IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Cataractogenesis of the basic science of lens protein

Yogita Channe[1], Samadhan Dahikar[2], Mukta Shinde[3] Rupali Munje[4]

Department of Zoology

Sanjivani Art commerce and science college Kopergaon, Maharashtra India.

Abstract

Cataractogenesis is the process of cataract formation. The aim of the present study was to estimate the copper, zinc, malondialdehyde and advanced oxidation protein produces stages of cataract formation.The causes for cataract are multifactorial and often related with different specific diseases such as diabetes mellitus, chronic renal failure, hereditary syndromes, as well as aging in the general population.The purpose of this review is to give an overview of contemporary research in cataractogenesis. Our study aims to investigate systemic oxidant and antioxidant markers in cataract patients.Several risk factors for cataract formation have been identified, including increasing age, genetic predisposition, oxidative stress and exposure to UV light. Recently, numerous authors have suggested that excess generation of highly reactive oxygen and nitrogen species is a key component in the development of complications invoked by hyperglycemia. This review has shown the large amount of evidence, laboratory based and, demonstrating a link between lenticular oxidation processes and cataract and between antioxidant intake and retardation in age-related cataractogenesis. We are studied the linkages of plasma status of antioxidant minerals and vitamins, oxidative stress, and lens opacity in commonly found in indian cataract patients. Other sources of cataractogenesis are the oxidative stress. Which can effect on the lens of eye and direct influence on the solubility of lens proteins, leading to an increase in the opacity of lens.

Keywords: Cataractogenesis, Oxidative stress, Lens protein and Antioxidant.

1. Introduction:

Cataractogenesis is the process of cataract formation. Cataract, which can be defined as any opacity of the crystalline lens, is the leading cause of avoidable blindness worldwide. Cataract, which leads to lens opacity, is one of the most common eye diseases and a leading cause of blindness, accounting for about half of the total visual impairments observed in humans (Asbell P, 2005; Foster A, 2005; Sacca S,2009). A significant number of cataract patients lose their vision due to inadequate access to eye care. Although around 16 million people worldwide have cataracts, congenital cataracts are rare and are generally caused by an intrauterine infection and other prenatal insults (Asbell P, 2005; Sacca S,2009, Shiels A 2017). In this review to the study of several factor and association of genetic mutations with the development of several cataracts (Shiels A 2017). It is estimated that about 25% of congenital cataracts are hereditary (Sacca S,2009). The age-related cataract is the most common type (Shiels A 2017). Age-related cataract is responsible for nearly half of all blindness worldwide (Beebe D 2010). In addition to increasing age, several other risk factors, such as diabetes and exposure to radiation and ultraviolet light, have been identified (Shiels A 2017). Although there is little information available about the loci and genes related to the age-related cataract as compared to the congenital cataract, previous reports have suggested the association of single nucleotide polymorphisms in several genes and genetic compositions of the patients with age-related cataracts (Shiels A 2017).

Lens opacification in cataract as a complication of diabetes mellitus is associated with increased oxidative and hyperosmolar stress. Oxidative damage to the lens has been linked with development of cataract and decrease in antioxidant enzyme activities in the cataractous lens points to the importance of antioxidant enzymes in the prevention of oxidative damage to the lens and subsequent development of cataract (Varma S, 2004). A wide range of drugs like aldose reductase inhibitors, non-steroidal anti-inflammatory drugs are being tried for their anticataract activity (Kyselova Z, 2004 9).

Zones of the lens are metabolically distinguishable: the epithelium, the cortex, and the lens nucleus or core (Blondin J 1987;11). Epithelial cells are found just under the collagenous capsule that surrounds the lens (Blondin J 1987 10). These are the most recently formed cells and they are the most metabolically active. Some of these cells divide to form lens fibres cells. It is in these cells that the major gene products of the lens, the crystalline, are elaborated (Blondin J 1987;Eisenhauer D, 1988; Boscia F 2000).The outer layers of such fibres cells comprise the cortex. Buried under the cortical cells are the oldest lens cells, called nuclear or core cells. Thus, there is a gradient, with the most recently elaborated proteins in the epithelium and the oldest proteins, which were elaborated during embryonic stages, in the nuclear cells (David L,1984).

