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Original Research Article

Role of oxidative stress in cataractogenesis

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ABSTRACT

Background: Cataract is a multifactorial disease and is a major cause of blindness in india. Oxidative stress is thought to be a major factor to initiate the process of cataractogenesis. It is today well established fact that oxidative stress participates in both age-related (senile) and diabetes-induced cataract (diabetic). Oxidative damage to the lens most likely arises as a consequence of an impaired antioxidant defence system, due to increased generation of ROS both by age and diabetes. The present study was designed to determine role of oxidative stress in cataractogensis and to compare levels of oxidative stress markers in senile and diabetic cataract patients.
Methods: Serum malondialdehyde (MDA) and serum protein carbonyl (PC) were measured as indicator of oxidative stress whereas antioxidant status was assessed by estimating serum Total antioxidant capacity (TAC) and dietary antioxidants levels i.e vitamin C and vitamin E in senile and diabetic cataract patients compared with healthy controls.
Results: The result reveal that the serum MDA and PC levels were significantly increased in patients with senile and diabetic cataract whereas serum TAC, vitamin C and Vitamin E were significantly reduced in senile and diabetic patients when compared with normal healthy controls.
Conclusions: From the result, it is concluded that oxidative stress is in the foreground of cataract formation which includes senile and diabetic cataract. Oxidative stress produced in diabetic cataract patients is more as compared to senile cataract patients.

Keywords: Cataract, MDA, PC, TAC, Vitamin C, Vitamin E

INTRODUCTION

Cataract is one of the major cause of impaired vision and blindness worldwide and is most simply defined as opacity of the crystalline lens.[1] Several risk factors have been identified for development of cataract; aging, diabetes, diarrhoea, malnutrition, sunlight, smoking, hypertension and renal failure. Cataract formation is mostly. Leading cause for cataract.[2] Over last decade there has been growing interest in the possibility that a diet rich in antioxidant vitamins might be able to reduce the risk of cataract by protecting the lens from oxidative modifications. Vitamin C and E are known to be effective at scavenging free radicals and eliminating provitamins.[3] Animal models have demonstrated that supplements of vitamin C can limit lens damage after oxidative insult.[4] Observational studies have provided some evidence that higher intake of these vitamins may be protective against cataract in humans.[5]

The definition of oxidative stress implies increased oxidant production and or a decreased antioxidant capacity in animal cells characterized by the release of free radicals, resulting in cellular degeneration.[6,7] The imbalance between the rate of free radical production and antioxidant defense causes cellular damage resulting in

many ocular diseases such as age related macular degeneration, retinopathy of prematurity, retinal light damage, and cataract.[7-9] Reactive oxygen species (ROS) are thought to play a role in variety of physiological and pathophysiological processes in which increased oxidative stress may play an important role in disease mechanisms. However, increased oxidative stress may also be a result of pathological process.[6,10]

In diabetic conditions, ROS are produced via glucose autoxidation and also via non-enzymatic protein glycation in various tissues. ROS is considered to have an important role in the development of microvascular complications in patients with diabetes.[11-15]

The objective of the present study was to evaluate the relationship between oxidative stress markers and antioxidant defenses in cataract formation and to compare the level of oxidative stress in both senile and diabetic cataract patients. The result of this study may be useful in deciding whether oxidative stress has any role in the development of diabetic/ senile cataract. Supplementation of antioxidant to the patients before the threshold age group would be able to minimize the occurrence of lens opacity.

METHODS

The study comprises of total 135 subjects divided into three groups aged between 50-75 years. The subjects were selected from ophthalmic OPD of B. J. Medical College and Sassoon Hospitals, Pune, Maharashtra, India.

- Group 1 - (n = 45) Senile cataract patients
- Group 2 - (n = 45) Diabetic cataract patients and
- Group 3 - (n = 45) Normal healthy controls.

