.13 %) additionally received a sodium glucose linked transporter-2 (SGLT2) inhibitor and 5 patients (5.21 %) – an agonist of glucagon-like peptide 1 (GLP 1). The study did not include patients with symptomatic AH, type 1 DM and other endocrinological disorders, clinical signs of coronary heart disease or severe concomitant chronic diseases.

All patients were anthropometrically measured; arterial pressure level was recorded as the arithmetic mean, three measurements were carried out with 2-minute intervals in a seated position on the dominant arm.

To study the antioxidant system status, the activity of glutathione peroxidase (GPO) and the level of sulfhydryl groups (SH-groups) were assessed. GPO plays an important role in protecting biological cell membranes against oxidative damage by increasing the concentration of reduced glutathione (oxidized glutathione ratio – GSSG-R) in the process of aerobic glycolysis. SH-groups are organic compounds containing a sulfhydryl group. Among all the antioxidants that are available in the body, they constitute the major portion of the total body antioxidants and play a significant role in defense against reactive oxygen species (ROS). The level of malondialdehyde (MDA) was used as a marker of lipid peroxidation (LPO) and oxidative system activity. The activity of GPO (EC 1.11.1.9) in Ethylenediaminetetraacetic acid (EDTA)-hemolizate was determined by the decrease in a reduced glutathione content within the 5-minute period of a test hemolizate sample incubation in the presence of an oxidizing substrate – cumene hydroperoxide by means of the photometric method [13]. The SH-groups and MDA were determined in the blood serum using the photometric method [13]. The following reagents were used: thiobarbituric acid (Organika, Germany), dithiobis nitrobenzoic acid (Merck, Germany), glutathione (Sigma-Aldrich, Japan), cumene hydroperoxide (Merck, Germany). The determination of 8-hydroxy-2-deoxyguanosine (8-OH-dG) in the blood serum as one of oxidative damage biomarkers, including oxidative DNA damage, was carried out by ELISA with "Bio-Vendor" kits (Czech Republic).

Among the wide variety of methods for determining BA, the method by V. P. Voitenko et al. has been extensively used in many studies on the problems of aging as the most accessible and integral one [1,2]. It consists in calculating the actual BA value for each examined patient and rationing its individual values by comparing with the estimated value appropriate to the population standard – PBA [1]. To calculate BA, the following indices were used: systolic blood pressure (SBP, mm Hg), pulse blood pressure (PBP, mm Hg), static balancing time on the left leg (SB) in seconds, time inspiratory capacity (TIC) in seconds, body mass (BM) and subjective health assessment (SHA, in relative value units) – the number of negative responses to the questionnaire. The SHA index was determined using a questionnaire containing 29 questions. With the number of negative answers equal to zero, health was considered ideal, with 29 – bad. The resulting SHA index value was included in the formula to determine the BA index.

The BA was calculated using the following formula:

BA of men = 26.985 + 0.215 × SBP – 0.149 × TIC – 0.151 × SB + 0.723 × SHA.

BA of women = (-1.463) + 0.415 × PBP – 0.141 × SB + 0.248 × BM + 0.694 × SHA.

PBA values were calculated using the formulas below:

PBA of men = 0.629 × CA + 18.56;

PBA of women = 0.581 × CA + 17.24,

where CA is the chronologic age of an individual in years.

The absolute deviation of BA from the population standard was judged by the biological age coefficient (BA-PBA), the relative deviation – by the BA/PBA index. With BA-PBA = 0 or BA/PBA = 1, the biological age matching with the population norm was recorded. Deviation from these values indicated accelerated or slow aging – the higher the BA deviation from its proper value (BA-PBA > 0, BA/PBA > 1), the faster an individual was aging, and vice versa, the more BA lagged behind PBA (BA-PBA < 0, BA/PBA < 1), the slower was the rate of aging [8,10].

The results obtained were presented as a mean value ± standard deviation from the mean (M ± SD). Statistic data processing was performed using the Statistica software package, version 8.0. To assess the differences between groups with the distribution close to normal, the Student's t-criterion and the Pearson's χ^2 were used. Differences were considered statistically significant at P < 0.05. The correlation between quantitative/qualitative variables was assessed using the Spearman rank correlation coefficient (R). Chaddock scale was used to assess the strength of an association.

The work was performed in compliance with the basic provisions of the World Medical Association (WMA) Declaration of Helsinki on ethical principles for medical research involving human subjects (1964–2000) and the MOH of Ukraine Order No 690 dated September 23, 2009.