2. Type of cataracts

1. Congenital cataracts

Congenital cataract reflects mainly genetically caused developmental alterations in the lens. Congenital cataracts, which are present at the birth and are, the less common cataract. Congenital cataract is a term used to define lenticular opacities at birth. Infantile cataract encompasses all lens opacities that develop within the first year of birth. The terms are used interchangeably due to some of these opacities being missed at birth only to be discovered later in life by ophthalmologists. They vary in severity from being non-progressive and visually insignificant to causing profound visual impairment (Rosenfeld and Blecher 2005). Visual loss in congenital cataract is predominantly caused by amblyopia, which arises in a number of ways.

2. Age related cataracts:

The age-related cataracts are nuclear sclerosis, cortical and posterior subcapsular. Nuclear cataracts form in the center of the lens and cause the nucleus to become hard or sclerotic with the deposition of brown pigment. Cortical cataracts are due to the opacity lens cortex and posterior subcapsular cataracts attack the back of the lens adjacent to the capsule.

3. Secondary cataracts

Secondary cataracts are caused by diseases like glaucoma and diabetes or medications such as steroids and radiations (Yanoff M and Duker J. 2008). Cataract is associated with the gradual reduction of visual quality and is accompanied by a series of pathways that associated with imbalance in oxidant-antioxidant status (Adedapo KS, Kareem ST 2012), membrane lipid peroxidation (Kisic B, Miric D 2009), defected cellular communication (Gao J, Sun X 2004), ion imbalance (Duncan G, Bushell AR 1975), modification, aggregation and accumulation of proteins (Boros S, Wilmarth PA 2008), lenticular cell death, inflammation (Klein BE, Klein R). Hence, based on a variety of model systems; including cell/ organ culture, animal and human studies, the review focused on exploring the various pathways relating to the pathology of cataract, current treatment modalities and therapeutic preventive measures.

3. Mechanism of Cataractogenesis:

1. Oxidant-antioxidant imbalance

The major enzymatic antioxidants in the lens are superoxide dismutase, Catalase, glutathione peroxidase, glutathione reductase, glutathione-S-transferase, thioredoxin system and non-enzymatic antioxidants are reduced glutathione, ascorbic acid, Vitamin A, E. (Bernstein P and Khachik F 2001). These antioxidants protect lens from damage induced by toxic radicals/species and oxidative stress is a metabolic state in which excessive levels of highly reactive and unstable compounds overwhelm the ability of antioxidants that quenches them. Decline in the activity of all these enzymes and molecules are reported in the formation of cataract (Kisic B 2012; Stamenkovic M, 2014).

2. Lipid peroxidation

The integrity of lenticular membrane is one of the important factors that keep lens transparency. Lens membrane serves as an impermeable barrier to cations and is equipped with membrane ATPases for the homeostasis of water, calcium, sodium and potassium. Lipid oxidation is a major harmful consequence of ROS formation as it produces irreversible oxidative changes of membranes. It has been shown to induce disorganization of the membrane, modification of membrane proteins, alters the physiological functions of cell membranes. Lipid peroxidation has been implicated in the pathogenesis of cataract because the lethal peroxidation products induce fragmentation of soluble lens proteins and damage critical membrane structures, epithelial cell apoptosis and correlating with an increase in lens opacity and changes in the refractive properties of the lens (Babizhayev M. 2016).

3. Ion imbalance

Lens membrane is equipped with various pumps for maintaining the optimal ion homeostasis. To maintain such steep ionic gradients, the lens must continually expend energy to drive sodium and calcium outward, at the same time functioning to accumulate other ions such as potassium. Cellular calcium homeostasis is achieved by a balance between the inward leak and out flow by plasma membrane Calcium ATPase and Na^{+} Ca^{2+} exchanger. Progressive elevation of sodium, marked loss of potassium and several fold increment of calcium are documented in the literature in the pathology of lens opacification (Shukla N. 1996). A prolonged increase in the calcium concentration would be expected to activate proteases such as calpain and could induce the formation of protein aggregates and irreversible breakdown of important structural proteins andlead to lens opacification. The decrease of calcium ATPase activity is also reported with cataract due to lipid structural changes (Sreelakshmi V. 2015), increase in the oxidation of sulf-hydrul groups (Ahuja R. 1999) and down regulated ATP utilization (Cooper K. 1986).

