

## **Therapeutic Role of carbonic anhydrase inhibitors in Treatment of Glaucoma: A Review**

### **Abstract**

eye disease may be a cluster of inveterately progressive disorders of the nervus opticus . during this article , I gift the medicine, Pathophysiology , risk factors , ophthalmic examination and therapeutic role of carbonaceous anhydrase inhibitors in treatment of eye disease . In European countries , the prevalence of eye disease is a pair of 93% among persons aged 40-80 years , reaching ten you tired of persons over ninety years old-time. There area unit many differing types of eye disease , and that they are classically divided into classes of open – angle and closed – angle eye disease. Use of topical selective or non selective beta- blockers are used in treatment of eye diseases. Second – line drug of alternative embody alpha – agonists and topical carbonaceous anhydrase inhibitors. Parasympathomimetic drugs, most ordinarily alkaloid, area unit thought-about third – line treatment . For patients United Nations agency don't reply to antiglaucoma remedy , optical laser incisional and tubeculoplasty surgery area unit more ways that may be accustomed lower the pressure. The inhibitors area unit used medication in treatment of symptom coronary failure , brain disease and hypoxia conjointly. A Corollary of Friedenwald's construct of hydrogen carbonate secretion within the formation of liquid body substance is that inhibition of the protein carbonaceous anhydrase could be expected to decrease the speed of secretion and lower IOP . The carbonaceous anhydrase matter, Diamox ( acetazolamide) is employed in treatment of eye disease. Preliminary trials of Diamox in rabbits created definite lowering of pressure to once ten to one hundred mg. carbonaceous anhydrase inhibitors diminish ocular high blood pressure in glaucomatous patients by reducing the hydrogen carbonate formation.

Keywords – acetazolamide, beta-adrenergic blocking agent, autacoid , antiglaucoma, Diamox

Introduction- eye disease is leading reason for international irreversible cecity. associate calculable fifty seven.5 million folks worldwide area unit suffering from primary open angle eye disease with international prevalence of two.2%. In Europe, 7.8% million folks area unit suffering from POGA and total prevalence is a pair of 5.1%. On the idea of accessible knowledge, there area unit or so eleven.2 million folks aged forty years and older with eye

disease in India. The calculable range with primary angle – closure eye disease is a pair of 54 million. Those with any style of primary angle-closure unwellness might compromise twenty seven.6 million persons. Eye disease may be a cluster of ailment that dissent in their pathophysiology risk factors, presentatios, therapy and prognosis. Their common feature is progressive deteoration of the cranial nerve, with loss of retinal bodily structure cell, cutting of its retinal nerve fibre layer and continuous ongoing unearthing of the blind spot. it's related to hyperbolic pressure that was appericated before long once Arminius Von Hemholtz fictitious the ophthalmoscope in 1850. once eye disease is left untreated, patients might step by step expertise visual view loss. it's second leading reason for cecity round the globe. There area unit 3 forms of eye disease – nonheritable, primary, secondary and absolute eye diseases. Open angle and closed angle are 2 varities of eye disease. The open- angle eye disease involves, iris in the right position, and therefore the uveoscleral voidance canals area unit clear. however the fibrous tissue meshing isn't exhausting properly. In closed – angle eye disease, the iris is squeezed against tissue layer, obstruction the uveoscleral drains and fibrous tissue meshing. The clinical identification of eye disease needs assessment of the anterior ocular section with the help of slit lamp biomicroscopy , that permits a pratician the acknowledging signs of conditions that may manufacture elevated IOP. once mensuration of IOP, the specialised chromatic lens known as a gonioscope are employed to look whether or not the angle is physically closed or open. The sole treatment that has been proven to be efficacious and is usually accepted for bar of the disease continuation is brought down of the pressure. The pressure in open angle glaucoma is reduced by autacoid analogs, beta-blockers, alpha a pair of -adrenergic agonists, carbonaceous anhydrase inhibitors area unit . Autacoid analogs like ( bimatoprost , latanoprost, travoprost) followed by beta blockers (levobunolol, beta blocker carteolol) alpha a pair of – adrenergic agonists like (brimonidine , apraclonidine) and carbonaceous anhydrase inhibitors like(brinzolamide , dorzolamide ) are used to lower IOP according to network meta- analysis. In, 1970's miotics were commonplace antiglaucoma medication. at the side of this, a spread of optical maser and surgical choices also are accustomed win the target IOP. optical maser medical aid could also be thought-about as a additional if native treatment doesn't adequately lower the IOP. It ends up in a moderate lowering of the IOP by approach of hyperbolic liquid body substance outflow once optical maser trabeculoplasty or diminished liquid body substance production once cyclophotocoagulation. Surgery is indicated if medical procedure treatment choices area unit scant to lower the IOP to the target pressure . Minimally filtering , invasive and non-filtering forms of eye disease incision area unit out there. Here carbonaceous Anhydrase

