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Glucose Metabolism and Cataract: Prevention and Treatment – A Review

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ABSTRACT

Glucose metabolic disorders and diabetic retinopathy is linked to an increased risk of cataracts. The anatomical components of the eye work together to focus a picture on the retina. The cornea, one of the eye's two major focusing structures, receives light. The pupil is the eye's next focusing component, and it is positioned directly after the crystalline lens, which is the eye's second focusing component. The cornea and lens focus light rays onto the retina, which initiates image processing and transmission to the occipital area of the brain. The lens of the eye becomes clouded, limiting light from reaching the retina. Blurred vision, glare, and reduced contrast sensitivity are all symptoms of cataracts. Studies have demonstrated that diabetic lenses have aberrant levels of electrolytes, glutathione, nucleotides, and carbohydrates. Cataracts are more common in those with type 1 and type 2 diabetes. Diabetes-related alterations in lens metabolism and cataract development are linked to hyperglycemia. According to a study of glucose metabolism pathways, several hyperglycemia-initiated activities are linked to cataract formation. Metabolic alterations in galactosemia-related cataracts are identical, indicating a similar biochemical origin. Aldose reductase ($NADP^+$ 1-oxidoreductase, EC 1.1.1.21) is a sugar alcohol synthase enzyme that transforms glucose or galactose into sugar alcohols (polyols). Increased intracellular polar alcohol levels promote lens fiber extension, vacuole formation, and opacification, while Aldose reductase inhibition prevents sugar cataract development. This article is a review on different studies and reports that encompasses diabetic retinopathy and cataracts.

***Keywords*:** Cataract, Diabetic retinopathy, Opacification, Glucose metabolism, Diabetes mellitus

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1. INTRODUCTION

Chronic hyperglycemia causes cataractogenesis, one of the early secondary consequences of diabetes mellitus. Because extracellular glucose diffuses into the eye unregulated by insulin, the lens is one of the most damaged organs in diabetes. Lens proteins are highly long-lived, with little protein turnover, allowing for post-translational modification (Abraham *et al*., 2006). The lens is drenched with aqueous and vitreous humor on either side. Since the lens lacks blood capillaries (which would obstruct light path), the aqueous humor nourishes and eliminates metabolic waste. The lens gets its energy from anaerobic glycolysis; the Krebs cycle in peripheral cells only provides around 5%. The pentose phosphate cycle generates NADPH required to maintain the redox state of lens proteins. Cataracts occur when crystalline proteins lose their solubility and aggregate. The different types of cataracts are associated with different metabolic aberrations an example is galactosemia, similar to diabetes (Yoshida *et al*., 2004).
The aqueous humor, a fluid that fills the front of the eye, feeds the lens. Hydrogen peroxide and glucose are found in aqueous humor. In uncontrolled diabetes, sugar levels grow in the aqueous humor and the lens. The lens swells due to high glucose levels, impairing vision (Hong *et al*., 2000). The lens also includes an enzyme that turns glucose into sorbitol. Sorbitol can alter cells and naturally existing proteins in the lens, making it less transparent and opaque. The disease causes cataracts, obscures or fades the world around the patient.

2. CATARACT

It is a progressive loss of eyesight caused by opacity in the clear natural crystalline lens. Thickening of the lens is a common symptom of this illness. As with gazing through a waterfall or waxed paper, the quantity of incoming light decreases due to lens cloudiness affecting eyesight. The crystalline lens is an ocular component that allows pictures to be focused on the retinal. Proteases are abundant in this translucent material. The lens is an avascular structure encased in a capsule. Fibers make up the rest of the ocular tissue, which includes epithelial cells below the tablet. It forms an onion-like structure as the new threads grow on top of the old. Because it does neither absorb nor scatter light, the lens is transparent. The fiber plasma membranes account for 5% of the lens's scattered light output. They are almost translucent due to their small volume (0.05%). Crystalline proteins are found in the cytoplasm of cells (35%) as biomolecules. Metabolic disorders and mistakes like hyperglycemia can cause changes in the lens and age (Srivastava *et al*., 2005).