Results

When analyzing the studied age characterizing indices (*Table 1*), the following results were obtained: there were statistically significant differences in all the studied parameters, except for the chronologic age, between patients with AH and T2DM and those of the control group. Patients with isolated AH did not demonstrate significant differences with the control group (except for PBA). The coefficients characterizing the rate of aging in AH and T2DM were changed to a greater extent than in isolated AH, which combined with the value of BA exceeding the PBA for this group of patients meant the premature aging signs presence.

When assessing the type of aging among patients with isolated AH, physiological aging (PhA, chronologic age = BA) was detected in 5 (12.5 %), delayed type of aging (DTA) – in 22 (55.0 %), accelerated type of aging (ATA) – in 13 (32.5 %) patients. Among individuals with a combined course of AH and T2DM, PhA was observed in 9 (9.4 %), DTA – in 30 (31.3 %), ATA – in 57 (59.4 %) patients.

When assessing the oxidant (OX) and antioxidant (AOX) systems status in the examined patients, only 5 patients (12.5 %) with AH and 3 patients (3.13 %) with AH and T2DM did not present any signs of OS.

Table 1. Comparative characteristics of age indexes in the studied groups (M ± m)

Index	Control (n = 22)	Patients with AH (n = 40)	Patients with AH and T2DM (n = 96)
Chronologic age (CA), years	58.30 ± 1.96	60.59 ± 2.37	62.66 ± 4.20
Biological age (BA), years	50.20 ± 1.68	52.73 ± 1.14	57.41 ± 1.30*,# #P = 0.009
Proper biological age (PBA), years	50.93 ± 0.42	53.46 ± 0.81*	56.22 ± 0.79*,# #P = 0.018
Coefficient of aging (BA-CA), years	-8.12 ± 0.97	-7.86 ± 1.23	-5.25 ± 1.10*
Index of aging (BA/PBA)	0.96 ± 0.02	0.98 ± 0.03	1.03 ± 0.04*
Biological age coefficient (BA-PBA)	-0.73 ± 0.33	-0.87 ± 1.34	0.19 ± 1.68*

*: P < 0.05 changes are significant compared with the control group; **#P:** significant difference between the isolated AH group and the AH with T2DM group.

Table 2. Comparative characteristics of oxidant-antioxidant system indices in the examined patient groups (M ± m)

Index	Control (n = 22)	Patients with AH (n = 40)	Patients with AH and T2DM (n = 96)
8-hydroxy-2-deoxyguanosine, ng/l	6.66 ± 0.97	16.26 ± 0.83*	15.89 ± 0.76*
Glutathionperoxidase, μkat/gHb	6.77 ± 0.52	5.78 ± 0.25*	5.41 ± 0.20*
Malonic dialdehyde, μmol/l	4.07 ± 0.22	6.11 ± 0.31*	6.55 ± 0.27*
SH-groups, μmol/l	712.26 ± 11.08	570.54 ± 12.64*	573.52 ± 10.91*

*: P < 0.05, changes are significant compared with the control group.

Table 3. Oxidative stress indexes depending on aging type of the examined patients (M ± m)

Index	Patients with AH (n = 35)		Patients with AH and T2DM (n = 87)	
Aging degree	DTA 1a (n = 22)	ATA 1b (n = 13)	DTA 2a (n = 30)	ATA 2b (n = 57)
8-hydroxy-2-deoxyguanosine, ng/l	17.80 ± 2.01	16.38 ± 1.01	17.76 ± 1.31	14.89 ± 0.97* P = 0.048
Glutathionperoxidase, μkat/gHb	6.09 ± 0.31	5.18 ± 0.38* P = 0.046	4.95 ± 0.30	5.40 ± 0.41
SH-groups, μmol/l	549.24 ± 18.00	573.48 ± 14.76	549.30 ± 12.34	578.05 ± 14.86* P = 0.05
Malonic dialdehyde, μmol/l	5.84 ± 0.30	6.25 ± 0.64	6.25 ± 0.37	7.06 ± 0.35* P = 0.025

DTA: delayed type of aging, **ATA:** accelerated type of aging, ***:** significant difference between ATA and DTA in the corresponding groups.

Comparative analysis showed significant differences in all OS indexes when comparing the studied groups with the control group. None of the indices showed significant differences between the studied patient groups (*Table 2*).

