Research Article

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On the Question of the Norm of some Laboratory Indicators of Homeostasis in People over 60

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BACKGROUND Currently, there are no reference values for many laboratory indicators of homeostasis for gerontological patients, which complicates the objective interpretation of their disorders.

AIM OF STUDY Based on a comparison of the reference values of some laboratory indicators of homeostasis of volunteers over 65 and people of working age, we offer their conditional norm for people of gerontological age.

MATERIAL AND METHODS Studies of laboratory indicators of homeostasis were carried out in 25 volunteers aged 60 to 85 years. The comparison group consisted of 50 donors aged 18–59 years. Investigated indicators: lipid peroxidation and antioxidant blood system; factors of endogenous vascular regulation; apoptosis of peripheral blood lymphocytes; blood rheology; endotoxemia, immunology. Statistical analysis of the data was performed using the Statistica 10 software package (StatSoft, Inc., USA); when comparing the indicators, the nonparametric Mann–Whitney U test (abnormal distribution) was used.

RESULTS In elderly and senile people, due to physiological aging, as well as the influence of endogenous and exogenous factors and concomitant diseases, there are significant differences in the reference values of some laboratory parameters from the parameters of the same name for people of working age.

Keywords: elderly and senile persons, laboratory parameters, reference values of laboratory parameters, geriatric patients

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ACE - angiotensin converting enzyme
APTT - activated partial thromboplastin time
CIC - circulating immune complexes
EA - early apoptosis
EAIM - erythrocyte aggregation index at rest
EAIM1 - erythrocyte aggregation index in motion
iNBT - induced nitro blue tetrazolium
INR – international normalized ratio
iNST - induced nitro blue tetrazolium
K - neutrophil stimulation coefficient
LA- late apoptosis
LCIC – large-sized circulating immune complexes
LPO - lipid peroxidation
MCIC – medium-sized circulating immune complexes
MDA - malonic dialdehyde
MMP – medium molecular peptides
NBT - nitro blue tetrazolium
NOx - nitrogen oxide
SCIC- small-sized circulating immune complexes
TAA - total antioxidant activity
TT - thrombin time

RATIONALE

According to WHO, in every country, including Russia, the proportion of people over the age of 60 is increasing faster than in other age groups. According to UNO, by 2050, one in 6 people in the world will be over 65 (16% of the population), compared to one in 11 people in 2019 (9% of the population). According to the forecast, the share of people aged 80 and older will increase 3-fold from 143 million in 2019 to 426 million in 2050 [4, 18]. Along with an increase in the proportion of people over 65 years of age among the population, their number is also increasing among patients seeking medical care, including those with acute poisoning. Thus, according to K. K. Ilyashenko et al., in recent years, there has been an increase in the number of patients with acute poisoning older than 60 years in the general structure, and their share on average is 12.5% [10].

Human aging is a universal and natural process characterized by gradual, uneven and steady progression, inevitably affecting to one degree or another all levels of biological organization. With age, the functional capabilities of the body's organs and systems gradually decrease, and their structure changes. Negative changes in the aging body occur due to: damage caused by endogenous changes; age-related damage caused by external factors; damage resulting from the development of age-related diseases [11].

Aging occurs strictly according to the genetic program, which is different for each species, and external causes only accelerate it. It should be noted that the concepts of "aging" and "old age" are ambiguous. Aging is a gradual process of cell damage and death in multicellular organisms, leading to disruption of the body's functions and its death.

Old age is not a process, but a condition of an organism that has undergone aging. Longevity is the result of physiological old age. Longevity is determined by the genetic safety margin that our body has.

Many changes that occur in the physiological state of the body's organs and systems become negative with age; they can be divided into those that reduce functional capacity, reduce functional response, and change homeostasis [12].

Currently, there are age norms for the period of formation and maturity. At the stage of extinction (aging), it is much more difficult to determine their boundaries, since there are no abrupt borderlines between the elderly, senile and the age of longevity [11]. In everyday clinical practice and when conducting scientific research, medical professionals have to assess disorders in the body caused by various factors: diseases, injuries, poisoning, etc., in particular, the degree of changes in laboratory homeostasis parameters in the elderly and senile. However, currently there are no reference values for many laboratory parameters for gerontological patients, which makes it difficult to objectively interpret their violations. When studying the laboratory parameters of homeostasis in this category of patients, for an objective assessment of the results

obtained, we determined the reference values of laboratory parameters in volunteers over 60 years of age, which we use in scientific research as a conditional norm [3, 9]. We want to present them to your attention.

The aim of the study was to compare the reference values of some laboratory homeostasis parameters of volunteers over 65 years of age and people of working age to suggest their conditional norm for people of gerontological age.

STUDY MATERIAL AND METHODS

Laboratory tests of homeostasis were conducted in 25 volunteers aged 60 to 85 years, including 17 women and 8 men. The comparison group consisted of 50 donors aged 18-59 years.