Cataracts have a varied etiology, making it difficult to pinpoint their source. A problem with the lens metabolism is the main reason. Diabetes and galactosemia are examples of metabolic errors. Lens metabolism is undeniably epithelial. The complex GAP-junction mechanism enables intercellular communication. A constant supply of ATP is required for structural component synthesis and transport system upkeep. For complete transparency, this is a vital step. It is metabolized by three routes: glycolysis, pentose phosphate shunt, and polyol pathways (Abraham *et al*., 2006).

These two glucose transporters, GLUT1 and GLUT3, carry glucose into the lens. The lens has a similar glycolytic mechanism as other tissues. It is worth noting that one of the pathway's key regulators, hexokinase, only has two isoforms, I and II, which have been identified. Although hexokinase type II is more common than type I, the Michaelis constant

(Km) is lower. When blood glucose levels rise, the latter is likely utilized (Liu *et al*., 2004). As people age, their hexokinase concentration drops. As ATP levels decline, the lens loses its ability to regulate electrolyte balance, which may be one of the reasons why cataracts develop in the elderly. The pentose phosphate shunt breaks down some of the glucose. The first enzyme in this system, glucose 6-phosphate dehydrogenase, produces substantial quantities of $NADPH^+$ and H^+.

Nitrogen is required for glutathione reductase and polyol pathway activity. This route metabolizes around 14% of glucose. Due to glutathione (GSH) requirement, this pathway is activated under oxidative stress (Kumamoto, 2007). The polyol pathway, commonly known as the sorbitol pathway, is the third metabolic process for glucose. Chung *et al*., 2003 characterized this method after confirming polyol buildup in the lens. High glucose, galactose, or xylose diets caused cataracts in his animal studies. Aldose reductase and polyol dehydrogenase are the only enzymes that produce sorbitol. The sorbitol route is thought to digest around one-third of the glucose entering the lens (Chung *et al*., 2003). Enzyme aldose reductase in humans has a Km for glucose of 200 mm and is found in the epithelia with 70% activity. Thus, the sorbitol concentration accumulates in a tiny region of the lens, resulting in a rise of 50 times the concentration predicted if the enzyme is distributed uniformly throughout the lens.

Sorbitol dehydrogenase is more uniformly distributed than aldose reductase. This enzyme is found in both the lens epithelium and cortex. However, it cannot metabolize inositol, glycerol, or dulcitol (unlike aldose reductase) (galactitol). Individuals with high sugar levels in plasma and aqueous humor need to take note of the polyol pathway. Aldose reductase does not operate in humans because blood glucose levels range from 0.7 to 2.2 mm. When glucose levels are 3–4.5 mm, aldose reductase has a chance. This mechanism is active in galactosemia, resulting in elevated galactitol levels. Another enzyme, hexokinase, whose activity declines with aging, is connected to this pathway. That is why it is vital to know how both enzymes interact to determine how glucose will be used. In high glucose concentrations, the hexokinase lens is saturated (Km = 100 mm). For people with diabetes, this makes the sorbitol route important. Sorbitol accumulates despite having a low polyol dehydrogenase Km compared to aldose reductase in the lens. In specific animal models, aldose reductase is thought to be 30 times more abundant than polyol dehydrogenase. It is 80 times greater in humans than aldose reductase (Mukesh, 2006; Fedirko, 2016; Ozgun, 2018).

3. GLUCOSE METABOLISM

The regular functioning of the body's organs requires energy. Some tissues, such as the brain and red blood cells, may use fat or protein as an energy source, but not all. Glycogen is the body's stored form of glucose. The liver is a significant glycogen storage organ. When blood glucose levels are low, gluconeogenesis mobilizes and converts glycogen to glucose. Gluconeogenesis produces glucose from non-carbohydrate precursors such as pyruvate, amino acids, and glycerol. Gluconeogenesis maintains blood glucose levels during fasting and strenuous activity (Olofsson *et al*., 2005).

