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Determining correlations between the grade of lens opacity and tear levels of total antioxidant activity and lipid peroxidation products in patients having both cataract and bacterial keratitis

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Purpose: *To determine correlations between the grade of lens opacity and tear levels of total antioxidant activity (TAA) and lipid peroxidation (LPO) products in patients having both cataract and bacterial keratitis treated versus not treated with methyl-ethyl pyridinol hydrochloride (MH).*

Methods: *Patients of the study group had both senile cataract and bacterial stromal keratitis; they received MH (nine four-week cycles of daily treatment with MH separated by four-week breaks) as an adjunct to the conventional antibacterial treatment. Patients that received the conventional antibacterial treatment only were used as controls. The development of senile cataract in patients with keratitis was followed up for 18 months. Severity of lens opacity was assessed by slit lamp biomicroscopy and scored on a scale of 0 to 5. Tear levels of TAA, malondialdehyde (MDA) and diene conjugate (DC) were determined in patients with keratitis only and those having both keratitis and cataract. Spearman's rank correlation was used to determine associations between the grade of lens opacity and tear levels of metabolic characteristics.*

Results: *Correlations between the grade of lens opacity and tear levels of TAA, MDA and DC were higher for patients having both cataract and keratitis and treated with MH than for patients with keratitis only. There were correlations of the grade of lens opacity with tear levels of TAA, MDA and DC (R=-0.85, R=0.80 and R=0.65, respectively) and of the tear level of TAA with tear levels of MDA and DC (R=-0.84 and R=-0.72, respectively) for patients having both cataract and bacterial keratitis and treated with MH.*

Conclusion: *Our findings of apparent correlations of the grade of lens opacity with the parameters of the oxidative-antioxidatiove system in the tear fluid of patients indicate a pathogenetic role of bacterial keratitis in the development of cataract. MH has antioxidative properties and may be used for correcting metabolic abnormalities and preventing structural and functional changes in the lens in cataractogenesis with corneal inflammation.*

Key words:

cataract, keratitis, lipid peroxidation, total antioxidant activity, antioxidant enzymes, methyl-ethyl pyridinol hydrochloride, lens, cornea, tear fluid

Introduction

Despite a variety of therapeutic and surgical options available and improvement in the quality of life, management of senile cataract remains a challenge. Effects of cataractogenic factors (excessive sunlight, presence of traumatic, inflammatory or degenerative disorders, etc.) on the eye and increased life span can increase the probability of the development of lens opacity among working age individuals [1-4].

Today, bacterial keratitis (BK) ranks among the leading causes of global ocular morbidity, with steep upward trends in disease frequency driven by the widespread use of contact lenses and a decline in the efficacy of broad-spectrum antibiotics and corticosteroids in a portion of patients [5].

Consequently, our attention was attracted by the effects of corneal inflammation on the development of cataract in patients with BK. Studies based on logistic regression analysis further emphasized the significance of managing systemic inflammation as a potential strategy for cataract prevention [6], which stresses the importance of early treatment of systemic inflammation in the prevention of corneal opacity [7]. Endothelial corneal dystrophy in cataract patients is associated with elevated levels of inflammatory chemokines in the aqueous humor [8].

Cataractogenesis in the presence of microbial keratitis, in turn, may be associated with effects of bacterial toxins as well as the toxicity of steroidal treatment. The potential for cataract formation must be considered when managing BK with the use of steroids and when planning surgical rehabilitation of the anterior segment [9]. Lens resistance to cataract can be improved with pathogenesis-based cataract prevention agents (antioxidants, lanosterol, etc.) [10-12]. Conflicting results have been seen with regard to multivitamin supplementation on the prevention of cataract [13].

Bridging the translational gap in the care of BK and cataract and taking into account the pathogenetic mechanisms with the identification of new therapeutic targets [5, 12] are important for effective use of anti-cataract agents under conditions of increased presence of cataractogenic factors and increased cataract prevalence in presenile individuals [3].

