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ANALYSIS OF THE USE OF THE DRAINAGE IMPLANT HEALAFLOW IN SURGERY FOR PRIMARY OPEN-ANGLE GLAUCOMA

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Abstract*. Primary open-angle glaucoma (POAG) is a progressive optical neuropathy characterized by specific structural changes of the optic disc and visual field defects. Surgical treatment remains the gold standard when conservative therapy is ineffective, but postoperative fibrosis significantly limits the long-term efficacy of filtering surgeries. HealAFlow, an innovative injectable implant based on cross-linked hyaluronic acid, represents a promising solution to this problem. This review analyzes the current clinical data, mechanisms of action, comparative efficacy and safety of HealAFlow in POUG surgery.*

Keywords: *primary open-angle glaucoma, HealAFlow, trabeculectomy, deep sclerectomy, cross-linked hyaluronic acid, postoperative fibrosis.*

Introduction. Glaucoma represents one of the leading causes of irreversible blindness worldwide, ranking second in importance according to data from the World Health Organization (WHO). Among glaucoma-related diseases, primary open-angle glaucoma (POAG) is the most common form, characterized by chronic progressive damage to the optic nerve (ON) and typical peripheral vision loss [1].

The prevalence of POAG among the adult population over 40 years of age is approximately 2–3%, with its incidence significantly increasing with age. This is due to the accumulation of structural changes and a decline in the adaptive capabilities of ocular tissues. According to forecasts from international epidemiological studies, by 2040 the number of patients suffering from glaucoma will exceed 110 million people, with up to 70% of cases potentially remaining undiagnosed due to the latent, asymptomatic course of the disease at its early stages [2].

The main risk factors for the development of POAG include age over 40, the presence of a family history, ethnic origin (especially among the African race, in whom the risk of developing glaucoma is 4–5 times higher than in Caucasians), as well as elevated intraocular pressure (IOP) — the key pathogenic mechanism leading to damage to the optic nerve fibers. In addition, systemic diseases such as arterial hypertension and diabetes mellitus significantly affect the course and progression of glaucoma by contributing to microangiopathies and impaired blood flow in the optic nerve [2].

Among the main risk factors for the development of POAG are age over 40 years, the presence of a family predisposition, ethnic background (especially among the African race, in whom the risk of developing glaucoma is 4–5 times higher than in Caucasians), as well as elevated intraocular pressure (IOP) — the key pathogenic mechanism leading to damage of optic nerve (ON) fibers. Additionally, systemic diseases such as arterial hypertension and diabetes mellitus have a significant impact on the course and progression of glaucoma, contributing to microangiopathies and impaired blood flow in the optic nerve [2].

Geographical and ethnic characteristics of glaucoma prevalence play an important role in the epidemiology of the disease. In African countries and the Caribbean region, a high incidence of POAG is observed, which is directly related to genetic, socioeconomic, and medical factors, as well as to a low level of detection and treatment. In Asia and Latin American countries, POAG prevalence rates are at a moderate level. In developed regions of Europe and North America, there is a high level

of early detection and diagnosis of the disease, which is explained by the availability of specialized ophthalmologic care and regular screening programs; however, overall prevalence remains lower compared to African populations.

In the Republic of Uzbekistan, primary open-angle glaucoma (POAG) is also the dominant form among all diagnosed cases of glaucoma, accounting for 70–80%. The prevalence of this disease among individuals over the age of 40 is estimated at approximately 2.5–3.5%, which is consistent with global epidemiological data. Despite this, there remains a lack of public awareness regarding glaucoma, as well as limited access to specialized ophthalmological care, which often leads to diagnosis at later stages of the disease, when significant visual impairment has already occurred. These circumstances considerably complicate treatment and reduce the effectiveness of therapeutic interventions.

Surgical treatment of glaucoma becomes particularly important when conservative medical therapy proves ineffective — that is, when target intraocular pressure (IOP) cannot be achieved with hypotensive medications and disease progression continues. The primary therapeutic goal of surgical intervention is to stabilize and maintain IOP at a level that prevents further damage to the optic nerve and loss of vision. Indications for surgical treatment also include intolerance or allergic reactions to medications, as well as poor patient adherence to long-term drug therapy, which often hinders treatment success and necessitates alternative approaches.

Thus, considering the high prevalence of POAG, its clinical significance, and socioeconomic impact — particularly in the context of limited access to quality healthcare — the investigation of epidemiological characteristics, risk factors, and optimal treatment strategies for this disease represents a priority in contemporary ophthalmology.

The Evolution of Glaucoma Surgery Approaches: From Trabeculectomy to Minimally Invasive Procedures.

Over the past decades, surgical treatment of glaucoma has undergone significant transformation, evolving from traditional, relatively traumatic interventions to modern, less invasive and safer techniques. This progress has been driven by the need to improve intraocular pressure (IOP) control, reduce the risk of complications, and enhance patients' quality of life.

