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Role of Malondialdehyde (MDA) in senile cataract

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Abstract

Cataract is characterized partial or complete loss of transparency of the lens that leads to loss of vision. Globally, cataract associated blindness is a major cause of morbidity in developing countries. The cataractogenesis is affected by a number of factors with redox imbalance at the top of list. This imbalance results either from an increased generation of free radicals and/or decreased production of antioxidants. The end products of lipid peroxidation are both mutagenic and carcinogenic. One such product, malondialdehyde (MDA) reacts with deoxyadenosine and deoxyguanosine in DNA, to form DNA adducts. Its role in cataractogenesis is due to its cross linking ability. The present study analyzed the role of MDA in the development of senile cataract. Its level was measured in 75 randomly selected senile cataract patients of different age groups and matched against suitable controls. The study found statistically significant increased levels of MDA in cataract patients but not in controls, indicating an oxidative stress. The present study concluded that increased levels of MDA increased the susceptibility to cataractogenesis.

Keywords: Malondialdehyde, Senile cataract, Redox, blindness, Lens opacity.

INTRODUCTION

Cataract is an established cause of blindness [1-3] and is causes loss of sight in a vast majority of cases in developing countries [4,5] along with India [6-8]. Presently, oxidative stress is believed to be a major factor cellular damage in cataractogenesis in addition to many other factors [9,10].

It is now well established that senile cataract is related to oxidative stress due to reactive oxygen species (ROS) like hydroxyl, peroxides and superoxides ions. Superoxide is instrumental in lens lipid peroxidation and various oxidative degradative processes as it is involved in the genesis of all kinds of oxidants including hydrogen peroxide and hydroxyl ions. When the antioxidants decrease, the lens becomes vulnerable to oxidative stress. Ultimately, the oxidized residues accumulate in lens proteins and enzymes and interfere in the normal metabolic processes and disrupt the healthy intracellular protein matrix to result in loss of lens transparency. Low concentration of hydrogen peroxide may be responsible for the oxidative modification of the lens proteins. Some evidences show that various cataractogenic events such as selenium, glucose and adriamycin are able to increase H_2O_2 in ocular humors in vivo prior to cataract formation compared to their respective controls. UV exposure, a source of oxidative stress, is known to contribute to cataract formation. It is possible that protein modifications linked with cataract could be the result of a reaction of lens crystallins with other oxidizing agents such as the hydroxyl radical. It is demonstrated that nuclear cataract is associated with the extensive hydroxylation of protein-bound amino acid residues, which increases with the development of cataract by up to 15-fold in the case of DOPA. Oxidized and hydroxylated amino acids such as DOPA, 3-hydroxyvaline (Val.OH1) and 5-hydroxyleucine (Leu.OH2) were synthesized after exposing lens proteins to Fenton-derived hydroxyl radicals Hydroxyl radical can also induce cross linking among proteins.

MATERIALS AND METHODS

The present study is a collaborative study of the Departments of Biochemistry and Ophthalmology, Govt. Medical College (GMC), Amritsar. The study was conducted after permission from ethical committee of the institute. It included 75 patients of senile cataract patients of both sexes and an identical number of control subjects with comparable age. They were studied for one year, i.e., from May 2012 to April 2013.

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All the subjects included in the present study belonged to Punjab. A written informed consent from all patients was obtained before the collection of samples. The MDA levels of both these groups were then analyzed and compared with each other.

Inclusion criteria

The 75 test subjects of senile cataract patients belonging to age groups of 40-70 years were selected from the Department of Ophthalmology, Ram Lal Hospital attached to GMC, Amritsar. A detailed history was obtained from each patient. The control group also comprised of same number of people in comparable age group. The control subjects had visual acuity of 6/6 or better in both eyes and no lens opacities in either eye as verified by slit lamp examination.

Exclusion criteria

The patients having a medical condition that is likely to involve the free radicals or influence the oxidative processed were excluded from the study. These were the patients on antioxidant drug therapy, chronic smokers, alcoholics, rheumatoid arthritis, hypertension, toxic cataract trauma, diabetes mellitus, ocular surgery, ischemic heart disease, infections, iridocyclitis, inflammatory conditions etc.

Collection and Processing of blood samples

After observing asepsis, 5 ml blood samples were collected from both cataract patients and control subjects by puncturing the antecubital vein using a dry, disposable syringe. The samples were then transferred to a sterile, dry and acid washed vial for biochemical analysis. 2ml of blood was taken in EDTA vials and plasma was separated for estimation of MDA.