4. Inflammation

Inflammation is a series complex biological response of body tissues to harmful stimuli; although Inflammation is a protective response, it is reported in various diseases. Nitric oxide (NO) is a free radical gas, signaling messenger and the role of the NO in inflammation are well established. Nitric oxide is normally present at a low concentration in the aqueous humor that bathes the lens (Er H and Gunduz A. 1999). Constitutive levels of NO production contribute normal ocular function, but in response to induction of inducible nitric oxide synthase (iNOS) by oxidant trauma, the production of NO is elevated. NO contribute to oxidation stress by developing more powerful oxidative agents suchas peroxynitrite with superoxide (Horton J.2003).

4. Risk factors causing cataracts:

Cataract is a multifactorial disease associated with several risk factors such as aging, diabetes, exposure to sunlight, and hypertension; however, free radical induced oxidative stress is postulated to be, perhaps, the major factor leading to cataract formation (Spector A 1995). Generation of reactive oxygen species (ROS), resulting in degradation, crosslinking, and aggregation of lens proteins, is regarded as an important factor in cataractogenesis (Spector A 1984 and Truscott R 2000).It has previously been reported that the age-related loss of vimentin, tubulin, and other cytoskeletal proteins in the nucleus of the human lens is not a direct initiator of nuclear cataract, since the same changes are evident even in old, clear lenses (Kuwabara T 1968 and Maisel H. 1984). Cataract can be congenital, age-related or secondary. Secondary cataract can be associated with ocular conditions such as retinitis pigmentosa or uveitis, or systemic conditions as in the case of diabetes or homocistinuria, or can be also drug-induced, mainly by steroids. Diabetes mellitus has been considered to be a major risk factor for cataractogenesis. It is known that in diabetics, the cataracts occur at comparatively an earlier age and 25 times more frequently. It is reported that about 20% cataract surgeries are performed for diabetics alone (Javadi M 2008).

5. Problem of cataracts formation:

Cataracts are a common problem among the old, which means that the aging process is mainly responsible for cataracts formation. Besides, if you have injuries in your eyes, cataracts may happen as well. Another popular cause for cataracts is the suffering from other serious diseases, such as diabetes or trauma.

6. **Discussion:**

In the present review support previous findings about antioxidant micronutrient deficiencies and their important contributory role to trigger the age-related oxidative insult. Further, an attempt has been made to highlight the relative role of plasma antioxidant micro-nutrient biomarkers for lens degeneration among the Indian cataract population with different socioecologic backgrounds. When we reviewed the literature for these aspects, most of the reports pertained to in vitro cell culture experiments and on limited study parameters. The data on ex vivo measurement of oxidative stress in human cataractous lenses, especially for Indian conditions, was scanty.

The lens in normal and cataractous stages contains a number of trace elements are responsible for copper, molybdenum, zinc, iron, selenium, chromium, and cobalt(Sethi A andNath K,1987).Copper in the lens may be associated with oxido-reduction and transamination reactions (Sethi A, and Nath K,1987). Selenium is the chief constituent of glutathione peroxidase, and iron and manganese act as important cofactors for catalase. Most of the literature reporting that micronutrient levels of lens in cataract are based on animal experiments including dietary habits. Further, there are limited studies on trace metal contents in cataractous lens, specifically in Indians. (Sulochana K. 2002 and Srivastava V 1992).

According to Sulochana et al., (2002.)was reported that the selenium, zinc, and copper stages in lens found whole blood for 53 smoker and non-smoker cataract patients.However, no comparisons for blood parameters could be made because their estimations were for whole blood, whereas ours concerned plasma and serum. Moreover, trace metal levels in lens are expressed as micrograms per gram of protein.

Although cataract is one of the major causes of preventable blindness throughout the world, there is no universally accepted pharmacological agent at present to either inhibit or regress the opacification in the human lens. Surgical removal is the only treatment method for human cataract. Oxidation of lens proteins may play an important role in the cataract. Biochemical evidence suggests that each of these compounds can delay photo-oxidative damage to lens proteins.

7. Conclusion:

This review has shown the large amount of evidence and epidemiological, demonstrating a link between lenticular oxidation processes and cataract and between antioxidant intake and retardation in age-related cataractogenesis. It is thus somewhat depressing to note the equivocal findings with regard to human interventional studies. One hopes that studies in companion animals might, in the future, be able to give more positive results. In these review we are concluded that the age related cataract is complex process and yet not understood properly. Oxidation may be a very early or initiating event in overall process in the sequence of events leading to cataract.