The content of LPO products was studied by measuring the level of malondialdehyde (MDA) in the blood serum, using the method of V. B. Gavrilov [6]. The total antioxidant activity (TAA) of blood serum was measured by spectrophotometric method on an Olympus AU2700 biochemical analyzer (Beckman Coulter, USA) using a TAS reagent kit (Randox, UK). The oxidative stress coefficient (Kos) was calculated as the ratio of normalized serum MDA to TAA values.

Impairment of endogenous vascular regulation was assessed by the content of stable nitric oxide (NOx) metabolites (nitrate/nitrite) in serum [7].

The concentration of angiotensin-converting enzyme (ACE) was determined photometrically on an Olympus AU 2700 biochemical analyzer (Beckman Coulter, USA) using reagents from Audit Diagnostics (Ireland).

The concentration of apoptotic lymphocytes and dead blood leukocytes (DC) was studied by flow cytometry using a YTOMIC FC500 device (Beckman Coulter, USA). The concentration of lymphocytes in the process of apoptotic death was determined using a set of Annexin V-FITC/7AAD Kit (Beckman Coulter, USA) using the vital DNA-specific dye 7-amino actinomycin D (7AAD): lymphocytes in the early stages of apoptosis (EA) (Annexin V+/ 7AAD−), lymphocytes in the later stages of apoptosis (LA) (Annexin V+/ 7AAD+).

The apparent blood viscosity was determined in the mode of decreasing the shear rate (γ) from 250 to 2.5 s-1 on a rotary viscometer AKR-2 (Russia), and the viscoelasticity of blood at shear rates of 62.8, 12.6, and 2.5 s-1 was determined on a BioProfiler capillary viscometer (USA) [13, 15]. Aggregation activity of erythrocytes was recorded on an MA-1 aggregometer (Myrenne GmbH, Germany), and collagen-induced platelet aggregation was recorded on an aggregometer with chrono–log model 590 (USA) [17]. Hematocrit and platelet count were determined on an Act diff 2 Beckman Coulter hematological analyzer (USA), hemostasis parameters – plasma fibrinogen content, INR, APTT, TT were measured on an S-1500 coagulometer (Sysmex, Japan) [16].

We investigated the concentration of immunoglobulins (Ig classes A, M and G), the state of phagocytosis (latex - and nitro blue tetrazolium [NBT] test, the neutrophil stimulation coefficient [K] and levels of circulating immune complexes [CIC]: large-sized (LCIC), medium-sized (MCIC) and small-sized (SCIC) ones [1, 2, 8, 14].

Endotoxicosis was tested by the content of medium molecular weight peptides (MMP) of fractions E254 and E280 [5].

Statistical analysis of the data was performed using the Statistica 10 software package (StatSoft, Inc., USA); and the nonparametric Mann-Whitney U-test (abnormal distribution) was used to compare the parameters

RESULTS

Table 1 shows the obtained reference values of the studied homeostasis parameters in volunteers over 60 years of age in comparison with the parameters of subjects under 60 years of age.

Table

Comparative assessment of laboratory indicators of homeostasis in volunteers under and over 60

