ARTICLE

Association between cataract progression and ischemia-modified albumin in relation to oxidant–antioxidant profiles in the serum, aqueous humor, and lens

Hesham M. Elmazar, MD, Ibrahim Elmadbouh, MD, PhD, Sameh S. Mandour, MD, Gehad M. Al Ariny, MD, Asmaa M. Ibrahim, MD

Purpose: To evaluate the levels of ischemia-modified albumin (IMA) in relation to oxidant–antioxidant profiles in the serum, aqueous, and lens in cataract patients.

Setting: Department of Ophthalmology, Menoufia University, Shebin El Kom, Menoufia, Egypt.

Design: Prospective case series.

Methods: Patients were divided into 2 groups. The cataract (study) group comprised patients with senile cataract and the control group, age- and sex-matched healthy persons. Patients with systemic disease or cataract formation secondary to identifiable causes were excluded. In all cases, a complete history was taken and a clinical examination was performed. In the cataract group, the lens was examined, and the cataract type and severity were graded. Blood levels of catalase, malondialdehyde (MDA), superoxide dismutase (SOD), and IMA were measured in all participants and in the aqueous and lens lysate of cataract patients.

Results: Each group comprised 30 participants. Cataract patients had significant higher levels of serum MDA and IMA than the control group but had lower levels of serum catalase and SOD. Patients with cortical cataracts had higher level of serum IMA, aqueous catalase, and SOD levels patients with nuclear cataracts but had a lower level of lens SOD. There was a significant positive correlation between serum MDA and the patient's age and serum catalase levels.

Conclusion: Patients with cortical cataract had increased local oxidative stress and diminished antioxidant activity compared with systemic oxidative activity, which was not the same in patients with nuclear cataract.

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Cataract is a major cause of diminution of vision in the aging population, especially in developing countries.[1,2] Ocular oxidative stress is a major factor in the development of cataracts.[3,4] Such stress occurs when the production of an oxidizing agent, such as reactive oxygen species (ROS), exceeds the antioxidant defense mechanisms.[5–7] This leads to the denaturation of many basic intracellular molecules, such as nucleic acids, proteins, and lipids.[3,8–10]

Ischemia-modified albumin (IMA) is a form of albumin that has been modified by oxidation and has been suggested to be a new marker for ischemia[11,12] and oxidative stress.[13] High serum IMA levels have been found in the serum and aqueous of patients with diabetic retinopathy (DR).[14,15]

Systemic or circulating antioxidants and oxidative stress markers can be useful tools for aqueous humor and lens changes in the pathophysiology of cataract progression. However, the exact signaling pathways in cataract regulated by ROS are unclear and require further study. In addition, the relation between IMA and systemic oxidative stress is not well established, although it has been implicated as a risk for cataract genesis and its severity.[16] Previous studies have evaluated the role of oxidative stress biomarkers in cataract pathogenesis; however, none has evaluated the role of IMA.[17]

The aim of this study was to evaluate the levels of IMA in relation to the oxidant–antioxidant profiles in the serum, aqueous, and lens of Egyptian cataract patients and the relation to cataract progression.

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From the Department of Ophthalmology (Elmazar, Mandour, Al Ariny, Ibrahim) and the Department of Medical Biochemistry (Elmadbouh), Menoufia Faculty of Medicine, Shebin El Kom, Menoufia, Egypt.

Corresponding author: Hesham M. Elmazar, MD, Department of Ophthalmology, Menoufia Faculty of Medicine, Shebin El Kom, Menoufia, Egypt. E-mail: helmazar@hotmail.com.

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PARTICIPANTS AND METHODS

This prospective nonrandomized case-control study comprised participants attending the Ophthalmology Department, Faculty of Medicine, Menoufia University, Menoufia, Egypt, from August 2015 to October 2016. All laboratory analysis was performed at the Medical Biochemistry Department, Faculty of Medicine, Menoufia University. After the Faculty Ethics Committee approved the study, patients were given a detailed description about the risk and benefits of the surgery and provided written consent. All procedures and protocols were in accordance with the tenets of the Declaration of Helsinki.

This study comprised 2 main groups. The cataract (study) group comprised patients with senile cataract and the control group, age- and sex-matched healthy persons.

Participants with hypertension, diabetes mellitus, cardiac, thyroid, hepatic, lung and renal dysfunction, anemia, osteoporosis, inflammatory arthritis, and who were smokers or alcoholics were carefully identified and excluded from this study. Patients with cataract formation as a secondary to identifiable causes such as diabetes, trauma, and steroid administration were also excluded. Exclusion criteria included eyedrops that may alter intraocular protein levels, such as cyclosporine or prostaglandins, inflammatory eye conditions, such as uveitis, or age less than 40 years. Only 1 member from a family was included in the study to eliminate genetic factors.