Therefore, a major task of visual science is the research on the mechanisms of interaction of factors contributing to the development of lens opacity and research on new methods of treatment (e.g., optimization of antioxidant therapy, given a profound effect of oxidative stress on cataractogenesis [10]). Methyl-ethyl pyridinol hydrochloride (MH) has potent antioxidant properties, exerts antihypoxic and anti-inflammatory effects, and has been widely used in the treatment of degenerative and inflammatory disorders [14].

The purpose of this study was to determine correlations between the grade of lens opacity and tear levels of total antioxidant activity (TAA) and lipid peroxidation (LPO) products in patients with cataract and/or bacterial stromal keratitis treated versus not treated with MH.

Material and Methods

The study was approved by the bioethics committee of SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine" (committee minutes dated March 4, 20009) and followed the ethical standards stated in the Declaration of Helsinki, the European Convention on Human Rights and Biomedicine and the relevant laws of Ukraine.

A total of 110 patients (136 eyes) were involved in the study. Of these, 26 (52 eyes) were somatically healthy patients with no eye disease who had their preventive medical check-up. Control group 1 including patients with bacterial stromal keratitis only (36 patients, 36 eyes) and control group 2 including patients having both bacterial stromal keratitis and lens opacity (24 patients, 24 eyes) received conventional antibacterial treatment. Group 3 including patients with bacterial stromal keratitis plus lens opacity (24 patients, 24 eyes) received MH (nine four-week cycles of daily treatment with MH separated by four-week breaks) as an adjunct to the conventional antibacterial treatment.

Severity and location of lens opacity was assessed by slit lamp biomicroscopy (Carl Zeiss Meditec, Jena, Germany) and scored on a scale of 0 to 5 [15].

Previously published data [16, 17] on the grade of lens opacity and tear levels of TAO and LPO products (malondialdehyde [MDA] and diene conjugate [DC]) were statistically analyzed. Parametric Student t-test was used for normally distributed data (biochemical parameters), and non-parametric tests (Kruskal-Wallis and Mann-Whitney tests) were used for the grade of lens opacity.

This paper presents the previously unpublished findings of the correlation analysis (namely, Spearman rank correlation analysis).

Results

For somatically healthy patients having no eye disease, there were moderate correlations of the grade of lens opacity with tear levels of TAA (negative correlation, $R = -0.56$, $p < 0.05$) and MDA (positive correlation, $R = 0.52$, $p < 0.05$); levels of TAA and MDA (negative correlation, $R = -0.67$, $p < 0.05$) and TAA and DC (negative correlation, $R = -0.58$, $p < 0.05$) in the tear fluid and a weak correlation of the grade of lens opacity with tear level of DC (positive correlation, $R = 0.34$, $p > 0.05$).

The correlations found between the characteristics of the oxidative–antioxidative system in the tear fluid and the grade of lens opacity in patients with BK only and those having both BK and cataract are presented in Figs. 1 and 2, respectively.

For patients with BK only, there were a statistically significant strong negative correlation of tear levels of TAA with MDA and moderate correlations of tear levels of TAA with DC and the grade of lens opacity with tear levels of TAA (Fig. 1).

For patients having both BK and cataract and not treated with MH, there were stronger negative correlations of the grade of lens opacity with tear levels of TAA and LPO products, a strong positive correlation of the grade of lens opacity with tear levels of MDA, and a moderate positive correlation of the grade of lens opacity with tear levels of DC (Fig. 2).

While comparing these findings with the normative data, attention should be paid to an increase in the Spearman correlation coefficient for patients with BK only and especially for those having both BK and cataract. Our findings may indicate the appearance of an imbalance in ocular tissue homeostasis and the development of metabolic and functional abnormalities in the structures responsible for biochemistry and production of the tear fluid in patients with both BK and cataract.