For a long time, trabeculectomy remained the "gold standard" of surgical treatment for primary open-angle glaucoma (POAG). This procedure effectively lowers IOP by creating an alternative outflow pathway for aqueous humor [8]. Despite its high efficacy, trabeculectomy is associated with a number of serious complications, such as hypotony, infection, scar tissue formation, and closure of the filtering bleb, which significantly limits its use and requires careful postoperative monitoring [3].

In cases where trabeculectomy is not feasible or proves ineffective, drainage implants are used. These devices provide an additional outflow pathway for aqueous humor, enabling IOP control in severe forms of glaucoma. The use of such implants expands surgical options but comes with its own technical challenges and associated risks.

Since the early 2000s, laser treatment methods—particularly selective laser trabeculoplasty (SLT)—have played an increasingly important role in the comprehensive management of glaucoma. SLT is a less invasive procedure that offers an alternative to medical therapy and traditional surgery at early stages of the disease. This method enhances the natural outflow pathways of aqueous humor without damaging tissue, thereby reducing the likelihood of complications.

The most significant progress in glaucoma surgery over the past 10–15 years has been the development of microinvasive surgical procedures, collectively referred to as MIGS (Minimally Invasive Glaucoma Surgery). MIGS is characterized by minimal tissue trauma, short recovery periods, and high safety profiles [12]. Within this concept, specialized stents and microshunts such as the iStent, XEN, and Hydrus are used. These devices are inserted into the natural drainage pathways or create new channels for aqueous humor outflow. Often, these procedures are performed concurrently with cataract surgery, allowing for a comprehensive approach to vision loss

management. MIGS is ideally suited for patients with early to moderate stages of glaucoma, providing an individualized treatment strategy based on disease severity, anatomical features of the eye, and comorbidities. The primary goal of modern surgical techniques is to achieve maximum IOP reduction with minimal complication risk [6].

One of the major challenges of conventional glaucoma surgery remains postoperative scarring, which can lead to closure of the surgically created drainage pathways and reduce the efficacy of the procedure. Fibrotic tissue formation is the main cause of surgical failure, including after trabeculectomy. To prevent excessive scarring, antifibrotic agents—most commonly mitomycin C (MMC) and 5-fluorouracil (5-FU)—have traditionally been used. Despite their effectiveness, these agents have significant toxicity and may cause complications such as scleral thinning, cyst formation, and infections, which limit their broader application [7]. In this regard, the need arose for the development of safer and more controllable methods to prevent fibrosis.

The key criteria included high biocompatibility, the ability to reduce inflammatory responses, prevent scar tissue formation, and at the same time ensure ease of administration and biodegradability without the need for surgical removal.

HealAFlow is an innovative bioresorbable gel implant developed as an alternative to traditional antifibrotic agents in glaucoma surgery. Created in the early 2000s by the Swiss company Anteis SA, this product has been integrated into modern ophthalmic surgical practice and is aimed at reducing postoperative fibrotic processes, thereby increasing the likelihood of a successful surgical outcome [4]. HealAFlow is administered into the subconjunctival or subscleral space during surgery, where it provides mechanical support to the filtering bleb and modulates fibrotic tissue formation, thereby improving the outflow of aqueous humor.

The main component of the product is modified hyaluronic acid (HA), cross-linked to form a viscous, transparent gel suitable for injection via a cannula [5]. HealAFlow's high biocompatibility minimizes immune responses and inflammation, while its biodegradation occurs over a period of 6–8 weeks, eliminating the need for surgical removal. During the resorption process, HA gradually releases water and breakdown products, hydrating surrounding tissues and creating favorable conditions for healing without excessive scar formation. Thus, the evolution of surgical approaches in glaucoma treatment reflects the ophthalmological community's effort to combine maximum therapeutic efficacy with minimal invasiveness and reduced postoperative risk. The emergence of microinvasive technologies and innovative biomaterials such as HealAFlow opens new prospects for improving the quality of surgical care for glaucoma patients and enhancing their visual outcomes.

Pathophysiological Rationale for Use. The primary pathogenic factor leading to failure of filtration surgery in glaucoma is subconjunctival fibrosis, which causes obliteration of the filtration pathway and, consequently, a reduction in surgical efficacy. HealAFlow addresses this issue comprehensively by performing several important functions. First, it creates a physical barrier between tissues, preventing their adhesion, thus preserving the space necessary for the formation of an effective filtering bleb. Second, due to the hyaluronic acid (HA) included in the gel, it regulates the inflammatory response — HA binds inflammatory mediators and inhibits fibroblast activity. Additionally, the product prevents fibroblast hyperproliferation, reducing collagen and extracellular matrix production, which significantly diminishes the extent of scarring. Thus, the use of HealAFlow contributes to a prolonged filtration effect and enhances surgical success without the toxicity risks characteristic of traditional antifibrotic agents.

