ISSN NO: 2770-2936
Date of Publication:30-11-2022

# Evaluation of Antiproliferative Activity of Hydroxypropyl Methylcellulose in Antiglaucomatous Surgeries

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**Abstract:** Glaucoma today remains an urgent problem of modern ophthalmology. Despite some progress in treatment methods, a high percentage of blindness, low vision and primary disability in this disease remains. The biological basis of glaucoma is poorly understood, and the factors contributing to its progression are not fully characterized. It is not possible to completely get rid of glaucoma today, but with correct and timelytreatment, it is possible to slow down the progression of the disease. The choice of the method of therapy directly depends on the severity of the pathological changes, the symptoms present, the form of glaucoma and consists in the use of medications, surgical interventionor laser therapy. Thex-surgical method of treating glaucoma remains the leading, but at the same time associated with some complications. This article considersthe complications of surgical intervention in glaucoma and the possibility of preventing them, in particular, the role of viscoelastics.

**Keywords:** glaucoma, hydroxypropyl methylcellulose, viscoelastic (VE), antiglaucomaatous surgery, drainages, intraocular pressure (IOP),open-angle glaucoma, angle-closure glaucoma, ciliochoriodeal detachment (CWC)

Glaucoma is a multifactorial pathological process, and its pathogenesis is not fully understood. In 2010, 2.1 million people worldwide went blind due to glaucoma. The prevalence of open-angle glaucoma increases with age, from 0.4% aged 40-44 years to 2.7% aged 70-74 years and 10% over 90 years in people of European descent. Men get sick more often than women. There are also differences in detection among different ethnic groups, in particular, in people of African descent, the prevalence of glaucoma is 2.8 times higher than in Europeans, while angle-closure glaucoma and normal-pressure glaucoma are more common in Asians. Congenital glaucoma and juvenile glaucoma in general are rare.

Although much attention is paid to the role of intraocular pressure (IOP), other factors such as abnormal ocular blood flow, abnormal structural susceptibility of the ethmoid plate, low intracranial pressure, and mitochondrial dysfunction may also be involved. The elevated intraocular pressure is thought to damage the ethmoid plate, resulting in a loss of normal structural and metabolic supportand axons of retinal ganglion cells and impaired axoplasmic transport. Reduced neurotrophic signaling to retinal ganglion cells likely leads to the initiation of apoptosis. Reduced IOP is the only proven means to stop or slow down progression of glaucoma. According to the age of patients, glaucoma can be divided into congenital (up to 3 years), infantile (from 3 to 11 years), juvenile (from 11 to 35 years) and adult glaucoma (over 35 years). Congenital glaucoma is caused by defects in the drainage system of the eye or the angle of the anterior chamber. Manifested in the first three years of a child's life, heredity is recessive. The basis forthe pathogenesis of the disease is the dysgenesis of the angle of the anterior chamber and an increase in IOP. Tothe line symptoms are diverse: photophobia, blepharospasm, lacrimation, an increase in the size of the eye, swelling of the cornea and an increase in its size, atrophy of the disc of the opticnerve with excavation. Infantile glaucoma occurs in children aged 3-10 years, heredity and pathogenesis are the same as with simple congenital glaucoma, intraocular pressure is increased, the size of the cornea and eyes are not changed, the excavation of the optic disc increases according to theprogression of glaucoma. Juvenile glaucoma occurs at the age of 11-35 years, heredity is associated with abnormalities in the chromosome, goniodisgenesis and trabeculopathy play a leading role in the pathogenesis of the disease. IOP is elevated, changes in the optic nerve disc and visual functionsflow through the glaucoma type. Adult glaucoma develops in persons older than 35 years and is a chronic pathological process characterized by a triad: a constant or periodic increase in IOP, characteristic changes in the visual field and marginal excavation of the optic nerve, in the absence of other ocular diseases or congenital pathologies. Also distinguish glaucoma of