Glycolysis breaks down a glucose molecule into two pyruvate molecules and stores the energy produced as ATP and NADH. Almost all species that digest glucose use the glycolytic process. Glucose regulation and product utilization are the significant differences across species. In some tissues and species, glycolysis is the sole energy source. This route is used in

both anaerobic and aerobic respiration. It comprises ten stages divided into two sections. It needs the breakdown of two ATP molecules in the first phase. Intermediates chemical energy is converted into ATP and NADH in process two. One glucose molecule breaks down into two pyruvate molecules which can be oxidized for additional fuel (Hong *et al*., 2000).

Glycolysis can be controlled at several stages through feedback regulation. The third phase has the most restrictions. This regulates the body's pyruvate production. This control permits glucose molecules to be stored as fatty acids. Various enzymes are employed during glycolysis. The enzymes upregulate, downregulate, and feedback regulate the process.

Gluconeogenesis

Gluconeogenesis is glycolysis's opposite, where non-carbohydrate molecules are turned into glucose. This route converts pyruvate, lactate, glycerol, alanine, and glutamine. This happens when the glucose levels are low. Gluconeogenesis occurs mainly in the liver, although it also occurs in the kidney. The liver degrades non-carbohydrate molecules and distributes them to other organs and tissues for gluconeogenesis. Different substances control this pathway. Glucagon, ACTH, and ATP stimulate gluconeogenesis. AMP, ADP, and insulin limit glucose synthesis. The most frequent regulators of gluconeogenesis are insulin and glucagon.

Glycogenolysis

Glycogenolysis occurs in the liver, muscles, and kidney. This happens to produce glucose. On cleavage a glucose molecule goes off a glycogen branch, which then becomes glucose-1-phosphate. In the glycolytic process, this molecule becomes glucose-6-phosphate. Then glycolysis can proceed. When glucose comes from glycogen, it just takes one molecule of ATP to start the process. To boost blood sugar levels, glucose-6-phosphate can be converted back to glucose in the liver and kidneys. When hypoglycemia (low blood sugar) occurs, the liver releases glucagon, which promotes glycogenolysis. In between mealtimes, the liver's glycogen can be used as a source of glucose. During the activity, adrenaline encourages the breakdown of glycogen in the muscle. Glycogen provides a quick supply of energy for muscular contractions.

Glycogenesis

Glycogenesis is the process of making glycogen. This is how people convert extra glucose to glycogen. This structure is made up of glucose in glucose-6-phosphate linked together, with more glucose molecules available for breakdown due to glycogen branching. It primarily occurs in the liver, skeletal muscles, and kidney.

Pentose Phosphate route

It is an alternate technique to oxidize glucose. Adipocytes and red blood cells use this route. It converts NADP to NADPH. G6PD activity regulates this pathway.

Metabolic Fructose

To reach the glycolysis pathway, fructose must go through a few more stages. Cellular enzymes can phosphatize fructose. These tissues may directly break down fructose-6-phosphate, which is produced by this phosphorylation. Muscles, adipose tissue, and kidneys all

have this route. As glyceraldehyde is converted into dihydroxyacetone phosphate by enzymes, fructose-1-phosphate is made in the liver.

Galactose oxidation

1 glucose + 1 galactose = lactose. Galactose is transported to the liver for glucose conversion. The enzyme phosphorylates galactose with one molecule of ATP. As glucose-6-phosphate is broken down in glycolysis, the phosphorylation of galactose is transformed to glucose-1-phosphate.

Hormones

Glucoregulation is the body's ability to maintain a constant glucose level. Pancreatic hormones control glucose metabolism. Each of these hormones is released in response to the availability of nutrients. The amount of insulin released into the bloodstream and the sensitivity of cells to insulin influence how much glucose are broken down by cells. Inhibition of glycogenesis occurs when there are increased glucagon levels. Insulin increases glycogenesis while inhibiting glycogenolysis. Carnitine and insulin are generated in response to changes in circulatory glucose (often known as "blood sugar"). Hypoglycemia causes glucagon release, while hyperglycemia causes insulin release. Diet affects significant elements of metabolism via insulin because dietary carbohydrate consumption determines the level of circulatory glucose. Hepatic cells store and release glycogen, while pancreatic beta cells produce insulin. Muscle cells' intracellular glycogen reserves do not release glucose into the blood regardless of insulin levels.