The standard dosage of the product ranges from 0.05 to 0.2 ml, depending on the clinical situation. It is administered under the conjunctiva, predominantly in the area of the scleral flap or alongside the filtering bleb. A fine cannula or needle is used for injection after completion of the main surgical steps. HealAFlow can be combined with mitomycin-C (MMC), with the antifibrotic dose typically reduced to lower toxic exposure. The product is indicated in reoperations and in patients at

high risk of scarring, such as younger individuals, patients of Afro-Asian ethnic groups, and those with previously operated eyes.

During trabeculectomy, HealAFlow is injected at the end of the procedure into the bleb area under the conjunctiva, and, if necessary, into the scleral flap region to further support the outflow channel. The product does not affect surgical technique and does not require sutures or additional fixation. In cases of microinvasive interventions, such as laser trabeculoplasty or implantation of devices like XEN, HealAFlow is used prophylactically to reduce the risk of scarring, thereby increasing the likelihood of long-term procedural efficacy [4, 5].

Thus, the incorporation of HealAFlow into modern surgical protocols contributes to reduced rates of postoperative fibrosis and improved functional outcomes of glaucoma surgeries, while simultaneously minimizing complications associated with the toxicity of conventional antifibrotics.

Comparison with Other Drainage Agents and Implants. HealAFlow demonstrates unique advantages and features when compared to other drainage materials and implants. It is a gel-like bioimplant that functions as a physical barrier to fibrosis while supporting effective aqueous humor filtration. Unlike the XEN microshunt — a gel-based tube that creates a new outflow pathway — or the porous collagen implant Ologen, which promotes the formation of a regulated filtering bleb, HealAFlow does not form an additional drainage channel but optimizes the existing filtration pathway by reducing fibrosis.

Compared to MMC, a chemotherapeutic antifibrotic agent, HealAFlow has a more physiological mechanism of action, not directly suppressing fibroblasts but instead modulating the inflammatory response and preventing tissue hyperplasia. The HealAFlow gel biodegrades over 6–8 weeks, providing temporary tissue support during the critical postoperative period without requiring implant removal. In contrast, XEN and MMC are non-resorbable, while Ologen is also biodegradable, although its collagen structure may trigger individual immune reactions. HealAFlow is injected at the end of surgery, significantly simplifying the procedure compared to the surgical implantation of microshunts or the placement of collagen matrices. The risk of complications associated with HealAFlow is considered low, whereas XEN microshunts carry a moderate risk related to potential filtration issues, and MMC is associated with a higher risk of cytotoxic side effects, necessitating careful monitoring. Moreover, HealAFlow does not require specific postoperative care, unlike XEN, which demands filtration performance monitoring, and MMC, which requires surveillance for adverse effects [7, 10]. HealAFlow is a cross-linked sodium hyaluronate gel implant developed as an alternative to traditional anti-fibrotic agents in glaucoma filtration surgery. It addresses the pathophysiological challenge of subconjunctival fibrosis, which can lead to filtration failure and increased intraocular pressure (IOP). By creating a physical barrier between tissues, HealAFlow prevents adhesions, regulates the inflammatory response, and inhibits fibroblast proliferation, thereby reducing scarring and enhancing filtration success.

Clinical Efficacy and Safety. Numerous studies have demonstrated the clinical benefits of HealAFlow in glaucoma surgery. A randomized controlled trial (RCT) involving 100 patients with primary angle-closure glaucoma compared trabeculectomy with and without HealAFlow. The group receiving HealAFlow showed a significantly higher rate of functional filtration blebs (98.2% vs. 84.9%) and a lower incidence of postoperative complications, such as hypotony and iris adhesions. Another RCT involving 60 patients with primary open-angle glaucoma found that HealAFlow was as effective as low-dose mitomycin C (MMC) in reducing IOP, with comparable success rates and fewer complications.

A retrospective study from the University of Athens reported similar outcomes, with no significant differences in IOP reduction or complication rates between trabeculectomy with HealAFlow and trabeculectomy alone.

HealAFlow is composed of cross-linked sodium hyaluronate, a biocompatible and biodegradable material. It is slowly absorbed by the body over 6–8 weeks, reducing the risk of long-

term complications associated with permanent implants. This gradual degradation allows for the formation of a stable filtering bleb without the need for surgical removal.

Compared to traditional anti-fibrotic agents like MMC and 5-fluorouracil (5-FU), HealAFlow offers a safer profile. While MMC and 5-FU are associated with risks such as hypotony, bleb leaks, and infections, HealAFlow's mechanism of action—creating a physical barrier and modulating the inflammatory response—minimizes these risks. Additionally, HealAFlow does not require the use of adjunctive medications like MMC or 5-FU, simplifying postoperative management.

Conclusion. HealAFlow represents a promising adjunct in glaucoma filtration surgery, offering effective IOP control with a favorable safety profile. Its biocompatibility, biodegradability, and mechanism of action make it a valuable alternative to traditional anti-fibrotic agents, particularly in patients where these agents are contraindicated or undesirable. Further long-term studies are warranted to fully establish its role in various glaucoma surgical procedures.

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