ORIGINAL ARTICLE

COMPARISON OF FREE RADICAL LIPID PEROXIDATION PROCESSES IN PATIENTS WITH PRIMARY AND SECONDARY GLAUCOMA

DOI: 10.36740/WLek202207116

Viktoriia V. Riadnova, Liudmyla K. Voskresenska, Iryna S. Steblovska, Olha Y. Maksymuk
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To investigate and compare the effects of free radical lipid peroxidation, antioxidant supply and the state of hydro- and hemodynamics of the eye on the course and progression of the glaucoma process in patients with primary and secondary glaucoma.

Materials and methods: We observed 123 patients with primary and secondary glaucoma and 58 apparently healthy individuals, constituting the control group. The first group included 62 patients diagnosed with primary compensated glaucoma. The remaining 61 patients, who constituted the second group of subjects, were included in the study with a diagnosis of secondary compensated glaucoma.

Results: Clinical examination of patients with primary compensated glaucoma in winter demonstrates a statistically significant decrease in intraocular fluid production, decreased outflow and reduced actual intraocular pressure, whereas in summer and autumn these figures were less pronounced. Observations of patients with secondary compensated glaucoma also showed a statically significant decrease in the production of chamber fluid and a decrease in the coefficient of outflow in winter. Similar tendencies were confirmed by hemodynamic changes. During this period, the relative pulse volume of the blood entering the eye is significantly reduced, in the summer and autumn period, the deficit of blood supply to the eye is less pronounced.

Conclusions: The results of the research indicate the proliferative form of peroxide mechanisms in the pathogenesis of glaucoma of both types, which is the basis for using inhibitors of free radical lipid oxidation – antioxidant preparations – in the comprehensive therapy of these diseases. The identified features of clinical and biochemical disorders, based on the season of examination, are the basis for the development of differentiated regimens for the use of antioxidants in the treatment of glaucoma.

KEY WORDS: free radical lipid peroxidation, primary and secondary glaucoma

Wiad Lek. 2022;75(7):1693-1698

INTRODUCTION

Glaucoma is a multifactorial disease, therefore, many factors of its pathogenesis are currently known. The causes of the development of primary open-angle glaucoma (POAG) are genetic factors, hydrodynamic, neurovascular and immunological changes, but a special role belongs to metabolic disorders [1,2]. The basis for the formation and progression of many pathological diseases and conditions and glaucoma in particular, as well as their unfavorable prognosis, is the activation of free radical peroxidation in organs and systems of the body against the background of reduced functionality of antioxidant defense [3,4]. Imbalance due to the stimulation of free radical oxidation (FRO) and decreased antioxidant activity (AA), often leads to the accumulation of FRO products, which have extremely high reactivity, inducing the modification of the structure of lipids, proteins and nucleoproteins, and other important molecules. This subsequently leads to the induction and progression of various pathological processes in humans. At present, glaucoma is also considered a neurodegenerative disease, since the development of degenerative changes is observed not only in retinal ganglion cells and healthy nerve fibers, but also in the tissues of the conduction tracts of the visual analyzer and cerebral cortex [5]. Also common to neurodegenerative diseases and POAG are selective death of nerve cells of a certain type by apoptosis, elderly age of patients, increasing incidence with age, genetic determinism and long latency. Therefore, determining the impact of metabolic disorders on the progression and course of glaucoma is a very important issue in modern ophthalmic practice.

THE AIM

The aim of the research is to investigate and compare the effects of free radical lipid peroxidation, antioxidant supply and the state of hydro- and hemodynamics of the eye on the course and progression of the glaucoma process in patients with primary and secondary glaucoma.

MATERIALS AND METHODS

We observed 123 patients with primary and secondary glaucoma and 58 apparently healthy individuals, of whom 30 were examined in the winter and spring period, and 28 – in summer and autumn, constituting the control

Table I. Biochemical parameters in healthy individuals depending on the seasonality of observation

Parameters	Number of observervations	Winter-spring	Number of observervations	Summer-autumn
β- and pre-β-lipoproteins, g / l	30	5.67 ± 0.20	28	5.20 ± 0.2 p<0.01
TBA reactants, units / ml	30	0.15±0.01	28	0.07±0.0001 p<0.001
AHP content, units / ml	30	4.79±0.40	28	3.59±0.5 p<0.01
SHE,%	30	11.77±1.04	28	8.82±0.41 p<0.02