The correlation analysis revealed the correlations between the AOXS indices and the age indices characterizing the aging degree, the most significant of which was the positive correlation between the coefficient of aging (BA-CA) and SH-groups (r = 0.390, P = 0.027 – in isolated AH group and r = 0. 354, P = 0.047 – in AH and T2DM group, respectively), the positive correlation between the index of aging (BA/ PBA) and SH-groups (r = 0.370, P = 0.037) and BA coefficient (BA-PBA) and the GPO level (r = 0.364, P = 0.040) in AH and T2DM group. No correlation was found between the levels of MDA and age characteristics.

To assess the effect of OS indices on the aging degree, both groups of patients were divided into subgroups: 1a (n = 22) and 2a (n = 30) subgroups included AH patients (1a) and AH with T2DM patients (2a) with DTA; 1b (n = 13)

and 2b (n = 57) included AH patients (1b) and AH with T2DM patients (2b) with ATA (*Table 3*).

Patients with PhA were not evaluated at this study stage due to a small number of observations in both of the groups.

According to the study results, it was revealed that the LPO rate (MDA) increased with the aging rate acceleration, regardless of the diagnosis, reaching significant differences only in patients of 2a subgroup (P = 0.025). However, the correlation analysis revealed the presence of MDA correlations only in AH patients of the DTA subgroup (with CA – r = 0.515, P = 0.034 and PBA – r = 0.495, P = 0.043).

Blood levels of 8-OH-dG decreased with ATA in both subgroups of patients, with AH and AH with T2DM, but significant differences were observed only when combined with T2DM.

The correlation analysis revealed the positive correlation of moderate strength between the 8-OH-dG level and BA in the DTA of 1a subgroup (r = 0.557, P = 0.020). The correlation analysis also revealed the presence of significant interactions between the 8-OH-dG level and such age characteristics as CA (r = 0.408, P = 0.038) and the aging rate (ATA, DTA or PhA; R = -0.520, P = 0.019), which confirmed the significance of this index not only as a marker of OS, but also as a biomarker of aging.

As it can be seen from *Table 3*, the thiol status in the DTA subgroups was characterized by the same level indicating the presence of mechanisms maintaining AOX protection at a certain level regardless of the metabolic processes disorder degree. The presence of ATA was accompanied by the thiol status activation; in the presence of comorbid pathology, an increase in SH-groups reached significant values (P = 0.05). The correlation analysis revealed the positive correlation of moderate strength between the concentration of SH-groups and the coefficient of aging (BA-CA) in individuals with DTA of both subgroups 1a (r = 0.615, P = 0.009) and 2a (r = 0.662, P = 0.01). In ATA, a correlation between SH-groups and age indices was only detected in the group of isolated AH (with the coefficient of aging (BA-CA) – r = 0.662, P = 0.01).

The presence of ATA in AH and T2DM group was accompanied by an insignificant increase in the GPO level as opposed to the dynamics of this index in isolated AH, where a significant decrease of the above index was observed (P = 0.046). However, no correlation was found between GPO and the age indices in ATA subgroups. In DTA, the presence of correlation relationships between GPO and the age indices was only revealed in 1a subgroup (with the coefficient of aging (BA-CA) – r = 0.615, P = 0.009).

Assessment of the relationship between the indices characterizing OS and the aging rate features was carried out using the Spearman rank correlation coefficient, which revealed the presence of negative correlations between the GPO level and the aging rate (R = -0.397, P = 0.024) in isolated AH group as well as between the blood level of 8-OH-dG and the aging rate (R = -0.520, P = 0.019) in AH with T2DM group.

Discussion

The urgency of determining the aging rate is due to the fact that it can have a real prognostic value for assessing the health of both an individual and groups exposed to one

or another risk (hereditary, environmental, social, occupational, etc.). In addition, the quantitative characteristics of the aging rate can serve as an objective efficacy measure of such impacts on humans as lifestyle changes, dietary intervention, various bioadditives, medications or other therapeutic effects [4].