ISSN NO: 2770-2936
Date of Publication:30-11-2022

normal pressure, which manifests itself in two of the main symptoms of the three mentioned above. According to the mechanism of increased intraocular pressure, glaucoma is divided into open-angle glaucoma (OUG) and closed-angle glaucoma (OUG), each andso of them further divided into primary or secondary, which indicates the absence or presence, respectively, of other clinically identifiable eye or systemic disorders that explainglaucoma. Most eyes with glaucoma have increased resistance to outflow through the trabecular network, which is usually associated with an increase in IOP. In eyes with open-angle glaucoma, this increase in resistance occurs in the absence of a clinically visible obstruction in the corner. In contrast, corner closure refers to an anatomical configuration in which the peripheral iris contacts the trabecular reticulum, thereby preventing the outflow of aqueous humor. There is a closure of the angle, which is called pupillary blockade, a condition in which abnormally tight contact between the iris and the lens can cause increased resistance to the outflow of fluid through the pupil. [1,2,3

A mandatorymeasurement of IOP (tonometry) in the initial diagnosis. Currently, intraocular pressure is the only modifiable risk factor for the onset and progression of glaucoma. Corneal thickness and curvature should be measured simultaneously to determine the likelihood that IOP results will be artificially high or low. Due to the fact that IOP changes during the course of a day, the wire measurementsare taken at different times of the day for the accuracy of the overall picture.

Gonioscopic examination of the angle of the anterior chamber during the initial diagnosis provides information about the pathogenesis of the disease. Visual fields also need to be examined to assess the extentof functional impairment associated withoptic nerve fibers. Visual field results may vary depending on the patient's concentration and cooperation, so identifying progression may not be easy. In this regard, patients are advised to examine the field of vision at least three times during the first year after diagnosis.

The basis for the diagnosis of glaucoma is the study of the fundus - the disc of the optic nerve and the layer of nerve fibers of the retina. Glaucomatous changes are manifested by the loss of neuroretinal rim tissue and the expansion of the excavationand optic nerve, not the physiological divergence of the excavaciand the optic nerve, thinning of the layer of nerve fibers of the retina and atrophy of the parapapillary tissue.

Optical coherence tomography allows you to examine the state of the optic disc, or ratherto measure the layer of nerve fibers of the retina and neuroretinal rim. The main goal of glaucoma treatment is to achieve a reduction in IOP. Conservative treatment consists in local instillation of drops. Different classes of drugs are available for topical use to reduce IOP. They differ in mechanisms of action, degree of reduction in IOP, dosage and side effects. IOP is most reduced by prostaglandin analogues, followed by beta-blockers, alpha2 adrenomimetics and carbonic anhydrase inhibitors.

Analogues of simpleandglandins are usually prescribed for initial treatment and used once a day, in the evening. These drugs improve uveoscleral and trabecular outflow and thereby reduce intra-eye pressure. Their side effects include conjunctival hyperemia, increased eyelash growth, decreased periorbital fiber and increased pigmentation of the iris and skin of the eyelids. Systemic conditions limiting the use of prostaglandin analogues include bronchial asthma, severe cardiovascular disease, and liver and kidney disease.

Analternative istopical beta-blockers. They are usually used twice a day they reduce intraocular pressure, reducing the productionof aqueous humor. The main side effect of beta-blockers is dry eyes or exacerbation of existing dry eye disease. Systemic contraindications include bronchial asthma, sinus bradycardia, congestive heart failure, severe allergic rhinitis, and beta-blockers can also aggravate hyperglycemia. and mask the symptoms of hypoglycemia in patients with diabetes mellitus.

Alpha2-adrinometics reduce the secretion of aqueous humor anduw are caused by uveoscleral outflow. Local side effects include conjunctival glaciation, intolerance in one third of patients. Caution should be administered to patients with bradycardia, arterial hypotension, atherosclerosis and impaired liver and kidney function.