Table II. The state of hydro- and hemodynamics of the eye in healthy individuals depending on the seasonality of observation

Parameters	Winter-spring n=30	Summer-autumn n=28
P0, mmHg	17.50±0.30	18.40±0.40 p<0.01
C, mm3/min	0.42±0.006	0.44±0.004 p<0.01
F, mm3/min	3.45±0.08	3.50±0.08 p<0.1
RQ, %	3.40±0.08	3.50±0.03 p<0.1
PV, mm3	13.90±0.40	13.50±0.10 p<0.01

group. The first group included 62 patients diagnosed with primary compensated glaucoma, 32 patients in this group were examined in the winter and spring period, and 30 patients – in the summer and autumn period. The remaining 61 patients, who constituted the second group of subjects, were included in the study with a diagnosis of secondary compensated glaucoma, of which 31 patients were examined in the winter and spring period, and 30 patients – in the summer and autumn period. All patients received traditional antiglaucoma therapy. The mean age of patients was 64.7 ± 8.43, from 54 to 81 years. All patients underwent general clinical and ophthalmological examinations, namely: visometry, tonometry, perimetry. To assess the hydrodynamics of the eye, we studied tonography according to A.P. Nesterov. The actual intraocular pressure (P0), the coefficient of outflow (C), the production of chamber fluid (F), and the Becker coefficient (BC) were determined. To assess the hemodynamics of the eye, ophthalmorheography was performed using a rheographic device 4RG-1A and an electroencephalograph according to the method of L.A. Katznelson. The obtained data were evaluated by the rheographic coefficient (RC) and pulse volume of the blood (PV). Along with ophthalmological examination, additional research methods were applied, namely: biochemical analysis of blood with the study of acylhydroperoxides (AHP) in the fraction of β- and pre-β-lipoproteins, 2-thiobarbituric acid (TBA-reactants), superoxide dismutase (SOD) and spontaneous hemolysis of erythrocytes (SHE). All results of biochemical studies and clinical observations were statistically processed using the software «Statistica for Windows».

RESULTS AND DISCUSSION

When observing patients of the control group (58 apparently healthy individuals), in whom the somatic status corresponded to the age norm, the following average indicators of biochemical examination were revealed: β- and pre-β-lipoproteins 4.94 ± 0.16 g / l, SHE 12.20 ± 0.49%, catalase activity 1.79 ± 0.03 units / 10^6 erythr., SOD – 2.36 ± 0.11 units / ml, ceruloplasmin 36.0 ± 0.63 units / ml, content of TBA reactants 16.63 ± 1.90 units extr / ml, AHP content 4.82 ± 0.33 units extr / ml.

Due to the seasonality of alimentary antioxidants, we analyzed biochemical parameters in this group of subjects in different seasons of the year (Table I).

Comparing the activity of antioxidant enzymes, we found that in the winter and spring period, the activity of SOD and catalase ($p<0.001$) in apparently healthy individuals is lower. We found a pattern of rising levels of β- and pre-β-lipoproteins in the winter and spring period ($p<0.01$). The results were interpreted as the norm. Hydro- and hemodynamic values in the control group, which were examined in different seasons, are given in Table II. We found no statistically significant difference in the values observed in this group by sex, age, and in different seasons.

During the examination of patients of group 1 (32 patients) with primary compensated glaucoma in the winter and spring period, significant changes in the hemodynamics of the eye were revealed. There was a decrease in the rheographic coefficient in patients with primary glaucoma, examined in the winter and spring period, as compared to the control group: in healthy individuals, this figure was 3.47 ± 0.06%, in patients of group 1 – 2.2 ± 0.04 %

Table III. The state of hydro- and hemodynamics of the eye in patients with primary glaucoma, examined in the winter and spring period

Parameters	Control group n=30	Group 1 n=32
P0, mmHg	17.50±0.30	16.00±0.08 p<0.001
C, mm3/min	0.42±0.006	0.52±0.004 p<0.1
F, mm3/min	3.45±0.08	5.60±0.08 p<0.1
RQ, %	3.40±0.08	2.20±0.04 p<0.01
PV, mm3	13.90±0.40	12.30±0.60 p<0.01