4. GLUCOSE METABOLISM AND DIABETES

The metabolic disease diabetes mellitus causes is hyperglycemia which is due to abnormalities in insulin production, action, or both. In people with diabetes, persistent hyperglycemia leads to long-term damage, malfunction, and failure of the eyes, kidneys, nerves, heart, and blood vessels. Diabetes causes aberrant glucose, lipid, and protein metabolism due to inadequate insulin activity on target tissues. The complicated routes of hormone action result in insufficient insulin secretion and tissue responses. Insulin secretion and insulin action abnormalities commonly occur in the same patient, making it difficult to determine which anomaly is the primary cause of hyperglycemia. (Yoshida, 2009)

Diabetes occurs when the pancreas does not generate enough insulin or when the body's cells do not respond appropriately to it. Types of diabetes mellitus include:

• Loss of beta cells in the pancreas causes type 1 diabetes. Previously called "insulin-dependent diabetes mellitus" or "juvenile diabetes". An autoimmune reaction destroys beta cells (Yoshida, 2009).

• Insulin resistance occurs when cells do not react appropriately to insulin. Lack of insulin may occur as the illness develops. Previously called "adult-onset diabetes" or "non-insulin-dependent diabetes mellitus". Obesity and lack of exercise are the most prevalent causes.

• Gestational diabetes develops when pregnant women who have never had diabetes acquire high blood sugar levels.

5. DIABETES AND CATARACTS

Chronic hyperglycemia in diabetes contributes to the development and progression of severe diabetic complications. Long-term exposure to high glucose produces both acute reversible metabolic alterations and permanent macromolecular abnormalities. The harmful consequences of hyperglycemia are often seen in tissues that do not require insulin for glucose entry into the cell (e.g., eye lens, kidneys) and so cannot decrease glucose transport when extracellular sugar concentrations rise. Multiple hypoglycemic mechanisms have been postulated to explain these anomalies (Trindade, 2007).

6. MAMMALIAN EYE LENS ANATOMY AND PHYSIOLOGY

The ocular lens is anatomically intended to transfer and concentrate light onto the retina for subsequent visual perception and circadian rhythm control. The lens must be translucent to transmit and focus light on the retina, which is done by carefully arranging and regulating volume inside lens cells (Stitt, 2005). These cells lack organelles and contain more stable proteins than the lens fluids, giving them a greater refractive index. To see, light must be focused on photoreceptors in the retina, which is translated into an electrical stimulation by the brain. The anterior section of the eye includes the lens, cornea, anterior chamber, iris, and posterior chamber. The lens is held in the regard by zonular fibers, thin projections of the non-pigmented epithelium of the ciliary body.

The aqueous humor is a complex solution of nutrients, growth factors, and minerals that provide nutrition to the lens. The vitreous humor functions in maintaining the volume and shape of the globe and may influence the differentiation of epithelial cells. The lens is an avascular tissue packed with protein that provides the high refractive index necessary for the fine focusing of light onto the retina. It also acts as an optical filter so that the access of the ultraviolet (UV) light to the retina is greatly minimized. As the lens ages, the proteins are damaged by photo-oxidation which aggregates, and accumulate in lens as opacities (Liao *et al*., 2003). These changes result in less flexibility and less flexibility of the lens as it ages.

7. CATARACTOGENESIS

To concentrate light on the retina, the lens must be clear. In diabetes, Oxidative stress increases around the lens protein, causing it to lose transparency and become opaque progressively. This causes light dispersion and a change in the refractive index. Cataract has been extensively studied, and opacity of the lens has proven clinically significant in recent decades. Blurred vision is the initial sign of a cataract. A cataract reduces the amount of light reaching the retina and distorts the light that does get it (Borenshtein *et al*., 2001).