Local carbonic anhydrase inhibitors also reduce the production of aqueous humor. Local undesirable effects include lacrimation, burning, and decompensation of the corneal endothelium. These drugs can be combined, taking into account their side effects and the state of healthof patients. Numerous studies show that patients tend to poorly adhere to local antiglaucomatous therapy. If pressure reduction is not achieved with the help of conservative treatment, laser therapy can be considered as complementary. Laser therapy

ISSN NO: 2770-2936
Date of Publication:30-11-2022

usually leads to a moderate decrease in IOP by increasing the outflow of aqueous humor after laser trabeculoplasty or reducing the production of aqueous humor after cyclophotocoagulation.

Surgical treatment of glaucoma today is used with insufficient effectiveness of conservative methods and laser therapy. Trabeculectomy is the most commonly performed incisional surgical procedure to reduce intraocular pressure. It consists in excising a smallpart of the trabecular network and adjacent corneosclerosing tissue to ensure drainage of aqueous humor from inside the eye under the conjunctiva, where it is absorbed. Anti-scar agents are often applied to the surgical area to reduce the fibroproliferative reaction and increase the likelihood of success of surgery, but they can increase the incidence of complications such as infections and damage due to very low intraocular pressure. An alternative to trabeculectomy are devices that drain aqueous moisture into the outer reservoir, which are just as effective at reducing intraoculard.arrhillation. Several alternatives to these procedures have been proposed and are being explored. These so-called minimally invasive surgeries for glaucoma potentially carry a lower risk of complications.

To date, these procedures do not have the same effectiveness in reducing intraocular pressure as trabeculectomy; however, they may be indicated in individual cases when the risk-benefit ratio is more favorable than with trabeculectomy. A recent meta-analysis comparing trabeculectomy with non-penetrating surgeries (deep sclerectomy, viscocanalostomy, and canaloplasty) concluded that while trabeculectomy is more effective at relieving pressure, it carries a higher risk of complications. [4,5,6]

Postoperative complications of antiglaucomatous surgeries include complications such as loss of the vitreous body, anterior small camera syndrome, hypertension, suprahoroidal hemorrhage, serous choroidal detachment, cataract progression, hypotonic maculopathy, vitreous hemorrhage, retinal detachment, inflammation of the filtration pillow, iridocyclitis and endophthalmitis. Prolonged hypotension of the eye can activate the proliferative process inthe newly created outflow pathways of the operation, therebyreducing the hypotensive effect of the operation. Awareness of these complications is necessary because their proper and timely treatment can preserve vision in the already affected eye. [7]

The history of viscosurgery dates back to the middle of the last century. It is believed that the greatest contribution to the creation and use of viscoelastics was made by Balazs [9, 10]. In 1958, he proposed the use of hyaluronic acid during the operation to eliminate retinal detachment as a replacement for the vitreous body, introducing it into the vitreal cavity [11], he also received a patent for Healon, a viscoelastic used to this day and is a kind of standard for new viscoprotectors. In 1977, Miller used sodium hyaluronate to implant an IOL in experiment [12], and in 1977. Feshner used it to maintain the depth of the anterior chamber. In 1979, Balazs proposed the term "viscosurgery" - manipulations using viscoelastic solutions to protect cells from mechanical trauma,rusting or creating spaces in tissues, separation, exposure of tissue surfaces. Until 2000, the term "viscoelastics" prevailed in foreign literature, which was later replacedby"ophthalmic viscoelastic device" (OVDD). ), literally - "ophthalmic viscoelastic device (instrument)", which emphasizes the breadth of functions of viscoelastics in surgery. Viscoelastics (VE) are pharmacologically inactive, transparent liquids with high viscosity and elasticity, simultaneously having the properties of gels and solids [13]. Their properties depend on the length of the polymer chain (molecular weight) and concentration, which determines their behavior during surgery. However, often viscoelastics with the same percentage of sodium hyaluronate may differ in the length of the polymer chain, the distribution of molecular weight and, accordingly, have different physical properties.

In ophthalmic surgery, VE perform various functions - create and maintain space, maintainpressure in the anterior and posterior chambers , stabilize tissues, divide the space of the anterior chamber and protect the corneal endothelium.