OBSERVATIONS

Based on the age, both the cases and controls were further divided into sets of three. Group I had 25 patients with an age range of 40-50 years. Group II had 23 patients with an age range of 51-60 years. Group III had 27 patients with an age range of 61-70 years (Table1). A highly significant statistical correlation ($p<0.001$) was detected in MDA levels after a suitable age matched comparison of two groups with considerably higher levels detected in cases as compared to controls (Table 2). Afterwards, both sexes in the two groups were compared. No statistically significant difference in the level of MDA was observed between the two genders (Table 3). A comparison of serum MDA in different age groups in controls and cases was done. Both controls and cases were divided into three groups according to age distribution and compared with each other. In cases, no statistical difference was observed among different age group when compared with one another (Table 4). A high statistical significance for MDA levels was observed when cases were compared with the controls of similar age (Table 4) with levels significantly higher in case ($p<0.001$).

Table 1: Division of cases and controls into three groups based on age

Group	Age (in years)	Cases	Controls
I	40-50	25	30
II	51-60	23	20
III	61-70	27	25

Table 2: Range of serum MDA in cases and controls

Subjects	No. of cases	Range (nmol/ml)	Mean±SD
Cases	75	2.4-6.9	4.96±0.89
Controls	75	0.35-1.9	0.76±0.25

Table 3: Gender wise differences of serum MDA levels in cases and controls

CONTROLS				CASES		
Sex	No. of Subjects	Range (nmol/ml)	Mean±SD	No. of Patients	Range (nmol/ml)	Mean±SD
Males	35	0.45 -1.9	0.77±0.34	33	3.2 – 6.0	4.91±0.96
Females	40	0.46-1.2	0.74±0.15	42	3.0 – 6.3	5.01±1.03

Controls
M/F t= 0.50
p >0.001 Not significant

Cases
M/F t =0.43
p >0.001 Not significant

Control Vs Cases
Male control/patients t = 22.3 p< 0.001 highly significant
Female control/patients t = 24.7 p< 0.001 highly significant

Table 4: Age wise difference of serum MDA levels in cases and controls

Age group (years)	No. of Subjects (control)	Range (nmol/ml)	Mean±SD	No. of patients (cases)	Range (nmol/ml)	Mean±SD
Group I (40-50)	30	0.35-1.3	0.69±0.14	25	2.4-4.8	5.0±1.2
Group II (51-60)	20	0.55-0.89	0.72 ±0.15	23	2.5-6.4	5.3 ±0.87
Group III (61-70)	25	0.86-1.9	0.92±0.35	27	2.8-6.9	5.8 ±1.34

Controls
Group I/II t = 0.63
p > 0.05 Not significant
Group I/III t = 0.45
p > 0.05 Not significant
Group II/III t = 1.90
p > 0.05 Not significant

Cases
Group I/II t = 1.08
p > 0.05 Not significant
Group I/III t = 0.52
p > 0.05 Not significant
Group II/III t = 0.80
p > 0.05 Not significant

Controls Vs Cases
Group I t = 2.3 p < 0.001 Highly Significant
Group II t = 8.74 p < 0.001 Highly Significant
Group III t = 8.30 p < 0.001 Highly Significant

DISCUSSION

The generation of ROS due to continuous exposure of lens to light and ambient oxygen causes photooxidative injury that results in cataract. These ROS adversely affect crystallins lens proteins, causing them to aggregate and precipitate to form opacities. In addition, the ROS impair the proper functioning of proteolytic enzymes resulting in accumulation of damaged proteins. The present study observed a significant increased MDA level in patients of senile cataract as compared to controls. Comparable results were obtained by other researchers [11-13]. The elevated MDA level in senile cataract patients probably point towards the redox imbalance tilting towards oxidative stress, and generating cataracts. Many researchers have postulated that diminished antioxidant activity in addition to elevated levels of free radicals plays a pivotal role in cataractogenesis in senile age group [14,15]. The increased MDA levels could be either be due to age related increased oxidative stress or diminished antioxidant defenses or both.

CONCLUSION

Our results indicate that oxidative stressed may be the initial events that initiate cataractogenesis. It is hoped that the antioxidants may act as an important impediment in the initiation and development of cataract. The authors recommend antioxidants to the senile cataract patients to retard the progression of the process and also educate the populace the benefits of an antioxidant rich diet. It is hoped that these measures will be able to control the menace of senile cataract.

Conflict of interest: The authors declare that no conflict of interest.

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