In the personal opinion cataract may be considered an illness with systemic echo, not only a local disease. But, it is still hard to say if the modified oxidative stress parameters are cause or effect on lens resulting on formation of cataract.

Reference:

1. Asbell, P.Dualan. I.Mindel. J.Brocks. D.Ahmad. M. and Epstein. S. 2005. Age-Related Cataract. Lancet. 365: 599-609.
2. Foster, A.and Resnikoff. S. 2005. The Impact OfVision 2020 On Global Blindness. Eye (London). 19: 1133-1135.
3. Sacca, S.Bolognesi. C.Battistella. A.Bagnis. A. andIzzotti. A.2009.Gene-Environment Interactions In Ocular Diseases. Mutate And Reserve. 2009; 667: 98-117.
4. Shiels, A. andHejtmancik. J. 2017. Mutations And Mechanisms In Congenital And Age-Related Cataracts. ExpectfOfEye Research. 156: 95–102.
5. Beebe, D.Holekamp. N.and Shui. Y. 2010. Oxidative Damage And The Prevention Of Age-Related Cataracts. Ophthalmic Reserch. 44: 155–65.
6. Javadi, M.and Zarei-Ghanavati, S. 2008. Cataracts In Diabetic Patients: A Review Article. Journal OfOpthalmic Visual Reserch. 3(1):52-65.
7. Varma, S.and Hedge. K. 2004. Effect Of Alpha-Ketoglutarate Against Selenite Cataract Formation. Expects Of Eye Reserch. 79: 913-8.
8. Kyselova, Z.Stefek, M.and Bauer. V. 2004. Pharmacological Prevention Of Diabetic Cataract. Journal OfDiabetic Complication. 18: 129-40.
9. Blondin, J. andTaylor A. 1987. Measures OfLeucineAminopeptidase Can Be Used To Anticipate UV-Induced Age-Related Damage To Lens Proteins: Ascorbate Can Delay This Damage. Mechanism OfAgeing Development. 41: 39-46.