8. TYPES OF CATARACTS

Cataracts come in several varieties. Their development in the eye determines their classification.

Age-related Cataracts

There are several age-related cataracts, each with its own unique development process, including oxidative damage, protein aggregation, glutathione breakdown, membrane damage, protein breakdown, increased calcium, abnormal lens epithelial cell migration, and lens fiber cell mutation.

Nuclear cataract

As oxidative stress increases in the lens cell cytoplasm, protein-protein interactions occur, altering protein and lipid structure. Light scattering occurs when the crystalline and lens fiber membrane contact. Age-related increases in oxidized glutathione in the lens nucleus imply protein and lipid oxidation and an imbalance in the endogenous glutathione-dependent reduction system. A nuclear cataract develops when the cytoplasm of lens cells separates into protein-poor and protein-rich phases.

Cortical cataract

The opacity rises from the lens' periphery to the lens' circumference in this cataract. An imbalance in calcium homeostasis may be implicated in cortical cataract formation. Because one of these elements affects the others, causing cortical opacity, they are interdependent. Opacity around the lens's periphery is caused by a high calcium content in the blood. Calcium increases peripheral opacity towards the lens nucleus, causing light scattering.

Posterior subcapsular cataract

This form of cataract is caused by environmental causes such as UV rays, diabetes, and medication consumption, back of the lens cluster of enlarged fiber cells located underneath the lens capsule. So light scattering occurs when the incoming light path is interrupted. This form of cataract is more susceptible due to improper epithelial cell migration and alterations in the lens fiber.

Extreme opacification alters the lens' transparency (Boscia *et al*., 2001). To produce an image, light enters the lens, travels through it, and hits the retina. A clouded lens scatters light, causing vision problems. Lenses with reduced transparency absorb light, reducing visual acuity and causing cataracts. This cataract can be caused by lens fiber cell breakage, cellular protein aggregation, and cytoplasm malfunction.

9. MECHANISM ASSOCIATED WITH CATARACT

The loss of lens transparency during cataract development is caused by a mix of metabolic and physiological processes that affect the lens' refractive index. During cataract development, post-translational modifications of lens protein include oxidation, glycation, Schiff base formation, proteolysis, transamidation, carbamylation, phosphorylation, and increased calcium levels. Lens protein aggregates and disrupts typical lens cell structure, causing lens opacification. Apart from this, the specific mechanisms are associated with cataract formation that includes:

Non-enzymatic glycation

Non-enzymatic glycation occurs when glucose interacts non-enzymatically with protein, tissues, or blood components. The chemical characteristics of advanced non-enzymatic glycation products play an important role in glucose/diabetic cataract development (Mulhern *et al*., 2006; Chung *et al*., 2003).

Polyol pathway

Polyol buildup within the lens is the leading cause of diabetes cataracts. Some bodily tissues, such as the lens, do not require insulin receptors to use glucose and other simple carbohydrates. Excess glucose in the aqueous humor passively diffuses into the lens in hyperglycemia. These polyols cannot passively diffuse out of the lens to collect or convert to fructose hence causing cataracts (Karel *et al*., 2003).

Lens proteins damage

In age-related cataracts, the reactivity of the thiol group in lens protein increases. Almost half of the methionine residue in the nuclear proteins oxidized to methionines sulfoxide, and more than 90% of protein sulfhydryl (PSH) groups are lost in most advanced cataracts. Damage to lens crystallins appears to be attributable primarily to UV radiation and various active oxygen species. Varma *et al*. suggested that denaturation, oxidation, and aggregation of crystallins leads to loss of transparency and can cause cataracts (Meyer *et al.*, 2005; Varma *et al.*, 2005).

Loss of Glutathione

In all cells, glutathione plays a role in metabolism, transport, and cell defense. The direction of oxidation is greatly affected by glutathione deficiency. Age-related nuclear cataract development may be preceded by a loss of decreased GSH concentration in the lens's center. Cataracts can occur here because of lack of GSH oxidation.

