Clear Vision Ahead: Cataracts Demystified

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***Abstract*— The crystalline material of the natural eye lens creates a clear path for light. Opacity within the clear lens of the eye is known as a cataract, and it is the primary cause of socio-medical problems, or blindness, globally. Surgery is the only known treatment for cataracts. However, post-operative difficulties and the lack of surgical facilities in underdeveloped and impoverished nations motivate researchers to explore alternative cataract treatment options.**

***Index Terms*—Cataract, Crystalline, Opacification, Oxidative stress**

INTRODUCTION

Worldwide, nearly 95 million people suffer from cataracts. The primary reason of blindness in middle class and lower-class nations is still cataracts. The development of small-incisional cataract surgery, that provides fast visual recovery, acceptable visual results, and few complications for the vast majority of patients, is the result of advancements in surgical techniques and methods[1]. Reduced lifespan and a lower quality of life are linked to cataracts. Age and oxidative stress are the main causes of cataracts, which affect most instances after birth. However, a number of modifiable and non-modifiable risk factors might hasten the formation of cataracts[2]. In all of medicine, cataract surgery utilizing an implant for an intraocular lens is one of the most popular and widely accepted medical procedures. Even though age is the most frequent cause, cataract formation has also been linked to other variable[3]. The human eye's crystalline lens is a clear, biconvex structure that works similarly to a camera's lens. A cataract is an anomaly of the lens that is characterized by increased cloudiness and decreased transparency. Worldwide, cataracts are the primary cause of both reversible vision impairment and blindness. People with lower socioeconomic position and those living in developing nations are more likely to suffer from the illness[4]. Globally, cataracts are the primary cause of blindness. Oxidative stress is the direct cause of the lens's opacity. Although age is the main cause of cataracts, diabetes is also a common cause, as higher superoxide levels in the mitochondria arise from hyperglycemia[5]. A majority of adults over 65 are thought to have developed cataracts in either one or both of their eyes to some extent. The Royal College of Eye specialists predicts that approximately 2.4 million individuals in the United Kingdom and Wales are 65 years of age or older possess a minimum of one cataract that impairs vision[6]. Because cataracts occur more frequently and at an earlier age in the third world, they pose a far bigger problem there. In India, where there are around 5 million blind people, cataracts cause 55% of all blindness. In Nepal, they cause nearly 60% of all blindness[5]. Many premature deaths and excruciating human suffering are brought on by blindness. In As per the World Health Organization, South-East Asia is home to half of the 1.5 million blind children worldwide and one-third of the 45 million blind adults worldwide. Blind people are frequently marginalized and lead terrible lives[14].

CATARACT

A "cataract" is a decrease in the amount of light entering the eye caused by the typically clear lens of the eye becoming opaque[8]. Excessive opacity of the lens that is crystalline, known as a cataract, is the result of the lens's refractive index changing dramatically across distances that roughly correspond to the wavelength of light that is transmitted[13]. Other than surgically removing the lens, there is no effective treatment available for the opacification. The mechanisms causing it are unknown. The lack of adequate *in vivo* or *in vitro* models has hindered research in this field[6]. Opacity within the clear lens inside the eye that reduces the amount of incoming light and causes vision to deteriorate; the natural lens is a crystalline substance with a precise structure of water and protein to create a clear passage for light; the experience of having a cataract is sometimes compared to looking through a waterfall or waxed

paper[14]. The effectiveness of a selection of topical and dietary antioxidant treatments in relation to our current knowledge of lens structure and function. Situated in the eye, behind the blood-eye barrier, the aqueous and vitreous humours supply the lens with nutrients and antioxidants. Additionally, the lens cannot rely solely on passive diffusion to supply nutrients and antioxidants to its many metabolic zones because it is a very big avascular tissue. Rather, we suggest that the lens actively delivers antioxidants to these various regions through a special internal microcirculation system, and the development of novel nutritional therapies to stall the onset and progression of lens cataract will depend on the antioxidants' ability to make use of this system.

TYPES OF CATARACT

Congenital cataract- unilateral or bilateral, arising from genetic or pregnant related conditions.

Subcapsular cataract: Anterior subcapsular cataracts are linked to fibrous metaplasia of the lens epithelium and are visible beneath the anterior lens capsule. When seen under an oblique slit lamp, the posterior subcapsular cataract, which is located in front of the posterior capsule, appears granular or plaque-like.

Nuclear sclerotic cataract: Nuclear sclerosis is typically an age-related occurrence. The nucleus appears brown and in rare instances, black, in advanced cases.

Cortical cataract: The anterior, posterior, or equatorial cortex may be affected. Cortical hydration is caused by the cortical opacities, which are visible as clefts and vacuoles between the lenticular fibers. This kind of opacity frequently causes glare and photophobia.

CAUSES OF CATARACT

Oxidative stress

Cataract is a frequent reaction to a chemical, mechanical, or physical injury and has various origins. The eye's lens is isolated in a particular environment by a capsule and epithelium, and its transparency is dependent on a distinct arrangement of densely packed fibers, which in turn depend on a particular protein structure. As a result, harm to the capsule, epithelium, or lens fibers itself may cause a cataract, and the harm may accumulate over a long period of time[7].