Fig. 3 shows correlations of the characteristics of the oxidative-antioxidative system in the tear fluid and the

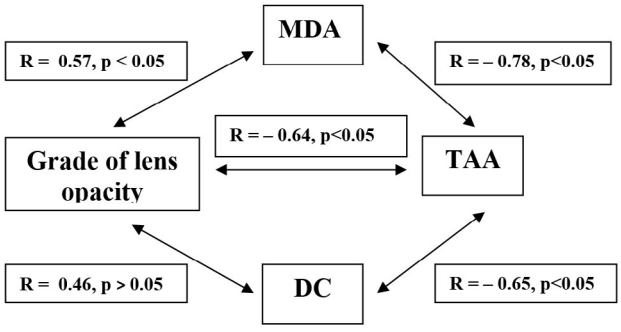

Fig. 1. Pattern of correlations between the grade of lens opacity and levels of total antioxidant activity (TAA) and lipid peroxidation products in the tear fluid in patients with keratitis. Note: DC, diene conjugate; MDA, malondialdehyde; p, correlation P-value; R, Spearman's rank correlation coefficient.

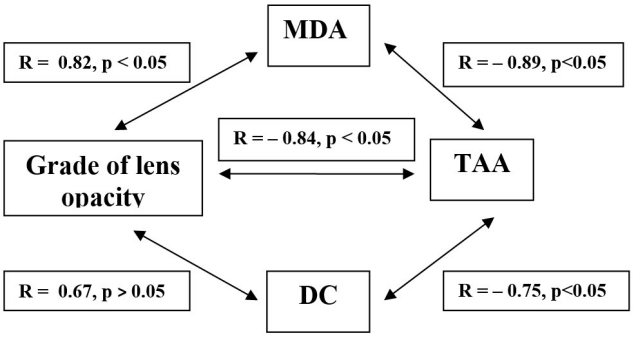

Fig. 2. Pattern of correlations between the grade of lens opacity and levels of total antioxidant activity (TAA) and lipid peroxidation products in the tear fluid in patients having both keratitis and lens opacity and not treated with methyl-ethyl pyridinol hydrochloride (MH). Note: DC, diene conjugate; MDA, malondialdehyde; p, correlation P-value; R, Spearman's rank correlation coefficient.

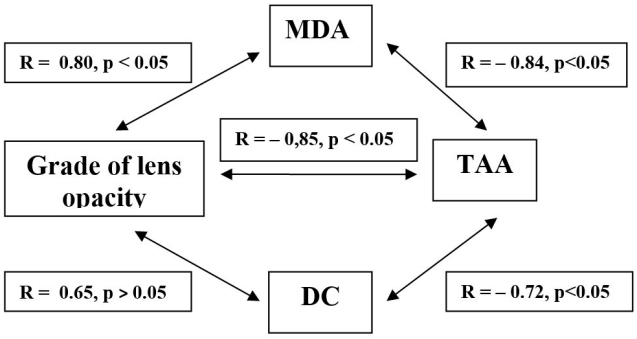

Fig. 3. Pattern of correlations between the grade of lens opacity and levels of total antioxidant activity (TAA) and lipid peroxidation products in the tear fluid in patients having both keratitis and lens opacity and treated with methyl-ethyl pyridinol hydrochloride (MH). Note: DC, diene conjugate; MDA, malondialdehyde; p, correlation P-value; R, Spearman's rank correlation coefficient.

grade of lens opacity in patients having both BK and cataract and treated with MH. For these patients, the grade of lens opacity was strongly and negatively correlated with tear TAA level, strongly and positively correlated with tear MDA level, and moderately and positively correlated with tear DC level. Additionally, we found strong and negative correlations of tear TAA with tear MDA and DC levels.

Therefore, given the presence of apparent correlations between the grade of lens opacity and the levels of TAA, MFA and DC in the tear fluid of patients having both BK and cataract and treated with MH, studies on these biomarkers may contribute to detection of early abnormalities in the lens, thus preventing complications in co-morbidities of patients with anterior segment disorders.