Damage of lens epithelial cells

To keep the lens healthy, epithelial cells act as the lens' first line of defense against damage. Aqueous humor's direct touch makes them phototoxic. Lens epithelial cell oxidative damage comprises protein oxidation, enzyme deactivation, DNA breakage, and lipid peroxidation.

10. PATHOGENESIS OF DIABETIC CATARACT

The polyol pathway enzyme aldose reductase converts glucose to sorbitol, a mechanism associated with diabetic cataracts. Polyol buildup causes lens fiber collapse and liquefaction, resulting in lens opacities. Due to the enlargement of cortical lens fibers, osmotic stress is critical in the fast cataract development in young individuals with type 1 diabetes. The buildup of sorbitol causes stress in the endoplasmic reticulum (ER), leading to free radicals. There is no evidence yet that these free radicals cause cataract formation but rather speed up and exacerbate it. Glycation and inactivation of lens antioxidant enzymes such as superoxide dismutases increase antioxidant depletion which can facilitate cataract development (Srivastava *et al.*,

2005; Wilson *et al.*, 2007 ; Oishi *et al.*, 2006 ; Kimamoto *et al.*, 2007 ; Chung *et al.*, 2003 ; Mulhern *et al.*, 2006 ; Hong *et al*., 2000 ; Olofsson *et al.*, 2005).

11. FACTORS INVOLVED IN CATARACTOGENESIS

There are several antioxidants (vitamin C, E, carotenoids, and glutathione GSH) and antioxidant enzymes in a juvenile lens that can help avoid damage. Proteases are proteolytic enzymes that selectively eliminate old proteins, adding a second layer of protection. In addition to oxidative stress, smoking and UV exposure tend to increase the risk of cataract development. (Vrensen, 2009; Delcourt *et al*. 2000).

Diabetes

Diabetic retinopathy and cataract cause visual loss. A cataract is a frequent consequence of diabetes caused by extreme hyperglycemia. Cataracts in diabetes are caused by high tissue sorbitol levels, lens protein glycation, and free radical generation.

Non-enzymatic glycation

Hyperglycemia causes non-enzymatic glucose reactions with proteins, tissues, and blood. This accelerates non-enzymatic glycation. Chronic, permanent problems include extracellular matrix, eye lens crystallins, and chromosomal DNA.

Oxidative stress and diabetes mellitus

The Maillard accelerated glycation, or AR-mediated osmotic theory, is plausible. Glucose, like other alpha-hydroxy aldehydes, may enolize and therefore decrease molecular oxygen under physiological circumstances. In hyperglycemia, the Amadori product autooxidizes, leading to oxidative protein damage. AGEs increase reactive oxygen species (ROS) while decreasing endogenous antioxidants like glutathione. The superoxide anion inhibits glyceraldehyde-3-phosphate dehydrogenase (GAPDH). The AGE-forming chemical methylglyoxal is elevated when GAPDH is inhibited. Methylglyoxal also causes substrate-induced AR upregulation, which may exacerbate diabetes problems. (Kowluru and Kennedy, 2001; Mario and Pugliese, 2001; Nishikawa, Edelstein, and Brownlee, 2000; Nishikawa, Edelstein, and Du, 2000; Chandra *et al*., 2002; Dixit *et al*., 2001; Salvemini and Cuzzocrea, 2002; Schleicher and Weigert, 2000; Chang *et al*. (2002),

Polyol pathway

Glucose is processed through the glycolytic route and the pentose shunt. Glucose elimination through these mechanisms tends to increase in hyperglycemia. The polyol pathway converts more glucose into sorbitol. Sorbitol is difficult to penetrate cell membranes and disrupts the osmotic equilibrium. AR initiates the cataractous process and helps explain the differences in cataract advancement rates between diabetic and galactosemic patients (Niwa and Majima, 2000). Increased glucose flow via the polyol pathway reduces GSH levels by competing with AR for NADPH. The most dramatic drop in lenticular GSH levels, an essential intraventricular antioxidant, was seen in an eye surgery patient (Lou, 2000)

12. SYMPTOMS OF CATARACTS

Various types of cataracts have different effects on visual symptoms. They include any one or all of the following:

Decrease in visual acuity

Eyesight sharpness and focus are measured utilizing visual acuity. Decreased visual acuity is considered as the first sign of a cataract. Capillaries (and other factors) can induce changes in visual acuity. Patients with advanced cataract symptoms may require more excellent lens correction. Ophthalmology experts advise using Snellen acuity testing to determine surgical needs. (Spector, 2000; Varma *et al.*, 2005).