Inclusion criteria

Senile cataract subjects had normal fasting blood glucose level with no history of diabetes. Diabetic cataract subjects were using oral hypoglycaemic agents or insulin since last ten years.

Exclusion criteria

Patients having history of steroid intake, ophthalmic disease, renal disease, anaemia, autoimmune disorders, infections, hypothyroidism, hyperthyroidism, cirrhosis and other systemic disorders are excluded from study. The study was approved by the Institutional Ethics Committee of B. J. Medical College Pune, Maharashtra, India.

A written informed consent was taken from the subjects. 10 ml of venous blood was collected during preoperative period in plain vacutainers under aseptic precaution. Serum was separated and analyzed on same day for the following parameters: malondialdehyde (MDA), protein carbonyl, total antioxidant capacity and dietary antioxidants as vitamin C and vitamin E.

Biochemical estimations

Serum MDA was estimated by thiobarbituric acid (TBA) reaction protein carbonyl by Levine et al, method.[16,17] The total antioxidant capacity was determined by FRAP method.[18] Vitamin C measured by Ayekyaw method.[19] Vitamin E measured by Baker and Frank method.[20]

Statistical analysis

The data was subjected to statistical Analysis of Variance (ANOVA) The results were expressed as mean± standard deviation (SD). The differences were compared with the use of an unpaired student's 't' test.

RESULTS

The present study was conducted to assess MDA and PC as biomarkers for oxidative stress and TAC, vitamin C and vitamin E as antioxidant defense parameters Table 1 shows age wise comparison of senile and diabetic cataract.

There was statistically significant ($p < 0.001$) difference between senile and diabetic cataract groups with regard to age. The average mean age of diabetic cataract patients was 60.36±7.46years and average mean age of senile cataract was 66.72±7.33 years. The values of serum MDA and PC are presented in Table 2 and the values of dietary antioxidants as vitamin C and vitamin E and TAC are presented in Table 3.

Table 1: Age wise comparison of senile and diabetic cataract.

	Senile cataract (n =45)	Diabetic cataract (n =45)
Age (years)	66.72±7.32	60.36±7.46**
Sex (f/m)	28/17	30/15

n = number of subjects; **= highly significant ($p < 0.001$).

A significant increase in serum MDA and PC levels in diabetic ($p < 0.001$) and senile cataract patients ($p < 0.001$) was observed as compared to control (Table 2). There was a significant decrease in dietary antioxidants as vitamin E and vitamin C and TAC in senile and diabetic cataract patients as compared to control (Table 3).

But in diabetic cataract decrease is more ($p < 0.001$) as compared to senile cataract patients. It is observed that in both cataract patient's protein oxidation is more than lipid peroxidation.

A significant negative correlation of MDA with vitamin E was seen in diabetic cataract patients ($r = -0.5188$, $p = 0.033$), but not in senile cataract patients. No such

correlation of MDA with vitamin C and TAC are seen in senile as well as diabetic cataract patients. Similarly, PC was not correlated with any antioxidant parameter such as vitamin C, vitamin E and TAC in senile as well as diabetic cataract patients.

Table 2: Lipid and protein peroxidation as oxidative stress marker in senile and diabetic cataract.

	Senile cataract (n=45) (Mean±SD)	Diabetic cataract (n=45) (Mean±SD)	Control (n =45) (Mean±SD)
MDA (nmol/ml)	3.26±0.29**	4.47±0.27**	2.97±0.17
Protein carbonyl (nmol/mg protein)	4.13±0.17**	6.08±0.22**	3.07±0.23

n = number of subjects; Comparision- Control vs Senile; **= highly significant (p < 0.001); Control vs Diabetic; Senile vs Diabetic.

Table 3: Vitamin C, Vitamin E, and TAC in senile and diabetic cataract patients.