Due tothe relative simplicity of execution, pronounced and prolonged hypotensive effect, trabeculectomy in various modifications remains a popular antiglaucoma intervention. However, surgical depressurization of the eyeball, accompanied by prolonged hypotension, a small anterior chamber and the potential possibility of ciliochorioidal detachment (CWC), contributes to the development of a number of complications in the early and late postoperative Period. Attempts to intraoperatively maintain the volume of the anterior chamber and restore it after suturing the scleral flap, mainly, were limited to the use of physiological solution, sterile air, which quite easily leave the anterior cavity with external compression or progression of the CSO. The use of VE gave hope for stable control of the depth of the anterior chamber and

ISSN NO: 2770-2936
Date of Publication:30-11-2022

ophthalmotonus, both intraoperatively and within a few days after the intervention up to the self-healing of the viscoelastic through the surgical fistula. In 1980. Pape and Balazs, and later Blondeau (1984) confirmed the assumption of maintaining the desired anterior chamber volume with Healon after trabeculectomy [14,15,16]. Blondeau demonstrated that when using sodium hyaluronate at observational dates of up to 1 year and above visual acuity, hypotensionis less common, and ophthalmotonus is controlled better. Wilson and Lloyd (1986) analyzed the results of intraoperative use of Healon on the material of 119 operations, noting a significant reduction in the number of complications compared to the control group [17,18]. Thus, the level of postoperative hyphema with the use of VE was 3% versus 20% without its use. Wand (1988), Charteris (1991) and Barak (1992) noted the stability of the deep anterior chamber, in particular in the early period, namely during intraoperative administration of VE [19,20]. In addition to longer compensation for ophthalmotonus, Barak (1992) noted a lower percentage of endothelial cell loss after performing trabeculectomy with viscoelastic [18]. In a prospective study, Gulkilik described the beneficial effect of sodium hyaluronate in terms of the incidence of early postoperative complications of trabeculectomy. In the main group, complications such as hypotension, small anterior chamber and detachment of the choroid were observed significantly less often than in the control [21,22,23,24,25]. The use of viscoelastic drugs is one of the main ways to increase the effectiveness of penetrating operations and reduce the numberof complications, such as hyphema, hypotension, cilio-choriodal detachment in the postoperative period. Experimental and clinical studies have revealed the positive effect of intraoperative use in penetrating operations of viscoelastics based on sodium hyaluronate and methylcellulose. Intraoperative administration of viscoelastic drugs into the anterior chamber of the eye contributes to the prevention of hemorrhagic complications, a smooth decrease in intraocular pressure during surgery and the early postoperative period, a decrease in complications such as hypotension, small anterior chamber syndrome and CSC almost twice. Viscoelastic drugs with prolonged exposure in the anterior chamber are well tolerated by the tissues of the eye, without causing visible inflammatory or dystrophic changes in the intraocular structures and membranes of the eye. Alekseev I.B. et al. (2006) with intraoperative administration into the anterior chamber of 0.2-0.3 ml of viscoelastic (Chealon - 1% sodium hyaluronate), through a fistula in the sinustrabeculectomy zone, a decrease in the frequency of CVO by 7% compared with the control group without the introduction of viscoelastic, as well as a decrease in the frequency of hyphema by 1.5 times. The authors note the hemostatic and tamponing effect of viscoelastic on damaged vesselswhen performing iridectomy. Gavrilova I.A. et al. (2011), Onishchenko A.L. et al. (2006) also revealed a decrease in the frequency of CWC and hyphema up to 10% with the introduction of viscoelastic into the anterior chamber of the eye during penetrating operations.

The authors noted the absence of inflammatory activity and progression of cataracts, as well as a decrease in the frequency of formation of gonosynechia and cicatricial changes in the outflow pathways formed by the operation [8].

Studies show that, undoubtedly, viscoelastics in ophthalmic surgery, in particular in glaucoma surgery, play an important role in preventing intra and postoperative complications. Therefore, further studies of their properties are needed to improve the quality of surgical care provided to patients.

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