REVIEW ARTICLE

Current Status of Epibulbar Anti-glaucoma Drainage Devices in Glaucoma Surgery

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SUMMARY

Background: The term “glaucoma” covers a heterogeneous group of progressive optic neuropathies that are accompanied by characteristic visual-field defects.

Primary open-angle glaucoma, the most common type, progresses insidiously and causes blindness if untreated. All current forms of treatment aim at lowering the intraocular pressure (IOP) in patients whose IOP is elevated. The implantation of anti-glaucoma drainage systems is one of the available options for surgical treatment.

Methods: This review is based on pertinent literature retrieved by a selective search, including glaucoma treatment guidelines from Germany and abroad.

Results: A paradigm shift is currently underway regarding the indications for the implantation of anti-glaucoma drainage systems. Trabeculectomy (a “fistulating” operation in which the aqueous humor is led out of the eye under the conjunctiva) is still considered the surgical gold standard, but drainage systems have been implanted with increasing frequency in recent years. Studies have shown that these systems are more likely to be beneficial the earlier they are implanted in the course of the patient’s disease. Five-year follow-up data from the randomized, multicenter Tube Versus Trabeculectomy (TVT) study have now revealed that anti-glaucoma drainage systems are equivalent to trabeculectomy with respect to long-term IOP reduction, complication rates, and absolute and relative clinical success rates.

Conclusion: Glaucoma is a major clinical and socioeconomic problem whose surgical treatment increasingly involves the implantation of anti-glaucoma drainage systems.

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Glaucoma is one of the main causes of blindness in the industrialized world. The term covers a highly heterogeneous group of diseases, ranging from congenital glaucomas in infants to primary open-angle glaucoma, which is more common with advancing age (1). By definition, the hallmark of glaucoma is slowly progressive atrophy of the optic nerve; the intraocular pressure (IOP) is not necessarily elevated, although it may be (*Figure 1*). Primary open-angle glaucoma, a “disease of old age,” is the most common type of glaucoma at present and will presumably become even more common in the future, because the population as a whole is aging. There will, therefore, be an increasing need for glaucoma treatment, including surgery. The current overall prevalence of glaucoma is 1.5% in persons over age 40 and 3.5% in persons over age 70. More than 350 000 persons in Germany now suffer from severe visual impairment or blindness due to glaucoma; 15% of all new cases of blindness are caused by glaucoma (1). Because the population is aging, it is predicted that more than 900 000 persons will have glaucoma needing treatment in Germany in the year 2030. 60 000 persons can then be expected to develop glaucoma each year, and there will be 30% more blind or visually impaired people in the population than at present (1, 2). The socioeconomic importance of glaucoma is clear.

Although much recent research has centered on neuroprotection and angiogenesis in glaucoma, elevated intraocular pressure is still the only risk factor that can be treated either medically or surgically (3). Long-term clinical trials have confirmed the need for effective pressure reduction, and the individualized setting of a target pressure at which the disease is unlikely to progress is now a key element of glaucoma treatment guidelines (2, 4). Evidence of this type comes, for example, from the recently published Advanced Glaucoma Intervention Study (AGIS), in which patients were followed up for seven years (5). Those whose IOP was below 15 mm Hg had, on average, no progression of their visual-field defect. Drugs remain the first line of treatment for glaucoma, yet many patients ultimately need surgery. Congenital

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Figure 1: Markedly advanced optic nerve atrophy in glaucoma (left). The neuroretinal border is attenuated, and the papillary vessels are stretched over the sharp scleral edge (arrow). A deep, dish-like excavation is seen, and there is an associated visual-field defect. The right papilla is normal

glaucoma is an exception to the “drugs first” rule and should be treated primarily by surgery. Surgery comes into play for various reasons, mainly the lack of adherence to medical treatment (6). Eyedrops can also cause side effects and allergies. They are poorly tolerated or contraindicated for many patients; for example, persons with asthma or cardiac arrhythmias may not be able to take beta-blockers. Moreover, if glaucoma is found to progress despite pharmacotherapy and the target IOP cannot be reached, this can constitute an indication for surgery. About 20% of patients need an operation at some point in the course of their disease, and 13% need operations on both eyes. Thus, as the coming decades see a rise in the number of elderly people, there will also be a marked rise in the number of glaucoma operations performed. Because glaucoma is often present for decades, successful visual-field preservation tends to be inadequately reflected in clinical studies of glaucoma treatment (particularly surgical treatment) and may be intrinsically hard to document.