inhibitors diminish ocular high blood pressure in patients of glaucoma by reducing the speed of hydrogen carbonate production and therefore , the secretion of liquid body substance. they're either used alone or together with alternative medication like adrenergic agonists\ antagonists .

Background – As eye disease is second leading reason behind sightlessness in world and carbonous anhydrase inhibitors have shown promising ends up in lowering down the pressure level created a lot of analysis to be done on medication associated with this category.

Objective- To review the articles associated with the therapeutic approach of carbonous anhydrase towards the treatment of eye disease.

Main text – eye disease a neurodegenerative disorder, will occur at any age.

**PATHOPHYSIOLOGY** -The neural structural cells of retina are neurons of the central systema nervosum that receives signal from the receptors that are sensitive to light, processes, and transfer them in axons by second cranial nerve to any centres within the brain .These nerve fibre run from the neural structure cell nuclei within the membrane to optic disk then beside to the retinal vessels through plate cribrosa, which is a sieve- like structure composed of albuminoid. Behind the cribrosa , the axons are encircled by medullary sheath , that continue because of the second cranial nerve. Increased IOP, low intromission pressure and less cerebral body fluid pressure will increase the gradient across plate cribrosa and lead to papillose hypoperfusion, resulting in structural exchange and transforming of the cribrosa and to weakned nerve fibre transmit within the second cranial nerve fibres.[1] In open – angle eye disease the spores within the anterior region of the plate cribrosa are elongated.. The progressive loss of retinal neural structure cells results in continous impairment of the field of vision, usually starting within the mid- fringe then advancing till solely a central island of intact vision remains. [2] the everyday course of open-angle glaucoma progresses perniciously over decades. Unless eye disease is related to significantly elevated IOP, it is not related to agony till the malady is subtle advanced, for many patients the malady is subtle in onset with a protracted and imperfectly outlined preclinical test. [3] The pathogenesis of glaucomatous damage is concerned with factors affecting nerve fiber health , with each factor

being interlinked in its effects to all others . The two main factors are- Mechanical changes due to raised Intraocular pressure.

Altered vascular perfusion of the optic nerve head.

It is believed that patients with primary open- angle glaucoma have chances of damage , because of presence of openings in the cribrosa that allow greater mechanical displacement of the nerve fibres coursing through.

ETIOLOGY-Etiological causes of eye disease embody trauma, contusion, inflammation, intraocular tumors and retinal anemia . Several medication will set off angle closure in patients UN agency are mechanically susceptible to the current condition.[4], and a few of medicine will manufacture bilateral angle closure eye disease albeit patient doesn't have antecedent slender retailers within the filtration equipment.

