Systemic Markers of Age-Related Changes in the Lens

Yu. V. Kudryavtseva[1,2], A. D. Chuprov[1,2], I. P. Ivanova[3], P. I. Tsapok[2], V. B. Tsibel'[4], and E. R. Bojko[4,5]

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 153, No. 3, pp. 355-358, March, 2012
Original article submitted October 6, 2010

A dependency was found between total protein content and cataract maturity (P=-0.91, p<0.01). LPO intensity sharply increased and remained stably high after appearance of lens opacity. A strict negative correlation was found between the content of polyunsaturated fatty acids in earwax and lens nucleus (P=-0.7, p<0.01). The content of conjugated dienes, crotonic aldehyde, and Schiff bases decreased during cataract development. The content of vitamins B_2, A, and E decreased with increasing brown coloration of lens nucleus. Studying the parameters of lipid metabolism in wax-producing glands of the external ear canal we can evaluate the disturbances in lipid metabolism in the lens, which was confirmed by the correlation between fatty acid composition of the earwax and lens nucleus. These data do not demonstrate the dependence of the lens state on earwax, but suggest general features of the process in organs and tissues during aging. Some markers in the blood of patients with cataract change during progress of lens opacity and intensification of brown coloration of lens nucleus, but these changes are inspecific and reflect general activation of peroxidation processes and antioxidant system.

Key Words: *cataract; lens; earwax, changes in the blood during cataract*

Studying changes in the lens as a partial event in the body we can hypothesize similar processes in other organs and systemic markers of cataractogenesis can be identified [8]. A sharp decrease in antiradical defense system of eye tissues as the pathogenetic basis of senile cataract seems to be a reasonable hypothesis [1]. An attempt was undertaken to study correlations between metabolic changes, in particular LPO and antiradical defense processes, in the lens and some other systems of the body.

Here we studied some systemic markers of changes in human lens during senile cataract development.

MATERIALS AND METHODS

The study included 134 patients with cataract of different maturity. Lens nuclei were collected during standard extracapsular cataract extraction. Before surgery, cataract maturity according to standard classification (initial, immature, and hypemature cataracts) was determined using Japanese Classification (The Japanese Cooperative Cataract Epidemiology Study Group (CCESG) system), when the degree of brown coloration is evaluated by a 4-point scale. Lens nuclei were studied *in vitro*; qualitative and quantitative composition of higher fatty acids was determined by gas-liquid chromatography (Hewlett Packard, model 5830 A). The intensity of free radical oxidation of antioxidant defense processes was evaluated by chemiluminescent analysis on Emilite El 1105 device by measuring maximum flash amplitude I_m and total luminescence over 60 sec (S, inversely proportional to antioxidant activity) [4]. In parallel, extinction ratios $E_{232/222}$ and $E_{278/222}$ (in arb. units) corresponding to conjugated dienes and ketotrienes were determined; TBA-reactive lipoperoxidation end-products were measured spectrophotometrically [2]. Total protein content was measured by the method of Lowry, total lipids were assayed by color reaction with sulfophosphovanillin

[1]Kirov Clinical Ophtalmological Hospital; [2]Kirov State Medical Academy; [3]Research Institute of Applied and Basic Medicine, Nizhnii Novgorod State Medical Academy; [4]Komi Branch of Kirov State Medical Academy, Syktyvkar; [5]Institute of Physiology, Komi Research Center, Ural Division of Russian Academy of Sciences, Syktyvkar, Russia. ***Address for correspondence:*** July_Kud@mail.ru. Yu. V. Kudryavtseva

0007-4888/12/1533-0375

TABLE 1. Correlation of Some Biochemical Parameters with Cataract Maturity

Parameter	Transparent lens (control)	Cataract		
		initial	immature	mature
Protein, g/liter	0.15±0.02	0.16±0.01	0.07±0.04*	0.043±0.006**
Total lipids, g/liter	0.013±0.001	0.005±0.001	0.03±0.01	0.007±0.003*
CL peak, imp.	50.9±7.8	54.5±5.6	77±28	77.6±36.5
CL sum, imp.	323.2±20.7	1535±425	1561.5±869.1**	1487±634**
TBA-reactive substances, μmol/g	0.25±0.08	1.11±0.12	1.06±0.2**	0.9±0.2**
CD, 233/222 nm	0	3.0±1.0	8.9±3.1**	11.9±6.0**
CT, 278/222 nm	0	2.0±1.0	6.9±3.0**	6.5±2.7**

Note. CL: chemiluminescence; CD: conjugated dienes; CT: conjugated trienes. *p<0.05, **p<0.01 in comparison with the control.

reagent [3]. Fifteen transparent lenses were used as the control.