In all cases, a complete history was taken and a ophthalmologic examination was performed. The examination included including visual acuity, slitlamp, intraocular pressure, and fundus evaluation. In the cataract group, the lens was examined, and the cataract type and severity were graded using the Lens Opacity Classification System II.[18] The cataracts were classified as pure (ie, single type of opacity [nuclear, cortical, posterior subcapsular]) or mixed (ie, more than 1 type of opacity), depending on the lens status in both eyes.

Oxidant–Antioxidant Profiles

Blood Blood samples were collected from the study group before cataract surgery and from the control group. The serum was separated from the cells by centrifugation at 2500 revolutions per minute (rpm) for 15 minutes.

Aqueous Aqueous samples were collected in cataract patients only. The samples were obtained through a paracentesis port before surgery as previously described.[19,20] In brief, 100 to 150 µL aqueous humor was collected using a 27-gauge needle attached to an insulin syringe. The samples were centrifuged at 10 000 rpm for 1 minute, and the supernatant was extracted.

Lens The lens (cortex and nucleus) obtained during extracapsular cataract extraction surgery was rinsed with cold physiologic saline, homogenized in a 10-fold volume (w/v) of cold buffer (0.2 mol/L potassium phosphate, 137 mmol/L potassium chloride, 60 mmol/L sodium dodecyl sulfate, pH 7.2), and spun (12 000 ×g; 40°C for 20 minutes). A clear supernatant was used for biochemical assays. The lens biochemical variables were expressed in correspondent units per gram tissue wet weight.[21,22]

The serum, aqueous, and lens lysate were stored at −80°C. Then, they were analyzed for malondialdehyde (MDA), catalase, superoxide dismutase (SOD), and IMA.

Statistical Analysis

Data obtained were computed using SPSS for Windows software (version 17, SPSS, Inc.) Continuous data were expressed as the mean ± SD, while categorical data were expressed in the form of count and percentage. Comparison of continuous data was performed using the Student *t* test and categorical data, using the chi-square test. The relation between variables was assessed using the Pearson correlation coefficient. A *P* value less than 0.05 was considered statistically significant.

RESULTS

The cataract group comprised 30 patients and the control group, 30 volunteers. Of the cataracts patients, 16 (53.3%) had pure cataract (8 nuclear, 8 cortical) and 14 (46.7%) had mixed cataract (corticonuclear). There were no significant differences in the age, sex, body mass index, or blood pressure between the cataract group and control group (Table 1). The cataract group had significantly higher serum of MDA and IMA levels but significantly lower levels of serum catalase and SOD than the control group ($P < .001$) (Table 1).

The diagnostic accuracy of serum MDA, catalase, SOD, and IMA were significantly impaired in the cataract group compared with the control group ($P < .001$), with a higher sensitivity and specificity percentage (Table 2 and Figure 1, *A*). Also, the levels of MDA, catalase, SOD, and IMA in the serum, aqueous humor, and lens were significantly impaired in the cataract group (Figure 1, *B* to *E*).

The serum IMA levels in eyes with cortical or mixed cataract than in eyes with nuclear cataract ($P = .02$). The higher aqueous catalase and SOD levels were significantly higher in eyes with cortical cataract than in eyes with nuclear cataract ($P = .03$ and $P = .028$, respectively); however, the lens SOD level was significantly lower in eyes with cortical cataract than in eyes with nuclear cataract ($P = .028$).

In the cataract group, there was a significant positive correlation between serum MDA level and the patient's age ($r = 0.42$, $P = .019$) and serum catalase level ($r = 0.44$, $P = .014$). There was also a significant positive correlation between the aqueous IMA and lens catalase levels ($r = 0.46$, $P = .009$). In patients with cataract, there was a significant positive correlation between the aqueous SOD level and the lens SOD level ($r = 0.46$, $P = .009$), between the serum IMA level and the serum MDA level ($r = 0.44$, $P = .014$) and aqueous MDA level ($r = 0.40$, $P = .026$), as well as between the lens IMA level and the diastolic blood pressure ($r = 0.37$, $P = .038$) and lens MDA level ($r = 0.41$, $P = .023$).

DISCUSSION

The prevalence of cataract type (cortical, nuclear, or posterior subcapsular) is different between different age and racial groups. These differences might be related to genetic elements, environmental circumstances, or dietary factors. However, oxidative damage has been implicated as a major contributor to the pathogenesis of cataracts regardless of the type.[23,24]

Reactive oxygen species are mostly generated in lens epithelium cells,[10] superficial fiber cells, and the aqueous humor.[25] They are highly reactive toxic substances and in higher amounts are harmful to macromolecules,[26] leading to lipid peroxidation of polyunsaturated fatty acids, loss of antioxidants, and insolubilization of crystallins. In particular, the lens is an avascular organ with limited efflux of substances to adjacent tissues, which would favor the accumulation of lipid peroxidation as MDA adducts within the lens fibers. Oxidation of proteins, lipids, and DNA has been observed in cataractous lenses.[27–29] Many of toxic

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