Our correlation analysis confirmed adequate efficacy of the use of MH for correcting metabolic abnormalities and preventing structural and functional changes in the lens of patients with cataract and BK.

Discussion

It has been established that the pathogenesis of cataract has multiple factors like age-related changes, vitamin deficiency in the diet, excessive exposure to ultraviolet radiation, and effects of comorbidities. Systemic and local oxidative stress develops due to an imbalance of the oxidative-antioxidative system, underlies the pathogenic impact of the above factors, and is a trigger for further development of lens opacity [18, 19].

Atalay and colleagues [20] evaluated the relationship between cataract and oxidative stress. They found a significant negative correlation between cataract grade and total antioxidant status level and concluded that the aqueous humor of patients with a high degree of cataract is characterized by low antioxidant capacity.

Ruban and colleagues [21, 22] found decreased activities of antioxidative enzymes (superoxide dismutase [SOD], catalase [CT], and glutathione peroxidase [GP]) and reduced glutathione (GSH) and an increased level of MDA in the cornea of rabbits with experimental keratitis.

Kravets and Regeda [23] also found decreased activities of SOD and CAT in the presence of increased levels of MDA and DC in blood in animals with experimental BK, which demonstrated a significant role of systemic oxidative stress in eye disease.

We have reported previously [24] that the grade of lens opacity was negatively correlated with activities of GP and CT, and positively correlated with the levels of MDA and DC in the tear fluid, aqueous and lens for rabbits with keratitis only, cataract only, and especially keratitis plus cataract.

We have also reported previously [16] a substantial imbalance in the oxidative-antioxidative system in patients with keratitis only, and especially in those having both keratitis and lens opacity, which caused increased LPO in the presence of substantially decreased total antioxidative activity in the tear fluid. Corneal inflammation had a negative impact on the lens and contributed to senile cataract progression in patients [17].

Our findings of apparent correlations of the grade of lens opacity with the levels of antioxidative marker TAA (R= – 0.84), MDA (R = 0.82) and DC (R = 0.67) in the tear fluid of patients having both BK and cataract indicate a pathogenetic role of these characteristics in the cataractogenesis, especially in the presence of corneal inflammation.

Up-to-date evidence on the pathogenetic mechanisms of senile cataract and its animal models facilitate the development of innovative methods for the prevention and treatment of this disorder. Given that the structural and functional changes in the lens are commonly mediated by oxidative stress in the ocular tissues and the body, especially in the presence of comorbid conditions (e.g., keratitis), novel therapeutic technologies (gene therapy, drug delivery nanotechnologies, etc.) are aimed at improving

the antioxidative defense of the anterior and posterior segments of the eye [10, 19, 25]. Aside from anti-inflammatory and antimicrobial options, Chen and colleagues [26] proposed synergistic antibiotic-antioxidant treatment of BK to reduce negative effects of active oxygen species and enhance the bioavailability of poorly soluble medications.

We have demonstrated [24] that that the grade of lens opacity was negatively correlated with activities of antioxidative enzymes (GP and CT), and positively correlated with the levels of MDA and DC for rabbits with keratitis plus cataract.

Findings of experimental studies have formed the foundation for subsequent clinical studies on MH in patients having both BK and lens opacity.

Thus, the use of the antioxidant MH in patients having both cataract and BK made the lens less susceptible to the negative effect of keratitis, and was accompanied by a reduction in LPO and normalization of TAA in the tear fluid [16].

Our findings of strong correlations between the grade of lens opacity and tear levels of TAA and LPO products in patients having both cataract and BK indicate that these parameters may be useful biomarkers for monitoring the inhibition of lens opacity progression and the development of complications in corneal inflammation under conditions of the use of MH.

Therefore, MH, a compound found to have anticaractogenic effects, may be effectively used in the modern comprehensive therapeutic treatment of patients having both cataract and BK.