Reduction in contrast sensitivity and glare

Cataract patients may have trouble seeing things in intense sunlight and may experience night vision loss. All cataracts diminish contrast sensitivity, but posterior subcapsular cataracts are the most severe. A modest degree of lens opacity causes light dispersion toward the front of the lens, causing glare (Truscott, 2005).

Myopic shifting

Myopic shifting occurs naturally when the human lens ages. Lens opacification, especially in the nucleus area, promotes short sightedness (a myopic shift). Myopic shift improves myopia. Also known as second sight (Spector, 2000).

Color shift and double vision

Double vision in one eye and change in color vision are the common symptoms reported in all types of cataracts. Cortical spoke cataract causes monocular diplopia (double vision in one eye). Water clefts produce radial wedges in cortical spokes, containing a fluid with a lower refractive index than the lens. Due to lens opacity, the light entering the lens is not bent equally.

13. OBSERVATION AND ASSESSMENT OF CATARACT

Slit-lamp biomicroscope is a binocular optical device used to diagnose cataracts. The eye lens is inspected with extreme magnification and a tiny slit. A funduscope is another optical tool for studying the lens and retina. Cataracts can be immature, mature, or hypermature. A hypermature cataract is a liquefied surface that seeps through the lens surface. This leaked substance may irritate other eye tissues (Behndig *et al.*, 2001).

Nuclear cataract

The central lens nucleus density rises in a nuclear cataract and eventually becomes yellow or brown at advanced stages.

Cortical cataract

In this type, the lens transparency changes at the peripheral (or cortex) region. This type of lens transparency changes at the cortex (periphery). Water diffusion from the lens cortex generates pockets that form vacuoles under the lens capsule. The vacuoles eventually fill with fluid.

Posterior subcapsular cataract

The posterior subcapsular cataract is distinct from the nuclear or cortical areas. In the posterior subcapsular cataract, granules, and vacuoles develop in front of the posterior lens capsule. They are rare, but their development and severity can be more severe than common cataracts because enlarged cells deposit toward the lens's rear where granules develop.

14. PREVENTION OF CATARACT

Generally, Drugs are being used to prevent the onset and progression of cataracts from interacting at the level of altered lens metabolism and physiology (Harding, 2001). The number of anti-cataract agents proven to be effective in vitro, in vivo, and epidemiological studies can be broadly classified into the following categories:

Aldose reductase inhibitors (ARI)

Aldose reductase inhibitors (ARI) include botanical extracts, animal tissues, and small chemicals. Plant flavonoids like quercitrin and genistein slow the development of diabetic cataracts in diabetic rats. Intrinsic ARI comprising human kidney and bovine lens extracts were injected into rats' lenses to decrease polyol levels (Kador *et al*., 2001. In a study by Matsumoto *et al*., 2008 it was reported that Compared to untreated diabetic rats, sorbitol buildup in the lens was reduced.

Non-steroidal anti-inflammatory drugs

The idea of using aspirin to prevent cataracts arose from its usage in rheumatoid arthritis and diabetic patients. NSAIDs' anti-cataract action has been attributed to several causes. Lens protein acetylation, glycosylation inhibition, and carbamylation (Matsumoto *et al*., 2008).