For detection of systemic markers of cataractogenesis, the blood and earwax from the external ear channel of patients were analyzed. The content of higher fatty acids (HFA) in earwax was qualitatively and quantitatively assayed by gas-liquid chromatography. In the blood, primary, secondary, and final LPO products of protein and lipid origin, antioxidant enzymes (glutathione peroxidase, glutathione reductase, SOD), natural antioxidants (retinol and tocopherol), and selenium content were measured. All measurements were performed on a Shectroninic Cienesys-6 spectrophotometer. The data were processed using SPSS 10 software.

RESULTS

Some authors believe that impaired transparency of the lens results from disturbances in barrier properties of cell membranes [1] and formation of protein aggregates due to disulfide cross-linking. According to our findings, a potent negative correlation exists between total protein content and cataract maturity (correlation coefficient -0.91, p<0.01; Table 1).

LPO intensity sharply increased and remained stably high after appearance of lens opacity, which is confirmed by the level chemiluminescence and content of TBA-reactive substances. This is confirmed by published data [5,7]. Comparison of HFA composition of the lens nucleus and earwax yielded interesting results (Table 2). Palmitic, stearic, and polyunsaturated HFA predominated in earwax and palmitic and polyunsaturated HFA predominated in the lens. Some HFA (lauric, linoleic, linolenic, and pentadecanoic acids) were present in minor amounts. A strict negative correlation was found between the content of polyunsaturated fatty acids in earwax and lens nucleus (P=-0.7, p<0.01). This stage of the study was based on general biological proposition on a correlation between some parameters of lipid metabolism in different (function-

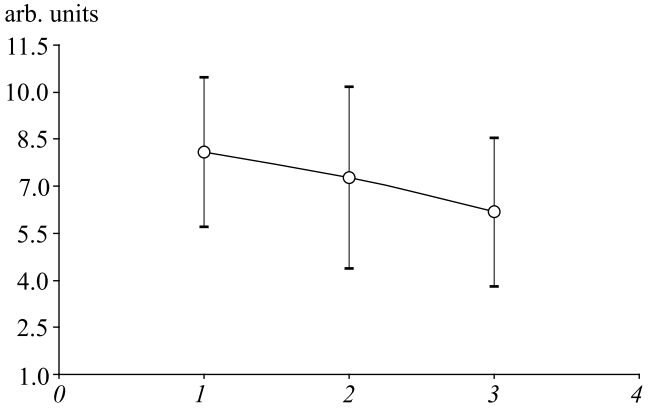

Fig. 1. Dependence of blood content of conjugated dienes (232 nm) on cataract maturity (p<0.05). Here and in Fig. 2: *1*) initial stage; *2*) immature; *3*) mature; *4*) hypermature.

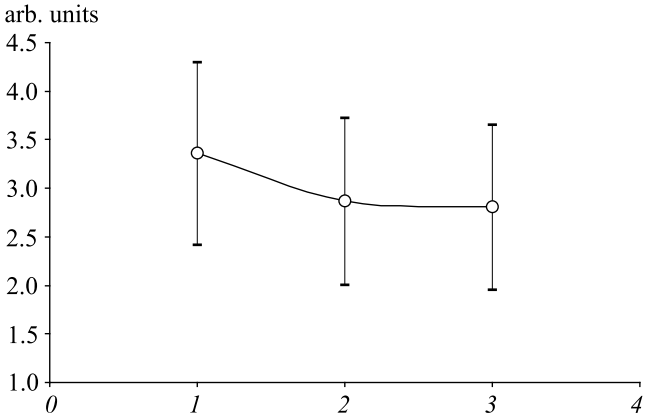

Fig. 2. Dependence of blood content of crotonic aldehyde (220 nm) on cataract maturity (p<0.05).