Genetics

The pathophysiology of all types of hereditary cataracts summarizes the lens's cell biology and development. Every newly discovered gene sheds light on the cellular and developmental biology of the lens, much as every novel mutation reveals more details on the relationship in structure or biological functioning of the impacted gene. In particular for age-related cataract, the list of genes now known to be linked to the condition is far from exhaustive, and more genetic research is needed to uncover a wealth of new information supplementary Data[8].

Steroid induce cataract

Black and associates initially observed the link between steroid use and cataract development in 1960. Researchers found that 39% of patients with rheumatoid arthritis who had received systemic steroid therapy went on to acquire Posterior Subcapsular Cataracts (PSCs). The steroid-induced cataract differs from the more prevalent forms of cataract in that it manifests bilaterally. Outlined the clinical characteristics of the cataract in a later publication[9]. PSCs, or posterior subcapsular cataracts, are linked to long-term steroid medication. Five steroid-associated cataractous lenses were examined with the use of transmission electron, scanning, and light microscopy. Three areas were analyzed the anterior, equatorial, and posterior. Five nuclear cataractous lenses without cortical opacities and five age-matched senile PSCs were used to compare the findings. There are two parts to the posterior polar area of steroid-associated cataractous lenses: a deep zone of segmentally enlarged lens fibers and a superficial zone of liquefaction. There are nucleated lens fibers in the areas of the posterior cortex[9].

Inherited cataract

Children's induced blindness is frequently caused by congenital cataracts, which are mostly caused by inherited cataracts. Certain genes, such as those encoding membrane transport and channel proteins, crystallines, gap junction proteins, the cytoskeleton, growth and transcription factors, have been linked to inherited congenital cataracts. Understanding the molecular flaws and pathophysiologic traits of hereditary congenital cataracts requires locating and identifying the genes and mutations implicated in cataractogenesis[10].

PATHOPHYSIOLOGY

The lens is made up of specialized proteins known as crystallines, whose hydration and three-dimensional structure must be carefully arranged to maintain their optical characteristics. The osmotic and ionic equilibrium across the lens is maintained by membrane protein channels, and the precise form of the lens cells—particularly the fiber cells of the nucleus—is provided by the lens cytoskeleton. High amounts of reduced glutathione, also known as the "mother of all antioxidants," shield the protein-bound sulfhydryl (SH)-groups of crystallines against oxidation and cross-linking. Higher spatial and temporal stability (heat-shock proteins) is primarily provided by their molecular compositions and tertiary and quaternary structures, which are primarily responsible for the larger crystallines ability to absorb electromagnetic radiation (shortwave visible wavelengths, ultraviolet, and infrared radiation) over longer timespan without significantly altering their optical properties. Glutathione and other protective antioxidants can't reach the nucleus of the lens in an aging eye due to the development of barriers that make the lens vulnerable to oxidation. Furthermore, the lens metabolic efficiency typically decreases with age, making it more susceptible to harmful substances. The process of aging creates conditions that allow "cataract noxae" to act and interact to cause a variety of cataracts, many of which are linked to increased light scattering and discoloration due to proteins. As a person ages, their glucose metabolic pathway performs less energetically efficiently and more aerobically, which causes issues with protein synthesis, transport, and membrane synthesis. Furthermore, the epithelium and the small number of fiber cells are required to maintain the syncytial metabolic function of the denucleated fiber cells[11]. Additionally, the proper amount of salt and calcium should be present in the intraocular irrigating solutions. The main cause of pupillary constriction during extracapsular cataract extraction is prostaglandins produced as a result of surgical trauma; topical indomethacin applied prior to surgery helps avoid this. Fluorophotometry has shown that preoperative topical non-steroidal anti-inflammatory drugs (Ptyethacin, flurbiprofen, and diclofenac) can avoid this effect. Breakdown of the blood-aqueous barrier during ophthalmic surgery may also result from a similar process. Following cataract surgery, topical indomethacin also helps to avoid cystoid macular oedema[12].

RISK FACTORS OF CATARACT

There are several causes of cataract development. Most people believe that the development of cataracts in humans is a complex illness. The majority of them have distinct etiologies that allow for diagnosis; examples include anterior (often brought on by steroid use) and posterior (often associated with senile cataracts)[14]. Wright examined the lenses of 4,000 outdoor labourers in two regions of India—one hot, dry, and cloudless, and the other cloudier—fifty years ago to test this theory. He discovered that the cloudier area had a higher prevalence of cataract and came to the conclusion that sunshine is most likely not a significant role in the high frequency of cataract in South India.

Cigarette smoking West and Valmadrid have evaluated the findings of several studies that looked at smoking as a risk factor for nuclear cataract. This analysis demonstrates that this link holds true for eight of the ten studies that were part of the review. There was evidence of a strong correlation, a dose response impact that was evident, and a lesser cataractogenic effect in former smokers compared to present smokers, which addresses the problem of reversibility[17],[18].