	Senile cataract (n=45) Mean±SD	Diabetic cataract (n= 45) Mean±SD	Control (n=45) Mean±SD
Vitamin C (mg/dl)	0.74±0.12**	0.53±0.08**	1.03±0.16
Vitamin E (mg/dl)	0.79±0.10**	0.54±0.06**	1.12±0.18
Total antioxidant capacity (mmol/L)	0.95±0.21**	0.69±0.07**	1.19±0.16

n = number of subjects; Comparision - Control vs Senile; **= p < 0.001) highly significant; Control vs Diabetic; Senile vs Diabetic

DISCUSSION

In this study attempt was to evaluate the oxidative stress and antioxidant status in serum of senile and diabetic cataract patients. High levels of serum MDA and PC in senile and diabetic cataract patients were observed as compared to controls. Oxidative stress is characterized by increase concentration of free radicals which can cause damage at different levels of cellular organization. MDA is the byproduct of lipid peroxidation whereas PC is a product of non-enzymatic oxidation or carbonylation of protein.[21] Oxidative stress plays an important role in pathogenesis of cataract, the most important cause of visual impairment associated with advanced age and diabetes.

In present study, it was observed high levels of MDA and PC in diabetic cataract patients compared to senile cataract patients. A 37% increase in the serum MDA levels and 47% increase in the serum PC was observed in diabetic cataract patients as compared to senile cataract patients (Table 2). In addition to this it is also observed that protein oxidation is significantly more than the lipid peroxidation in senile as well as diabetic cataract patients. But if compared senile and diabetic cataract patients in diabetic cataract there was significant increase in PC levels as compared to MDA. These results are supported by the study of Obara et al.[22] The increased levels of lipid peroxidation product (MDA) in diabetes are due to increased production of reactive oxygen species caused by hyperglycemic status, hyperinsulemia and hyperlipidemia which are commonly associated with diabetes.[23,24] The increased levels of MDA and PC in diabetic cataract patients as compared to senile cataract patients might accelerate the process of cataract formation in diabetic patients which is observed in this study.

In present study antioxidant status i.e serum TAC, vitamin C, and vitamin E found to be significantly decreased in diabetic cataract as compared to senile cataract, when compared with controls.

There was 28% decrease of TAC in diabetic cataract as compared to senile cataract. This is supported by the studies done by Gul et al.[25]

The dietary antioxidants vitamin C and vitamin E levels were significantly decreased in diabetic cataract patients may be due to increased oxidative stress. Vitamin C is considered the most important antioxidant in the extracellular fluids and the only endogenous antioxidant that can completely protect the lipids from detectable peroxidative damage induced by aqueous peroxyl radical. Vitamin C act as co-antioxidant by regenerating α tocopherol from α tocopheroxyl radical produced during scavenging ROS.[26] The decreased levels of vitamin C in diabetic cataract may be due to its utilization by counteracting ROS.[27]

Vitamin E is an important chain breaking antioxidant and can directly scavenge ROS. It is a major lipid soluble antioxidant present in cellular membranes which protect against LPO. Low levels of vitamin E in diabetic cataract may be due to its utilization by counteracting ROS which increases the risk of cataract.[28] As the oxidative stress due to lipid peroxidation is increased there is concomitant decrease in vitamin E level and this is supported by

observed negative correlation between MDA and vitamin E.

CONCLUSION

Our present data indicates that the intensity of oxidative stress in diabetic cataract patients is higher as compared to senile cataract patients. Oxidative stress is more in diabetic cataract due to diabetes i.e. hyperglycemia and hyperlipidemia. Decrease in antioxidant status in diabetic cataract as compared to senile cataract is may be due to their utilization for counteracting oxidative stress.

So, by comparing the average mean age of senile and diabetic cataract it is inferred that diabetic patients are subjected to more oxidative stress at much earlier age than senile cataract patients. Oxidative stress might have a role in pathophysiology of cataract. Hence supplementation of an adequate dose to be antioxidant to diabetic patients at a much earlier age may be beneficial by delaying the cataract formation.

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