In this article, we provide an overview of the episcleral anti-glaucoma drainage implants that are used in glaucoma surgery. A paradigm shift is currently underway regarding the use of such implants because of the findings of recently published studies. We will present the clinical results of the technique, its complications, and the potential for improvement in the near future.

The pathogenesis of glaucoma remains unclear

The underlying cause of elevated intraocular pressure (a common, though not universal, accompaniment of glaucoma) has not yet been definitively

identified. A combination of hydrodynamic factors and abnormal perfusion is presumed to be at work.

In most types of glaucoma, most patients have a so-called outflow disturbance, i.e., increased resistance to outflow in the trabecular meshwork proximal to the canal of Schlemm.

The aqueous humor, secreted by the ciliary body, normally flows through the trabecular meshwork and into the canal of Schlemm, then passes into the collector canals and the episcleral veins. The greatest resistance to outflow along this pathway is normally at the level of the trabecular meshwork; in glaucoma patients, the resistance here is even higher (7).

Glaucoma surgery is intended

- either to reduce the secretion of aqueous humor by the ciliary body (cyclodestructive surgery at the ciliary body with lasers or cryotherapy),
- or to lower or circumvent the resistance in the trabecular meshwork and thereby increase the outflow of aqueous humor from the eye.

The latter can be achieved either by trabeculectomy or by the implantation of a drainage system. In either case, the aqueous humor is diverted into an artificial (non-physiological) space between Tenon’s capsule and the sclera of the eye, from which it flows into the deep venous plexus of the orbit. Both operations result in the formation of an extraocular filtering bleb, with the potential problem of an excessive wound-healing reaction around the bleb.

The history of implantable anti-glaucoma drainage devices

The idea of using artificial material to shunt the aqueous humor out of the eye is an old one. Gold and

silk threads were used for this purpose in the mid-eighteenth century.

In 1969, Molteno developed the first system composed of silicone and polypropylene, which came onto the market a year later (8). Molteno designed the basic model of anti-glaucoma drainage systems that still prevails today, with a base plate fixed to the outside of the sclera and connected to a tube.

This thin silicone tube connects the base plate with the interior of the eye and enables the aqueous humor to flow out of the eye (*Figure 2*). A cyst or filtering bleb usually forms over the base plate; this structure can receive the aqueous humor and then conduct it into the deeper layers of the orbit. The earlier models (Molteno and Baerveldt) had no valve; the Ahmed drainage implant, introduced in 1993, was the first to have one.

Silicone base plates and tubes

Today, nearly all anti-glaucoma drainage systems have a small silicone base plate (of variable size and strength) and a thin silicone tube. Models with a valve have been introduced very recently (9).

If the system to be implanted has no valve or other restriction to outflow, the tube is usually tied off during surgery with a resorbable ligature, or its lumen is occluded with a prolene thread, so that the desired lowering of the intraocular pressure is not induced until some weeks after the procedure.

Silicone has become the usual material for the base plate in recent years, as clinical studies have shown that polypropylene base plates tend to evoke a more intense wound-healing response with a higher rate of encapsulation. They are also more difficult to handle than silicone ones, which are softer and more flexible (10, 11).

Children with glaucoma who undergo surgery of the classic type can have a complicated clinical course. The manufacturers of anti-glaucoma drainage implants now sell children's models with smaller base plates. The thickness of the base plate and the dimensions of the valve mechanism and the tube are the same as in the adult models. As a rule, the tube is implanted into the anterior chamber (*Figure 3*).