OPHTHALMIC EXAMINATION- The diagnosis is made after looking for a combination of symptoms and sign . The result as POGA can be made if at least two of the abnormalities are detected .In, PACG the presence of raised intraocular pressure is enough to make a conclusion of eye disease.In eye disease, Snellen acuity is conserved till the malady is progressed. In progressed malady, affected are allowed to browse the chart a bit slowly or move one's head in order to decide to see round the fault within the field of vision. Till the malady is advanced the Red – inexperienced color vision , which is recorded with Ishihara plates . On the opposite side, blue–yellow color vision, which is never taken down outside the clinical analysis circles, has to be rumored to slow down fast within the malady method. The second cranial nerve signify the afferent branch of the aperture miosis, and the corticoefferent branch is carried by sympathetic and parasympathetic nerves to the pupil[5]. This is a automatic act is accordant, which means that if the reflex is set off in one's eye, each pupil contract because of spat of the aperture miosis within the neural structure. Therefore unilateral or markedly uneven eye disease doesn't alter the pupil size however it'll manufacture Associate in Nursing afferent aperture defect on swinging electric lamp take a look at. Associate in Nursing correct designation of eye disease subtype needs careful evaluation of the anterior phase of eye for pathological signs that are either a result of or a proof for increased IOP. ] The pathogenesis of glaucomatous damage is concerned with factors affecting nerve fiber health , with each factor being interlinked in its effects to all others . The two main factors are- Mechanical changes due to raised Intraocular pressure.

. Unless eye disease is related to significantly elevated IOP, it is not related to agony till the malady is subtle advanced, for many patients the malady is subtle in onset with a protracted and imperfectly outlined preclinical test.

The progressive loss of retinal neural structure cells results in continuous impairment of the field of vision, usually starting within the mid- fringe then advancing till solely a central island of intact vision remains

Gonioscopy is necessary technique for satisfying glaucomas as open – angle and closed – angle varieties] The pathogenesis of glaucomatous damage is concerned with factors affecting nerve fiber health , with each factor being interlinked in its effects to all others . The two main factors are- Mechanical changes due to raised Intraocular pressure.

The neural structural cells of retina are neurons of the central systema nervosum that receives signal from the receptors that are sensitive to light, processes, and transfer them in axons by second cranial nerve to any centres within the brain.

The pathogenesis of glaucomatous damage is concerned with factors affecting nerve fiber health , with each factor being interlinked in its effects to all others . The two main factors are- Mechanical changes due to raised Intraocular pressure.

MOA OF element ANHYDRASE INHIBITORS -The chemistry and physiology of element anhydrase square measure revived in regard to medical specialty progress within the development of antibacterial inhibitors. The neural structural cells of retina are neurons of the central systema nervosum that receives signal from the receptors that are sensitive to light, processes, and transfer them in axons by second cranial nerve to any centres within the brain .These nerve fibre run from the neural structure cell nuclei within the membrane to optic disk then beside to the retinal vessels through plate cribrosa, which is a sieve- like structure composed of albuminoid. element anhydrase square measure is prohibited primarily by 2 important categories of compounds: the metal complexing inorganic anions and unsubstituted sulphonamides .The first form of inhibition was vital for understanding intimately the chemical action and repressing mechanism , whereas the second crystal rectifier to the event of many categories of medical specialty agents. Sulphonamides represent the most category of CA inhibitors , that cohere to the metal particle from the catalyst situation. The physiology of body fluid formation with reference to particle transport is vital and key event is that the chemical action formation of  $\text{HCO}_3^-$  from carbon dioxide and  $\text{OH}^-$ . The freshly shaped  $\text{HCO}_3^-$  is connected to  $\text{NA}^+$  and movement of fluid to provide body fluid. The pressure is

lowered by Inhibition of  $\text{HCO}_3^-$  synthesis sulfonamides which reduces binary compound formation.[6]

At least 3 isoforms of CA II, IV, XII square measure chosen by the antibacterial inhibitors, a number of these are square measure of clinically used medication. Acetazolamide, Methazolamide and dichlorophenamide square measure initial generation CA inhibitors still used as general medication for management of this illness. The second class of inhibitors include Dorzolamide and Brinzolamide are getting used locally as eye drops , with less aspect effects in contrast to the primary class medication. Exploitation tail approach has developed third generation inhibitors., however they failed to reach the clinics nevertheless. The foremost hopeful of such derivatives square measure the sulfonamides integrate either with gas cathartic moiety or hybrid medication having autacoid F agonist moieties in the molecules or tails.[7] element anhydrase inhibitors is also administered through IV routes topical or oral . Samples of presently on the market medication square measure acetazolamide, brinzolamide, ethoxzolamide and zonisamide. used for eye disease divide into topical and general subgroups division is done under the CAI medications. dorzolamide and brinzolamide together along with topical element anhydrase inhibitors, will reach the membrane through tissue layer perforation.