TABLE 2. Mean Content of Some HFA in the Lens and Earwax

Symbolic notation	Name	Mean content in earwax, %	Mean content in cataract lens, %
12:0	Lauric	0.70±0.08	0.16±0.04**
14:0	Myristic	2.6±0.5	2.04±0.20
15:0	Pentadecanoic	1.37±0.27	1.34±0.20
16:0	Palmitic	24.1±2.6	32.2±3.7*
18:0	Stearic	12.9±2.3	2.41±0.43**
18:1	Oleic	9.2±1.3	3.69±0.59**
18:2	Linoleic	3.2±0.4	1.07±0.08**
18:3	Linolenic	1.3±0.1	0.46±0.04**
	Pool of polyunsaturated HFA	28.8±2.8	52.9±5.8**

Note. *p<0.05; **p<0.01.

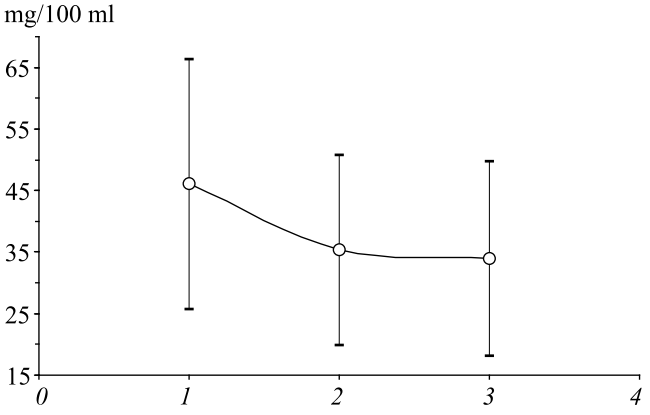

Fig. 3. Dependence of blood content of vitamin A (232 nm) on intensity of brown coloration of lens nucleus (p<0.05). Lens color: *1*) gray, *2*) yellow, *3*) blown.

ally and genetically identical) organs. These data do not demonstrate the dependence of the lens state on earwax, but suggest common features of the process in organs and tissues during aging.

The blood is the main biological fluid in the body and reflects variousl including age-related shifts in the organism. Many attempts at identification of changes specific for cataract patients were undertaken [9,6]. Our findings suggest that progression of senile cataract is accompanied by a decrease in the content of LPO products (conjugated dienes, crotonic aldehyde, and Schiff bases; Figs. 1, 2).

Using color classification of cataracts, we found that intensification of blown coloration of the lens nucleus is associated with a decrease in the content of vitamins B_2, A, and E in the blood (Fig. 3).

Our study demonstrated a variety of changes in the blood during cataract development. No single marker unambiguously reflects the degree of lens opacity. The processes are unspecific and attest to general activation of peroxidation and antioxidant defense processes.

REFERENCES

1. A. I. Deev, A. V. Aseichev, and Yu. A. Vladimirov, *Vestn. Ross. Akad. Med. Nauk.,* No. 2, 22-26 (1999).
2. G. A. Vinikova, Ch. F. Camilov, I. S. Orlov, Klin. Lab. Diagn., No. 7, 7-9 (1999).
3. V. T. Kolb and V. S. Kamyshnikov, *Clinical Biochemistry* [in Russian], Minsk (1982).
4. P. I. Tsapok and A. A. Galkin, *Chemiluminescent Analysis of Lipid Peroxidation in Blood Serum* [in Russian], Information Bulletin No. 75-98, Kirov Center of Scientific and Technical Information (1998).
5. R. P. Bhatia, R. Rai, and G. R. Rao, *Ann. Ophthalmol*., **38**, No. 2, 103-106 (2006).
6. B. Virgolici, I. Stoian, C. Muscurel, *et al., Rom. J. Intern. Med*., **45**, No. 1, 59-65 (2007).
7. B. Kisic, D. Miric, L. Zoric, *et al., Vojnosanit Pregl.,* **66**, No. 5, 371-375 (2009).
8. M. Mirsamadi and I. Nourmohammadi, *Ophthalmic Res*., **35**, No. 6, 329-34 (2003).