Parameter		Age up to 60 years n = 50	Age after 60 years n = 25
Hematocrit,%		2	3
Apparent viscosity of blood, mPa* s at a shear rate of 250 s-1		40.4 (40.05; 40.76)	41.8 (39.6; 43.1)
Apparent viscosity of blood, mP* s at a shear rate of 10 s-1		4.9 (4.84; 4.96)	5.10 (4.8; 5.6)
Plasma viscosity, mPa*s		9.50 (5.46; 9.54)	9.5 (9.2; 12.0)
Blood viscosity mPa* s at shear rate	2.5 s-1	5.90 (5.75; 6.05)	5.70 (5.56; 6.16)
	12.6 s-1	4.8 (4.68; 4.92)	5.04 (4.74; 5.35)
	62.8 s-1	4.1 (4.02; 4.18)	4.61 (4.25; 4.77)
Viscoelasticity mPa* s at shear rate	2.5 s-1	3.13 (3.02; 3.24)	4.36 (4.05; 4.93) *
	12.6 s-1	1.55 (1.48; 1.62)	1.93 (1.75; 2.35) *
	62.8 s-1	0.61 (0.57; 0.65)	0.90 (0.79; 1.10) *
Erythrocyte aggregation index at rest (EAIM)		15.6 (15.02; 16.18)	17.13 (15.43; 19.42)
Index of aggregation of erythrocytes in motion (EAIM1)		18.9 (18.17; 19.63)	24.37 (22.63; 31.1) *
Platelet aggregation, % opt.pl.		13.0 (12.6; 13.6)	17 (16; 19) *
Absolute platelet count, 109 /L		196 (187.6; 204.4)	183 (141; 219)
Prothrombin index,%		86.1 (84.7; 87.5)	94.1 (83.8; 102.3)
APTT, s		36.2 (35.9; 36.5)	26.5 (25.6; 27.1) *
Fibrinogen, g/L		2.8 (2.7; 2.9)	2.53 (2.30; 2.77)
Antithrombin III, %		103 (102.2; 103.76)	97.0 (93.7; 100.3) *
Thrombin time, s		17.6 (17.59; 17.61)	18.8 (18.2; 19.3)
MDA, μmol/L		2.27 (2.11; 2.47)	4.59 (4.02; 6.01) *
TAA, mmol/L		1.61 (1.56; 1.68)	1.55 (1.49; 1.64)
Kos , cU		0.96 (0.91; 1.11)	2.33 (2.0; 2.73)
MMP, fraction E 254 , rel. Unit		0.239 (0.223; 0.246)	0.229 (0.218; 0.248)
MMP, fraction E 280 , rel. Unit		0.322 (0.292; 0.345)	0.322 (0.274; 0.387)
NOx, μmol/L		18.61 (17.70; 23.62)	22.85 (18.55; 30.36)
ACE, μmol/L		45.00 (36.45; 55.15)	41.95 (19.65; 62.5)
Absolute leukocyte count, 109 /L		6.4 (6.17; 6.63)	6.0 (5.1; 7.45)
Relative leukocyte content (dead cells), %		0.65 (0.56; 0.71)	0.93 (0.60; 1.29) *
Absolute leukocyte count (dead cells), 109 /L		0.041 (0.03; 0.046)	0.059 (0.03; 0.07)
CD 95,%		44.5 (43.8; 45.3)	26.6 (24.3; 30.7) *
EA,%		2.74 (2.70; 2.98)	7.25 (5.87; 12.71) *
LA,%		0.1 (0.08; 0.12)	0.12 (0.07; 0.20)
NBT, %		17.1 (12.0; 21.2)	11, (8.0; 19.0)
Induced NBT, %		34.0 (23.8; 45.3)	37 (27; 46)
K, cU		2.0 (1.43; 2.54)	2.75 (2.0; 3.86)
CIC L, cU/mL		20.8 (11.2; 30.5)	8.0 (6; 18) *
CIC M, cU/mL		45.5 (38.0; 52.0)	91 (77; 109) *
CIC S, cU/mL		98.0 (69.4; 126.6)	240 (212; 296) *
CIC total cU/mL		165 (122; 210)	329 (288; 390) *

Note: * - p <0.05 statistically significant difference from the value of subjects aged 18-59; APTT, activated partial thromboplastin time; ACE, angiotensin-converting enzyme, K, neutrophil stimulation coefficient, Kos, oxidative stress coefficient; MDA, malonic dialdehyde; NBT, nitro blue tetrazolium; TAA, total antioxidant activity; LA, late apoptosis; EA, early apoptosis;, CIC, circulating immune complexes, NOx, nitric oxide metabolites (nitrites/nitrates)

The data presented in Table 1 demonstrate that there are differences between some indicators of the same name in the compared groups. Thus, in individuals over 60 years of age, the aggregation activity of platelets and red blood cells in motion and blood viscoelasticity were statistically significantly higher. At the same time, APTT and the percentage of antithrombin III were reduced. The concentration of MDA in the blood was 2 times higher than the indicator of the compared group. Noteworthy is the higher content of total CIC, especially their fractions of medium and small sizes, and its decrease for large-sized CIC, as well as the relative number of dead leukocytes and the proportion of cells in early apoptosis (EA), with lower values of CD 95 in the blood of subjects of gerontological age.

It follows from the above that in elderly and senile people, due to physiological aging, as well as the influence of endogenous and exogenous factors and concomitant diseases, there are significant differences in the reference values of some laboratory parameters from the same parameters of people of working age.

CONCLUSIONS

The conducted studies revealed a statistically significant increase in the parameters of lipid peroxidation, erythrocyte aggregation in motion, platelet aggregation, the absolute number of dead lymphocytes, the readiness of lymphocytes for apoptosis, the proportion of lymphocytes at the stage of early apoptosis, the total number, as well as fractions of medium and small size of circulating immune complexes in persons of gerontological age. Along with this, a statistically significant decrease in APTT, antithrombin, the readiness of lymphocytes for apoptosis, and the absolute number of circulating complexes of small sizes were found. These changes in the gerontological age are primarily caused by the processes of physiological aging, which lead to changes in the structure and functions of various organs and systems of the body, as well as concomitant diseases that contribute to the identified homeostasis disorders.

It follows from the above that the obtained results of homeostasis laboratory parameters of volunteers from the older age group can be used as reference values for assessing their disorders in individuals with various somatic pathologies, in particular, with acute chemical poisoning.

FINDING

1. Volunteers of gerontology age as compared to able-bodied people have blood viscoelasticity higher by 1.24 to 1.47 times at different rates of shear capacity; higher erythrocyte aggregation index in motion by 1.29 times, platelet aggregation higher by 9%, MDA by 2 times, the contents of dead cells by 1.4 times, the proportion of lymphocytes in the early stages of apoptosis 2.6 times higher, the total amount of CIC more by 1.9 times.

2. APTT, antithrombin, CI9595, and LCIC values were reduced in volunteers over 60 years of age by 1.36 times, 6%, 1.67, and 2.6 times, respectively, as compared to those of working age.

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