Several medication will set off angle closure in patients UN agency are mechanically susceptible to the current condition.[4], and a few of medicine will manufacture bilateral angle closure eye disease albeit patient doesn't have antecedent slender retailers within the filtration equipment.

- The diagnosis is made after looking for a combination of symptoms and sign . The result as POGA can be made if at least two of the abnormalities are dected .In, PACG the presence of raised intraocular pressure is enough to make a conclusion of eye disease. These medications is also used as a single drug however square measure usually employed in combos with alternative eye disease medications. Dorzolamiode complex preparation is out there as two answer and brinzolamide as I Chronicles suspension. The counseled indefinite quantity for medications is one call each eyes 3 times daily. Acetazolamide is out there generically beneath the name Diamox in one hundred twenty five, 200, five hundred mg tablets. Patients with eye disease like glaucoma might take approximately 250 mg to a thousand mg per day.

Methazolamide is out there in twenty five mg and fifty mg tablets. The counseled dosing for eye disease is fifty to a hundred mg doubly daily.[8] Recommendations for patients take element anhydrase inhibitors embrace potable at the time of taking the drug to prevent formation of urinary organ stone thanks to inflated urinary alkalinization.[9] – As eye disease is second leading reason behind sightlessness in world and carbonous anhydrase inhibitors have shown promising ends up in lowering down the pressure level created a lot of analysis to be done on medication associated with this category.

- The diagnosis is made after looking for a combination of symptoms and sign . The result as POGA can be made if at least two of the abnormalities are dedcted .In, PACG the presence of raised intraocular pressure is enough to make a conclusion of eye disease.

Novel bi-functional compounds with gas – cathartic moiety absolute to a dorzolamide platform were conjointly examined. Many compounds were produced and their action as fastidious element anhydrase inhibitors was evavulated inside a cell on recombinant hcA kind II,I , IV catalyst isozymes wherever they showed totally unlike degrees of efficiency and property to hcA II A high resolution X- ray crystal structure for the CA II adduct with eight, confirmed high attachment of this category of compounds for this catalyst. Several medication will set off angle closure in patients UN agency are mechanically susceptible to the current condition.[4], and a few of medicine will manufacture bilateral angle closure eye disease albeit patient doesn't have antecedent slender retailers within the filtration equipment .Compound four and six exerted strong IOP lowering effects , thereby employed in treatment of eye disease.[10]

Carbonous Anhydrase inhibitors might have several adverse effects conjointly, together with change in style, abdominal pain, diarrhea, fatigue ,vomiting, symptom and headache.[11-16]

Sulphonamide element anhydrase inhibitors also are helpful as diuretics and helpful in treatment of altitude sickness, peptic ulceration, symptom coronary failure and neurologic disorders.

**CONCLUSION-** The symptomatic analysis of disease rests on many aspects, all of that ought to be thought of for introducing the designation and deliver the products the normal target pressure. on an individual basis tailored pressure – lowering treatment got to be evaluated oftentimes thus on attenuate the possibility of progression. – As eye disease is second leading

reason behind sightlessness in world and carbonous anhydrase inhibitors have shown promising ends up in lowering down the pressure level created a lot of analysis to be done on medication associated with this category. the possibility and edges of each kind of treatment should be rigorously thought of to maximize the treatment's edges whereas minimizing adverse effects.