10. Eisenhauer, D.Berger. J.and Peltier. Z.1988.Protease Activities In Cultured Beef Lens Epithelial Cells Peak And Then Decline Upon Progressive Passage. Expects Of Eye Research. 46:579-590.
11. Boscia, F.Grattagliano. I.and Vandermiale. G.2000.Protein OxidatonAndLens Opacity In Humans. Investigation OfOphthalmology Visual Science. 41: 2461-2465.
12. David,L.andShearer. R. 1984. State Of Sulfhydryl In Selenite Cataract. Toxicology OfAppllied Pharmacology. 74: 109-115.
8. Rosenfeld, S.Blecher. H.Bobrow. C.Bradford. A.Glasser. D. andBerestka. S. 2005. Lens AndCataract. Section 11. Basic AndClinical Science Course. American Academy OfOphthalmology. 33-9.
5. Yanoff, M.and Duker. J. 2008. Ophthalmology. 3rd Edn. Mosby Inc: St. Louis.
6. Adedapo, K.Kareem. S.Bekibele. C. and Nwobi. N. 2012. Increased Oxidative Stress And Non Enzymatic Antioxidant Levels In Senile Cataract. Arch Applied Science Research. 4: 2461-2466.
7. Kisic, B.Miric. D.Zoric. L.Dragojevic. I.and Stolic. 2009. A. Role Of Lipid Peroxidation In Pathogenesis Of Senile Cataract. VojnosanitPreglogy. 66: 371-375.
8. Gao, J.Sun. X.Martinez-Wittinghan. F.Gong. X.White. T. and Mathias. R. 2004. Connections BetweenConnexins, Calcium, And Cataracts In The Lens. Journal OfGenes And Physiology. 124: 289-300.
9. Duncan, G. and Bushell. R.1975.Ion Analyses Of Human Cataractous Lenses. Expects Of Eye Reserch. 20: 223-230.
13. Boros, S.Wilmarth. P.Kamps. B.and De Jong. W. 2008.Bloemendal H, Lampi K. Tissue Transglutaminase Catalyzes The Deamidation Of Glutamines In Lens ßb2 And ßb3 Crystallins. Expects Of Eye Reserch. 86: 383-393.
9. Klein, B.Klein. R.Lee. K.Knudtson. M. and Tsai. M. 2006. Markers Of Inflammation, Vascular Endothelial Dysfunction, And Age-Related Cataract. American Journal OfOphthalmology. 141: 116-122.
10. Bernstein, P.and Khachik. F.2001. Identification And Quantitation Of Carotenoids And Their Metabolites In The Tissues Of The Human Eye. Expects Of Eye Reserch. 72: 215-223.
11. Kisic, B. and Miric. D. 2012.Antioxidant Capacity Of Lenses With Age-Related Cataract. Oxidative Medical Cell Biology. 2012: 467-130.
12. Stamenkovic, M.Radic. T.and Stefanovic. I.2014. Glutathione S Transferase Omega-2 Polymorphism-Asn142Asp Modifies The Risk Of Age Related Cataract In Smokers And Subjects Exposed To Ultraviolet Irradiation. ClinExpOphthalmol. 42: 277-283.
13. Babizhayev, M. and Yegorov. Y. 2016. Reactive Oxygen Species And The Aging Eye: Specific Role Of Metabolically Active Mitochondria In Maintaining Lens Function And In The Initiation Of Theoxidation-Induced Maturity Onset Cataracta Novel Platform Of Mitochondria-Targeted Antioxidants With Broad Therapeutic Potential For Redox Regulation And Detoxification Of Oxidants In Eye Diseases. American Journal Therapy. 23: 98-117.
14. Shukla, N. and Moitra. J. 1996. Determination Of Lead, Zinc, Potassium, Calcium, Copper And Sodium In Human Cataract Lenses. Journal OfScience And Total Environment. 181: 161-165.
15. Sreelakshmi, V.Sasikala. V. and Abraham. A. 2015.Luteolin Supplementation Prevents Selenite-Induced Cataractogenesis In Sprague DawleyRat Pups. Chemical Biodiversity. 12: 1881-1890.
16. Ahuja, R.and Borchman D.1997. Effect Of Oxidation On Ca^{2+} -Atpase Activity And Membrane Lipids In Lens Epithelial Microsomes. Free Radicals AndBiological Medicin. 27: 177-185.
17. Cooper, K.Tang. J.Rae. L.and Eisenberg. S. 1986. A Cation Channel In Frog Lens Epithelia Responsive To Pressure And Calcium. Journal of Membrane and Biology. 93: 259- 269.

18. Er, H.and Gunduz. A. 1999.Effects OfNG-Nitro L-Arginine And Corticosteroids On Aqueous Humor Levels Of Nitric Oxide And Cytokines After Cataract Surgery. Journal OfCataract Refraction Surgiry. 1999; 25: 795-799.
19. Horton, J. 2003. Free Radicals And Lipid Peroxidation Mediated Injury In Burn Trauma: The Role Of Antioxidant Therapy. Toxicology. 2003; 189: 75-88.
14. Spector, A. 1995. Oxidative Stress Induced Cataract: Mechanism Of Action. Journal OfFASEB 1995; 9:1173-82.
15. Spector, A. 1984. The Search For A Solution To Senile Cataract. Investigation OfOphthalmology Visual Science. 25:130-46.
16. Truscott, R. 2000. Age-Related Nuclear Cataract: A Lens Transport Problem. Ophthalmic Of Reserch. 32:185-94.
17. Kuwabara, T. 1968.Microtubules In The Lens. Archive OfOphthalmology. 79:189-95.
18. Maisel, H. andEllis. M. 1984. Cytoskeletal Proteins Of The Aging Human Lens. Current Research Of Eye. 3:369-81.
20. Javadi, M. and Zarei-Ghanavati. S. 2008. Cataracts In Diabetic Patients: A Review Article. Journal OfOpthalmic Visual Reserch. 3(1):52-65.
21. Sethi, A.Nath. K. and Ahmed N.1987. Trace Elements And Cataracts: A Comparative Study Of Trace Element Levels In Patients With Mature Senile Cataracts In: Proceedings Of The International Symposium Paris France.1987:151
19. Sulochana, K.Punitham. R.and Ramkrishnan. S. 2002. Effect Of Cigarette Smoking On Cataract: Antioxidant Enzymes In Lens And Blood Of Humans. Indian Journal of Pharmacology. 34: 428.