In our study, the absence of significant differences in the aging characterizing indexes between the control group and patients with isolated hypertension is explained, on the one hand, by the presence of stable antihypertensive therapy, which allows patients to maintain stable blood pressure levels, which was the criterion for inclusion in the study, and on the other hand, patients with complicated and uncontrolled hypertension were not included in the study. The simultaneous presence of DM significantly affects the aging indicators, which is evident from significant differences not only in relation to the control group, but also in relation to the isolated course of hypertension. Currently, there is no doubt that insulin resistance, which plays a major role in the pathogenesis of diabetes and its complications, is also one of the leading factors in the development of age-related and accelerated aging process diseases [14]. The data of this work confirm the hypothesis that biological age is a dynamic indicator that reflects not only the state of the body, but also the therapeutic and preventive measures effectiveness.

The study of OS was mainly conducted in hypertension without diabetes or diabetes without hypertension [15–17].

In patients with a combined course of AH and DM, previous studies of OS were mainly focused on its effect on carbohydrate metabolism, blood pressure levels, risk factors [18]. The effect of OS on the aging process in this comorbid pathology has not been practically studied.

The lack of OX-AOX systems stabilization in the most patients of this study, in our opinion, is due to insufficient medicamentous correction particularly of blood pressure and partly of carbohydrate metabolism at the time of inclusion in the study, which, in its turn, is characterized by the processes leading to OS development and progression.

Thus, despite the permanent blood pressure control, which was the criterion for inclusion in our study, the target levels (as recommended by the European Society of Cardiology [19]) of SBP in group with isolated AH were not reached by 16 (40.00 %) patients, in group with AH and T2DM – by 57 (59.38 %) patients. The target level of the DBP were not reached by 23 patients (57.50 %) in group with isolated AH and by 77 (80.21 %) – in group with AH and T2DM.

Hyperglycemia is known to cause glycosylation and inactivation of antioxidants, which is also observed in our work. The presence of insignificant differences in OS indices between patients of groups with isolated AH and with AH and T2DM may be explained by the fact that a significant proportion of AH and T2DM group patients (50 patients — 52.08 %) had a compensated status of carbohydrate metabolism (glycosylated hemoglobin was less than 7.5 %) on antidiabetic therapy. In addition, the beneficial effect of metformin, received by all patients with AH and T2DM in this study, on OS has been shown in many studies [20].

Considering the above, to clarify the role of OS in this comorbidity, it is necessary to conduct large-sample comparative studies on the oxidative-prooxidant balance state when reaching and not reaching the target blood pressure levels and T2DM compensation. This will make it possible to consider OS not only as a pathogenetic and prognostic factor of these diseases, but also as a marker for controlling therapeutic measures.

In groups of patients, changes in the parameters characterizing AOX system (AOXS) were not unidirectional, which is probably due to the varying degree of the studied AOXS parameters compensatory activation in response to the increased free radical processes, as well as to the degree of AOX inhibition in response to long-term LPO activation.

The presence of significant differences between subgroups, taking into account aging degree, not for all indices characterizing the OS, may indicate a sufficiently pronounced compensation at this stage (the study did not include patients with pronounced cardiovascular and diabetic complications). Nevertheless, ATA with comorbid pathology was still characterized by a significant activation of LPO, stimulation of antioxidant protection compared to persons with the DTA, which was not so typical for patients with isolated AH.

The observed decrease in 8-OH-dG plasma levels in the ATA was more pronounced in patient with comorbid pathology confirming, on the one hand, the current opinion on the antioxidants inactivation during hyperglycemia and its negative impact on the levels of DNA damage products caused by the oxidative process [21], and on the other hand, indicates the depletion of AOX reserves in the ATA.

In our opinion, such an ambiguous and multidirectional status of the OX-AOX system with the ATA can be explained by the fact that the mechanisms triggering the process of accelerated aging at the body level seem to include processes providing both negative and protective (stimulating) action on the antioxidant protection system, which requires further study.

Conclusions

1. Oxidative stress in most cases accompanies the course of both isolated AH and its combination with T2DM, regardless of the aging rate, including mediation of DNA oxidative damage development.

2. Patients with a combined course of AH and T2DM, have a more pronounced oxidative stress than those with an isolated AH course, which is one of the significant factors leading to the premature aging development.

3. The accelerated rate of aging, regardless of the existing pathological processes and states, is accompanied by more significant manifestations of oxidative stress than the delayed rate of aging.

Thus, determination of BA and the aging rate in the period of late ontogenesis with a high degree of accuracy reflects the degree of the physiological body adaptation impairment, resulting from a combination of age-dependent and pathological processes including OS, therefore OS evaluation together with age characteristics can be used not only to assess the body status, but also as an integral indicator characterizing the treatment and prevention measures efficacy.

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