Table IV. Biochemical parameters in patients with primary compensated glaucoma, examined in the winter and spring period

Parameters	Control group n=30	Patients of group 1 n = 32
β- and pre-β-lipoproteins, g / l	5.67±0.20	6.49±0.38 p<0.05
TBA reactants, units / ml	0.15±0.01	1.01±0.03 p<0.001
AHP content, units / ml	4.79±0.40	15.40±0.10 p<0.001
SHE,%	11.77±1.04	14.50±1.10 p<0.02

Table V. The state of hydro- and hemodynamics in patients with primary compensated glaucoma, examined in the summer and autumn period

Parameters	Control group n=28	Patients of group 1 n=30
P0, mmHg	18.40±0.40	23.60±0.30 p<0.001
C, mm3/min	0.44±0.004	0.50±0.04 p<0.001
F, mm3/min	3.50±0.08	4.48±0.05 p<0.001
RQ, %	3.50±0.03	2.70±0.04 p<0.001
PV, mm3	13.50±0.10	12.30±0.90 p<0.5

(p<0.001), there was also a decrease in the relative pulse volume of the blood entering the eye (Table III).

Analyzing biochemical parameters in patients with primary compensated glaucoma, examined in the winter and spring period, we revealed moderate hyperlipidemia. The content of atherogenic fractions of lipoproteins reliably exceeded the same values in the subjects of the control group (p<0.05) (Table IV). In patients of group 1, there is a sharp intensification of free radical lipid oxidation, which indicates a slightly higher level of TBA reactants and AHP in lipoproteins as compared to the same indicators of the control group, which were examined in the winter and spring period.

The examination of patients of group 1 (30 patients) in the summer and autumn period also revealed significant changes. The rheographic coefficient decreased statistically significantly in comparison with apparently healthy individuals of the control group (p<0.001), a similar situation was observed with the indicators of minute blood volume in patients of this group (Table V).

When evaluating the results of functional methods of examination in patients of group 1 in the summer and autumn period, there is a statistically reliable and significant increase in the production of chamber fluid, as compared with those of the control group (p<0.001). These changes were observed against the background of a decrease in the coefficient of outflow (p<0.001), as well as an increase in actual IOP (Table 5). When analyzing the biochemical parameters in patients with primary compensated glaucoma, who were examined in the summer and autumn period, moderate changes in lipid metabolism were identified (Table VI). Intensification of free radical lipid oxidation

Table VI. Biochemical parameters in patients with primary compensated glaucoma, examined in the summer and autumn period

Parameters	Control group n=28	Patients of group 1 n=30
β- and pre-β-lipoproteins, g / l	5.20±0.2	11.70±0.08 p<0.001
TBA reactants, units / ml	0.07±0.0001	0.80±0.001 p<0.001
AHP content, units / ml	3.59±0.5	8.34±0.05 p<0.001
SHE,%	8.82±0.41	12.40±0.03 p<0.001

Table VII. The state of hydro- and hemodynamics in patients with secondary compensated glaucoma, examined in the winter and spring period

Parameters	Control group n=30	Patients of group 2 n=31
P0, mmHg	17.50±0.30	25.70±0.04 p<0.001
C, mm3/min	0.42±0.006	0.52±0.002 p<0.001
F, mm3/min	3.45±0.08	7.12±0.08 p<0.001
RQ, %	3.40±0.08	1.43±0.08 p<0.001
PV, mm3	13.90±0.40	11.20±0.60 p<0.001

Table VII. Biochemical parameters in patients with secondary compensated glaucoma, examined in the winter and spring period

Parameters	Control group n=30	Patients of group 2 n=32
β- and pre-β-lipoproteins, g / l	5.67±0.20	8.5±1.20 p<0.05
TBA reactants, units / ml	0.15±0.01	1.1±0.01 p<0.001
AHP content, units / ml	4.79±0.40	15.43±0.20 p<0.001
SHE,%	11.77±1.04	23.60±1.02 p<0.001

(FRLO) was detected in patients of this group, the level of TBA reactants and AHP was statistically significantly higher than in the control group (p<0.001). The above changes occurred against the background of declining antioxidant levels.