References

1. Hashemi H, Pakzad R, Yekta A, Aghamirsalim M, Pakbin M, Ramin S et al. Global and regional prevalence of age-related cataract: a comprehensive systematic review and meta-analysis. Eye. 2020;34:1357-70. https://doi.org/10.1038/s41433-020-0806-3.
2. Latebo AA, Assefa NL, Ferede TW, Bekele MM, Demilew KZ. Prevalence of cataract and its associated factors among adults aged 40 years and above living in Durame town, Southern Ethiopia, 2023: a community-based cross-sectional study. BMJ Open. 2024;14(12):e089741. doi: 10.1136/bmjopen-2024-089741.
3. Sarkar D, Sharma R, Singh P, Verma V, Karkhur S, Verma S et al. Age-related cataract - Prevalence, epidemiological pattern and emerging risk factors in a cross-sectional study from Central India. Indian J Ophthalmol. 2023;71(5):1905-12. doi: 10.4103/ijo.IJO_2020_22.
4. Yeh LJ, Shen TC, Sun KT, Lin CL, Hsia NY. Periodontitis and Subsequent Risk of Cataract: Results From Real-World Practice. Front Med (Lausanne). 2022;9:721119. doi: 10.3389/fmed.2022.721119.
5. Ung L, Chodosh J. Foundational concepts in the biology of bacterial keratitis. Exp Eye Res. 2021;209:108647. doi: 10.1016/j.exer.2021.108647.
6. Li X, Du GL, Wu SN, Sun YQ, Zhang SQ, Zhang ZJ et al. Association between systemic immune inflammation index and cataract incidence from 2005 to 2008. Sci Rep. 2025;15(1):499. doi: 10.1038/s41598-024-84204-7.
7. Huang J, Wu H, Yu F, Wu F, Hang C, Zhang X et al. Association between systemic immune-inflammation index and cataract among outpatient US adults. Front Med (Lausanne). 2024;11:1469200. doi: 10.3389/fmed.2024.1469200.
8. Fiolka R, Wylęgała E, Toborek M, Szkodny D, Czuba Z, Wylęgała A. Fuch's Endothelial Corneal Dystrophy in Cataract Patients Is Associated with Elevated Levels of Inflammatory Chemokines, but Not Growth Factors, in the Aqueous Humor. Int J Mol Sci. 2024; 25(3):1894. https://doi.org/10.3390/ijms25031894.
9. Lotti R, Dart JKG. Cataract a s a complication of severe microbial keratitis. Eye.1992;6:400-03. doi: 10.1038/eye.1992.82.
10. Kulbay M, Wu KY, Nirwal GK, Bélanger P, Tran SD. Oxidative Stress and Cataract Formation: Evaluating the Efficacy of Antioxidant Therapies. Biomolecules. 2024; 14(9):1055. https://doi.org/10.3390/biom14091055.
11. Zhang Y, Jiang W, Xie Z, Wu W, Zhang D. Vitamin E and risk of age-related cataract: a meta-analysis. Public Health Nutr. 2015;18(15):2804-14. doi: 10.1017/S1368980014003115.
12. Xu J, Fu Q, Chen X, Yao K. Advances in pharmacotherapy of cataracts. Ann Transl Med. 2020;8(22):1552. doi: 10.21037/atm-20-1960.
13. McCusker MM, Durrani K, Payette MJ, Suchecki J. An eye on nutrition: The role of vitamins, essential fatty acids, and antioxidants in age-related macular degeneration, dry eye syndrome, and cataract. Clin Dermatol. 2016;34(2):276-85. doi: 10.1016/j.clindermatol.2015.11.009.
14. Gupta DS, Bagwe Parab S, Kaur G. Promising effects of emoxypine and its succinate derivative in the management of various diseases-with insights on recent patent applications. Curr Res Pharmacol Drug Discov. 2022;3:100121. doi: 10.1016/j.crphar.2022.100121.