Exposure to UV-B According to a thorough analysis of the epidemiologic data from 22 human studies by McCarty and Taylor and a review of earlier ecological studies by West24, there is a direct correlation between lifetime UV radiation exposure and the prevalence of cortical cataracts[17].

Diabetics Long before there was a medical cure, "sugar cataracts" were identified through case observations. The correlation between these two forms of cataract and galactosaemia and diabetes mellitus has been demonstrated by experimental and biochemical research. Clinical studies have revealed a higher frequency and early onset of posterior subcapsular opacities and cortical cataract in diabetes patients[15].

Steroids According to reviews by West and Valmadrid and Hodge *et al.,* the consistency of the findings, biologic plausibility, and strength of the correlation suggest that topical and systemic steroids are important risk factors for posterior subcapsular cataract development. Cataract risk has also been demonstrated to be elevated by inhaled steroids[15].

Alcohol consumption Even though a number of studies have demonstrated that alcohol consumption increases the incidence of various forms of cataract, particularly posterior subcapsular opacities, there are a number of potential biases. The primary cause for concern is that, although data on alcohol consumption is regularly gathered, a significant percentage of studies did not report on this link[17].

Other factors Numerous other risk variables have been investigated; however, the findings vary somewhat throughout the investigations. This holds true for severe thirst, malnourishment, and tachycardia. Disease causation, where it can be challenging to discern the medication's cataractogenic effect from the disease's inherent effect, requires more research[19].

PREVENTION OF CATARACT

There's growing proof that the unchecked Ca^{2+}-mediated proteolysis of vital lens proteins by calapains could be a significant. Furthermore, the molecular specifics of the activation mechanism employed by these proteases have been revealed by recently solved calpain structures, opening the door to the structure-based design of strong calpain inhibitors that may function as anti-cataract medicines. Global respite from a life-depreciating condition and the first genuine prospect of an urgently needed alternative to surgical treatment of at least some forms of cataract are provided by these drugs[16]. the effectiveness of a selection of topical and dietary antioxidant treatments in relation to our current knowledge of lens structure and function. Situated in the eye, behind the blood-eye barrier, the aqueous sand vitreous humours supply the lens with nutrients and antioxidants. Additionally, the lens cannot rely solely on passive diffusion to supply nutrients and antioxidants to its many metabolic zones because it is a very big avascular tissue. Rather, we suggest that the lens actively delivers antioxidants to these various regions through a special internal microcirculation system, and the development of novel nutritional therapies to stall the onset and progression of lens cataract will depend on the antioxidants' ability to make use of this system[19]. Many medicinal plants, including the leaves of amethyst, passion fruit, and ginger, have strong antioxidant activity, according to an online study of the literature. A number of plants exhibit bioactivity as anticataracts, according to some reviewed research. Thus, it may be inferred that high-antioxidant plants can be included in attempts to prevent cataracts, and that more research on treating cataracts can use plants as a natural source of antioxidants that slow the development of cataracts[19].

TREATMENT OF CATARACT

Cataract surgery : Phacoemulsification became popular in 1996 despite its invention in 1967 to become the standard cataract surgery procedure because it delivers reduced postoperative inflammation with quicker vision recovery and a lower likelihood of capsulotomy formation. The examination of the fundus becomes impossible whenever the lens develops enough opacity in diabetic patients so cataract surgery should be performed. The complications resulting from diabetes include rapid development of retinopathy along with changes to the macular area. Postoperative inflammation together with macular edema affect diabetics at an elevated rate. Research indicates that cataract surgery possesses the potential to cause progressive worsening of diabetic retinopathy at levels ranging between 21% and 32% specifically within patients who have proliferative diabetic retinopathy.

Aldose-Reductase Inhibitors: The clinical trials for diabetic cataract prevention using Sorbinil alongside other aldose reductase inhibitors proved unsatisfactory due to their inefficient results and negative side effects. The promising potential of new ARIs including Lidorestat needs additional research studies for proper evaluation. The activation of calpain protease occurs with elevated calcium levels found within the lens tissue. Calpain 2 which resides in human lens epithelial cells functions by decomposing proteins resulting in cataract. The prevention of cataract caused by calcium levels might be attainable through calpain inhibition strategies.

Antioxidant therapies: Laboratory tests demonstrate that antioxidants alongside oxysterols succeed in restoring or halting the progression of cataracts in experimental lens models. Two oxidate compounds - N-acetylcysteine amide and N-acetylcarnosine - demonstrate better bioavailability than their original substances which solves the problems experienced during topical applications. Research indicates that applying N-acetylcarnosine through eyes results in lens opacity reduction based on clinical findings. Both lanosterol and 5-cholesten-3b,25-diol (VP1-001) and recently lanosterol have shown potential in

reducing crystallin aggregation patterns in living animals and laboratory tests. The use of nanotechnology has enhanced delivery while scientists need to conduct more studies about these compounds' therapeutic activities towards cataract and better lens-targeted delivery methods.

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