Observing the change in biochemical parameters in patients of group 1 depending on the season, we noted the stability of the level of lipid metabolism. In the winter and spring period in patients with primary compensated glaucoma, there was a significant intensification of FRLO. Therefore, the content of TBA reactants in patients examined in the winter and spring period was 1.01 ± 0.03 units extr / ml, while in the summer and autumn period – 0.80 ± 0.001, respectively (p<0.001). Similar changes were observed in relation to the content of AHP, which was equal to 15.40 ± 0.1 units / ml in the winter and spring period, and 8.34 ± 0.05 units / ml in the summer and autumn period (p<0.001). The intensity of free radical reactions in the winter and spring period is twice as high as the same values in patients examined in the summer and autumn seasons. There is a tendency of reduced antioxidant activity in the winter and spring period (14.50 ± 1.10) as compared to the summer and autumn (12.40 ± 0.03) (p<0.1). When comparing the activity of antioxidant enzymes, it was found that in the winter and spring period, their activity was statistically significantly higher (Tables 4 and 6).

When observing patients of the **second group** with secondary compensated glaucoma in the winter and spring period, it was found that the indicators of hydrodynamics are statistically significantly different from the control group. First of all, this concerns the increase in the production of chamber fluid, which in turn led to a compensatory decrease in the coefficient of outflow (p<0.0001). We also found a statistically significant increase in actual IOP (Table VII).

Significant intensification of FRLO was observed in

patients of this group, which is indicated by a higher level of TBA reactants ($p<0.001$) and AHP in lipoproteins ($p<0.001$) when compared with the values of the control group, which were examined in the same period. However, we noted a high degree of intensity of free radical reactions, about 5 times higher than in the control group. The increase in the level of autooxidation detected by us was observed against the background of lower antioxidant activity (Table VIII).

After analyzing antioxidant enzymes in patients of group 2, we found a progressive increase in the activity of catalase, SOD and ceruloplasmin ($p<0.001$). Data from functional examination methods showed significant changes in eye hydrodynamics in patients of group 2 in the winter and spring period. The production of chamber fluid in patients of this group increased in the summer and autumn period in comparison with the control group, 3.50 ± 0.08 and 8.16 ± 0.02, respectively ($p<0.001$). There was a significant decrease in the coefficient of fluid outflow ($p<0.001$). Significant changes were also found in the hemodynamics of the eye in patients with compensated secondary glaucoma examined in the summer and autumn period. Patients had a statistically significant reduction in rheographic ratio as compared to healthy individuals, which leads to a decrease in the relative pulse volume of the blood, and thus to a deterioration in the blood supply to the eye. In healthy individuals, this figure was $4.0 \pm 0.08\%$ versus $1.0 \pm 0.05\%$ in patients with secondary glaucoma ($p<0.001$).

When observing the biochemical changes in patients of group 2 in the summer and spring period, changes were found that are similar to those patients who were examined in the winter and spring period. In patients, there was an intensification of FRLO, an increase in the level of TBA reactants and AHP, respectively, which exceeded these values in the control group. The intensity of free radical reactions was also statistically significantly higher. These changes were observed against the background of reduced antioxidant supply of patients with secondary compensated glaucoma, as evidenced by a higher level of spontaneous hemolysis of erythrocytes ($p<0.01$). Analysis of the activity of antioxidant enzymes in patients of group 2, examined in summer and autumn, showed that the activity of superoxide dismutase was statistically significantly lower than in the control group, whereas the activity of catalase and ceruloplasmin did not differ significantly.

When comparing clinical and biochemical parameters in patients of group 2 in different seasons, it was found that in the winter and spring period, there is a moderate decrease in chamber fluid production as compared to the summer and autumn period (0.61 ± 0.003 and 0.52 ± 0.002, respectively) ($p<0.001$). Patients in group 2 in the winter and autumn period had a statistically significant deterioration in the blood supply to the eye ($1.30 \pm 0.08\%$ and $1.90 \pm 0.05\%$ $p<0.001$) as compared to the group of patients examined in the summer and autumn period.

Analysis of biochemical parameters in patients of group 2 depending on the season showed that in the winter and spring period, there is an increase in the level of AHP (15.43 ± 0.07 units extr / ml and 9.54 ± 0.01 units extr / ml $p<0.001$). The intensity of free radical reactions in the winter and spring period is almost 2 times higher than in patients of group 2 in the summer and autumn period ($p<0.001$). We found a decrease in antioxidant supply in patients of group 2 in the winter and spring period as compared to summer and autumn ($23.6 \pm 0.20\%$ and $12.45 \pm 0.12\%$, respectively) ($p<0.001$). Comparison of the activity of antioxidant enzymes showed that in the winter and spring period, the activity of all of the above was statistically significantly higher.