Agents acting on Glutathione (GSH)

Glutathione (GSH) is needed to neutralize free radicals. GSH is produced in two ATP-dependent stages within the lens cell cytoplasm. Melatonin, a free radical scavenger, has been proven to boost GSH synthesis. This is useful in preventing cataracts. (Drel *et al*., 2008; Kador *et al*., 2006)

Vitamins

Vitamins such as Vitamin C and E can act as antioxidants and UV filters; this helps preserve normal lens physiology. Lens Ascorbate level was observed to be reduced in Vitamin C insufficiency, thus showing susceptibility to cataracts. In guinea pigs, Ascobate therapy

reduced galactose-induced cataractogenesis Vitamin E has been shown to protect against galactose, steroid, and UV-induced cataracts (Yoshida *et al*., 2004; Varma *et al*., 2005).

Minerals

Micronutrients including zinc, copper, and manganese can prevent cataract development by lowering the free radical burden. Metal protein and superoxide dismutase catalysis require copper and zinc (SOD). Zinc and copper plasma levels were found to be low in cataract patients. (Meyer *et al*., 2005).

Antioxidants

Antioxidants are essential preventive agents against oxidation-induced cataracts. Carotenoids, natural lipid-soluble antioxidants available in dietary supplements, have been shown to decrease cataract incidence. Curcumin, an antioxidant phytoconstituent in turmeric, is an active phytoconstituent. Stobadine, a new synthetic pyridoindole, is an effective antioxidant in lipid environments (Kador *et al.*, 2006; Wolf *et al*., 2007)

Use of herbal drugs

For many years, natural resources have been employed to avoid cataracts. This illness has been proven to be delayed by several therapeutic herbs and their preparations. Green tea (*Camellia sinensis*) has anti-cataract properties due to its antioxidant content. Green and black teas have hypoglycemic properties that slow diabetic cataractogenesis. The flavonoids in *Emilia sonchifolia* inhibit lens opacification and regulate oxidation.

Other anticataract agents

Numerous substances with diverse chemical structures and properties have been investigated to be prophylactic in treating cataracts. Iton, a polyherbal mixture containing over 19 herbal medicines, functions as an antibacterial and non-irritant lotion without harming the eye tissues. The antioxidant and anti-cataract properties of alpha-lipoic acid, Pantethine, DL-penicillamine, and Deferoxamine have been reported, but none have been tested clinically.

15. CATARACT TREATMENT

Cataracts cannot be fixed with glasses or contact lenses. Thus far, cataract surgery has been the most effective.

Cataract Surgery in Diabetic Patients

Nowadays, most cataracts are treated by phacoemulsification (Lin, 2004). But it wasn't until 1996 that this approach became generally adopted. It reduces postoperative irritation and astigmatism, speeds up visual recovery, and reduces capsulotomy with contemporary foldable lenses (Babizhayev, 2002). But diabetic people may have worse vision than non-diabetics.
Krepler *et al*. found that in 50 individuals with type 2 diabetes, 20% of the operated eye and 16% of the non-operated eye had diabetic retinopathy progression. They were statistically

different from eyes without preoperative retinitis pigmentosa—retinopathy associated with worsening visual acuity. (Krepler *et al*., 2002; Schmier *et al.*, 2007; Hong *et al.*, 2009).

16. CONCLUSION

In older people, cataract is one of the most prevalent causes of blindness. It can also impact kids with metabolic issues or other hereditary issues. Since diabetes is an underlying factor for cataract formation, diabetic patients should work closely with their doctors to maintain healthy blood glucose levels. Having the proper glucose levels might help keep the eyes healthy.

Anticataract medication should delay cataract development; thus, it may require extended therapy. Cataracts in animals can be prevented by glycation inhibitors, antioxidants, and ARIs. Detailed scientific studies are needed to ascertain the efficacy of some of these ethnic herbal drugs used in treating cataracts. Also, it is necessary to investigate further the mechanisms of action of NSAIDs and its usage as an anticataracts in various circumstances and experimental models.

Futhermore, novel techniques such as the siRNA technique should not change the interest of pharmaceutical firms' in developing medicines to cure lens opacifications. Lastly, it is expedient to explore how fast novel biochemical methods can fix or halt pathological diseases like cataracts in time.

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