15. Brown NA, Bron AJ, Ayliffe W, Sparrow J, Hill AR. The objective assessment of cataract. Eye (Lond). 1987;1(Pt2):234-46. doi: 10.1038/eye.1987.43.
16. Usov VIa, Tarik Abou Tarboush. [Longitudinal changes in the levels of lipid peroxidation and total antioxidant activity in the tear fluid of patients with keratitis treated with emaksipin]. Oftalmol Zh. 2011;4:26–9. Russian.
17. Usov VIa, Tarik Abou Tarboush. [Clinical observations of the development of cataract in patients with keratitis]. Problemy ekologichnoi ta medychnoi genetyky i klitynnoi imunologii. Kyiv-Lugans'k. 2013;6(120):323–32. Ukrainian.
18. Nsonwu M, Ozims SJ, Nnodim JK. Perspective of cataract and oxidative stress. Series Clin Biomed Res. 2024;1(1):1-10. doi:10.54178/2997-2701.v1i1a1994.
19. Goodman D, Ness S. The Role of Oxidative Stress in the Aging Eye. Life. 2023; 13(3):837. https://doi.org/10.3390/life13030837.
20. Atalay E, Oğurel T, Derici MK. The role of oxidative damage in cataract etiopathogenesis. Ther Adv Ophthalmol. 2023;15:25158414231168813. doi: 10.1177/25158414231168813.
21. Ruban VV, Archana PT, Sundararajan M, Geraldine P, Thomas PA. Inflammation and oxidative stress in corneal tissue in experimental keratitis due to Fusarium solani: Amelioration following topical therapy with voriconazole and epigallocatechin gallate. Mycoses. 2018;61(3):159-71. doi: 10.1111/myc.12718.
22. Ruban VV, Anbukkarasi M, Anand T, Thomas Ph A, Geraldine P. Oxidative stress in corneal tissue in experimental keratitis due to Aspergillus flavus: Effect of topical voriconazole therapy. Biocatalysis and Agricultural Biotechnology. 2019;21:101323. doi.org/10.1016/j.bcab.2019.101323.
23. Kravets BB, Regeda MS. [The role of corvitin in the correction of violations of lipid peroxidation processes and the activity of the antioxidant system in guinea pigs blood in experimental bacterial keratitis against the background of bronchial asthma and pneumonia]. Medychna ta klinichna khimiia. 2015; 17(2): 69-71. Ukrainian. http://nbuv.gov.ua/UJRN/Medkh_2015_17_2_17.
24. Usov VIa, Tarik Abou Tarboush, Kolomiichuk SG. [Correlations of parameters of the oxidative-antioxidative system in the lens, aqueous humor and tear fluid with the grade of lens opacity in

rabbits with cataract and/or bacterial keratitis: an experimental study]. J of Ophthalmology (Ukraine). 2025;2:49-57.
25. Honisch C, Rodella U, Gatto C, Ruzza P, Tóthová JD. Oxidative Stress and Antioxidant-Based Interventional Medicine in Ophthalmology. Pharmaceuticals (Basel). 2023;16(8):1146. doi: 10.3390/ph16081146.
26. Chen Q, Han X, Liu L, Duan Y, Chen Y, Shi L et al. Multifunctional Polymer Vesicles for Synergistic Antibiotic-Antioxidant Treatment of Bacterial Keratitis. Biomacromolecules. 2023;24(11):5230-44. doi: 10.1021/acs.biomac.3c00754.

Disclosures

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Data Availability Statement: *The data obtained and/or analyzed during this study are available from the appropriate author upon reasonable request.*

Abbreviations: *CT, catalase; DC, diene conjugate; LPO, lipid peroxidation; MDA, malondialdehyde; MH, methyl-ethyl pyridinol hydrochloride; TAA, total antioxidant activity.*