CONCLUSIONS

Clinical examination of patients with primary compensated glaucoma in winter demonstrates a statistically significant decrease in intraocular fluid production, decreased outflow and reduced actual IOP, whereas in summer and autumn these figures were less pronounced. Observations of patients with secondary compensated glaucoma also showed a statically significant decrease in the production of chamber fluid and a decrease in the coefficient of outflow in winter. Similar tendencies were confirmed by hemodynamic changes. During this period, the relative pulse volume of the blood entering the eye is significantly reduced, in the summer and autumn period, the deficit of blood supply to the eye is less pronounced. This is confirmed by the established close correlations between the level of blood supply to the eye and the content of intermediates of FRLO – TBA reactants and AHP.

The results of clinical observations were also confirmed by biochemical changes. Estimation of FRLO levels in patients with primary and secondary compensated glaucoma provides evidence of a proliferative form and a significant increase in the level of autooxidation intermediates. Intensification of FRLO occurred against the background of decreased antioxidant supply of patients. It is necessary to admit the greater intensity of free radical reactions in patients with secondary glaucoma. In terms of the influence of seasonal factors on the development of changes in different types of glaucoma, we analyzed seasonal differences in biochemical parameters. In patients with glaucoma in the summer and autumn period, there is a lower intensity of FRLO and a higher antioxidant supply of hydrophobic and hydrophilic antioxidants. The activity of all studied antioxidant enzymes in the summer and autumn period was compared to the winter and spring period. The greater intensity of autooxidation in glaucoma patients in the winter and spring period of the year against the background of low antioxidant supply and, consequently, more pronounced clinical manifestations and biochemical changes are due to nutritional deficiency of natural biologically active substances with antioxidant action. Their lack leads to disruption of the antioxidant defense system of the vascular wall in patients with glaucoma, thus creating conditions for increased reactions of FRLO and damage to the structures of the vascular wall, which leads to morphofunctional changes characteristic of glaucoma.

Thus, the results of the research indicate the proliferative form of peroxide mechanisms in the pathogenesis of glaucoma of both types, which is the basis for using inhibitors of FRLO – antioxidant preparations – in the comprehensive therapy of these diseases. The identified features of clinical and biochemical disorders, based on the season of examination, are the basis for the development of differentiated regimens for the use of antioxidants in the treatment of glaucoma.

REFERENCES

1. Alekseev V., Gazizova I. Neurodegenerative changes in patients with primary open-angle glaucoma [Electronic resource]. http://pmarchive.ru/nejrodegenerativnye-izmeneniya-u-bolnyx-pervichnojotkrytougolnoj-glaukomoj/ [date access 15.10.2021]
2. Astakhov Yu., Rakhmanov V. Heredity and glaucoma. Ophthalmol. payroll. 2012;4:51–57.
3. Bezdetko P. Neuroprotective treatment of glaucoma [Electronic resource]. Access mode: http://healthua.com/articles/11999 [date access 15.10.2021]
4. Rakhmanov V., Nikitina N., Zakharova F. Mutations and polymorphisms of myocilin and optineurin genes as genetic risk factors for the development of primary open-angle glaucoma. Genetics. 2005;11:1567–1574.
5. Kovaceva O. Differences in activities of antioxidant superoxide dismutase, glutathione peroxidase and prooxidant xanthine oxidoreductase/xanthine oxidase in the normal corneal epithelium of various mammals. Physiol. Res. 2007; 56:105–112.

ORCID and contributionship:

Viktoriia V. Riadnova: 0000-0001-8815-7827 [A-F]
Liudmyla K. Voskresenska: 0000-0001-6389-8928 [A-F]
Iryna S. Steblovska: 0000-0002-9151-2524 [A-F]
Olha Y. Maksymuk: 0000-0002-1451-7997 [A-F]

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Iryna S. Steblovska
Poltava State Medical University
24 Shevchenko st., 36000 Poltava, Ukraine
tel: +480666871079
e-mail: irunasteblovska@gmail.com

Received: 10.02.2022
Accepted: 29.06.2022

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article