#### **COMPETING INTERESTS DISCLAIMER:**

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

#### **REFERENCES-**

1. Masini E, Carta F, Scozzafava A, Supuran CT. Antiglaucoma carbonic anhydrase inhibitors: a patent review. Expert opinion on therapeutic patents. 2013 Jun 1;23(6):705-16.
2. Supuran CT, Altamimi AS, Carta F. Carbonic anhydrase inhibition and the management of glaucoma: a literature and patent review 2013-2019. Expert opinion on therapeutic patents. 2019 Oct 3;29(10):781-92.

3. Yadav KS, Rajpurohit R, Sharma S. Glaucoma: current treatment and impact of advanced drug delivery systems. *Life sciences*. 2019 Mar 15;221:362-76.
4. Miglior S, Zeyen T, Pfeiffer N, Cunha-Vaz J, Torri V, Adamsons I. 2005. Results of the European Glaucoma Prevention Study. *Ophthalmology* 112: 366–375
5. Bianchi-Marzoli S, Rizzo JF III, Brancato R, Lessell S. 1995. Quantitative analysis of optic disc cupping in compressive optic neuropathy. *Ophthalmology* 102: 436–440
6. Maren TH. Carbonic anhydrase: General perspective and advances in glaucoma research. *Drug Development Research*. 1987;10(4):255-76.
7. Scozzafava A, Supuran CT. Glaucoma and the applications of carbonic anhydrase inhibitors. *Carbonic Anhydrase: Mechanism, Regulation, Links to Disease, and Industrial Applications*. 2014:349-59.
8. Supuran CT. Drug interaction considerations in the therapeutic use of carbonic anhydrase inhibitors. *Expert opinion on drug metabolism & toxicology*. 2016 Apr 2;12(4):423-31.
9. Detailed insight for future development as anti-glaucoma agents. *Bioorg Chem*.2020
10. Steele RM, Benedini F, Biondi S, Borghi V, Carzaniga L, Impagnatiello F, Miglietta D, Chong WK, Rajapakse R, Cecchi A, Temperini C. Nitric oxide-donating carbonic anhydrase inhibitors for the treatment of open-angle glaucoma. *Bioorganic & medicinal chemistry letters*. 2009 Dec 1;19(23):6565-70.
11. Mincione F, Scozzafava A, Supuran CT. The development of topically acting carbonic anhydrase inhibitors as antiglaucoma agents. *Current topics in medicinal chemistry*. 2007 May 1;7(9):849-54.

12. Gajbhiye, Varsha, and Yeshwant Lamture. "Minoxidil a Youth Elixir for Eyebrow Hypotrichosis." *JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH* 14, no. 2 (February 2020). <https://doi.org/10.7860/JCDR/2020/42801.13474>.
13. Kedia, Palak, and Bhushan Madke. "Unilateral Molluscum Contagiosum Following Eyebrow Grooming." *JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH* 13, no. 11 (November 2019): WD01–2. <https://doi.org/10.7860/JCDR/2019/42600.13283>.
14. Khasbage, Suwarna Dangore, and Arvind S. Bhake. "Cervical Lymphadenopathy in a Dental Patient: An Eye Opener Case Report." *SPECIAL CARE IN DENTISTRY* 39, no. 1 (February 2019): 59–64. <https://doi.org/10.1111/scd.12336>.
15. Laad, Gaurish, Bhushan Madke, and Balkrishna Nikam. "Cirroid Aneurysm of Upper Eyelid." *JOURNAL OF DERMATOLOGY DERMATOLOGIC SURGERY-JDDS* 23, no. 2 (December 2019): 109–10. [https://doi.org/10.4103/jdds.jdds\\_30\\_19](https://doi.org/10.4103/jdds.jdds_30_19).
16. Mahatme KG, Deshmukh P, Sable P, Chakole V. Ultrasonography: The Third Eye of Anaesthesiologist. *JOURNAL OF PHARMACEUTICAL RESEARCH INTERNATIONAL*. 2021;33(37A):235–8.

UNDER PEER REVIEW