Data from clinical studies

In assessing the currently available data from clinical studies of various types of anti-glaucoma drainage system (either tested individually or compared against each other), one should bear in mind that, when these systems first came onto the market, they tended to be implanted in patients with complicated clinical courses, most of whom had already undergone multiple operations on the affected eye (12, 13). Indeed, this is often still true today because of the cautious attitude with which these systems are viewed, especially in Europe. The reluctance to implant such systems is also partly due to their relatively high price—in the region of 800 euros when bought from the manufacturer. At first, the relative and absolute success rates of these

Figure 2: Size comparison of glaucoma drainage implants. In each, a silicone base plate is connected to a thin silicone tube that protrudes into the interior of the eye, providing a diverting path for the aqueous humor

Figure 3: Left eye after implantation of a drainage device in the upper temporal quadrant in the area of the sclera and the equator of the eye. The tube is just barely visible in the anterior chamber, in front of the iris and behind the cornea (arrow). There is marked conjunctival injection

systems were poor, and the rates of complications, re-operations, and even enucleations were high. The number of prior operations and cyclodestructive procedures has a direct effect on the rate of encapsulation and on the long-term therapeutic benefit (14). It was only recently demonstrated that these systems work better if implanted early (15, 16), where success is measured in terms of effective pressure reduction and low rates of re-operations and postoperative complications. Budenz et al., in a recently published randomized trial, found no difference between the success rates of two different anti-glaucoma drainage systems—the Ahmed system, which has a valve, and the Baerveldt system, which does not—after 1 year of follow-up (17). All other published studies of these systems have been retrospective and thus of lesser informative value. A case-control study published by Syed et al. in 2004 also revealed no significant

TABLE

Data from 5-year follow-up in the Tube Versus Trabeculectomy (TVT) study^{*1}

	Trabeculectomy	Drainage implant
Number of patients	105	107
Intraocular pressure at 1 year	12.7 ± 5.8	12.5 ± 3.9
Intraocular pressure at 5 years	12.6 ± 5.9	14.4 ± 6.9
Number of drugs at 1 year	0.5 ± 0.9	1.3 ± 1.3
Number of drugs at 5 years	1.2 ± 1.5	1.4 ± 1.3
Reoperation rate at 5 years	29%	9%
Cumulative probability of failure	46.9%	29.8%
Number of serious complications	28	24

^{*1}modified from Gedde SJ et al. (15, 16)

difference between the Ahmed and Baerveldt systems, although the intraocular pressure with the Ahmed system was somewhat higher after a year of use. The complication rates in this study were notably high: 9% in each group. This may reflect the complicated pre-surgical situation of the patients (18).

The Tube Versus Trabeculectomy (TVT) study

The state of knowledge from clinical studies was markedly improved recently by the publication of the Tube Versus Trabeculectomy (TVT) study, in which implantation of the Baerveldt system was compared with fistulating trabeculectomy. One of these two procedures was chosen at random to be performed as either a first or a second operation (15). The multicenter trial involved procedures on 212 eyes of 212 patients. The allowable previous operations were restricted to cataract surgery or trabeculectomy; thus, some patients received implantable drainage systems as their first operative treatment of glaucoma. The avoidance of multiple prior operations gave the drainage systems a better chance of success. The results of this study clearly confirmed what had already

been suspected from clinical experience: Implanting such systems as a last resort in patients with advanced disease leads to a high rate of failure. The main findings of the study are shown in the *Table*. In general, the Baerveldt system was found to be clinically equivalent to the standard technique (trabeculectomy) in terms of reduction of intraocular pressure, complication rate, and failure rate. After one year of follow-up, the patients who had received an implanted system needed slightly more medication to achieve their target IOP than the trabeculectomy patients did (an average of 1.3 versus 0.5 drugs). The data after five years of follow-up are highly promising (16): They reveal not only that the two treatments are of equivalent benefit for the reduction of IOP, but also that the anti-glaucoma drainage systems have a lower probability of failure. After five years of follow-up, the “tube” patients still needed somewhat more medication to achieve their target IOP than the trabeculectomy patients did (1.4 versus 1.2 drugs), but trabeculectomy had markedly higher rates of failure and reoperation.

Complications and encapsulation

Despite the high success rates, many surgeons still advise caution. The spectrum of complications is broad and depends crucially on the preoperative condition of the eye (19). Postoperative bulbar hypotonia is a feared early complication, with a frequency of 16% in the TVT study. It can, however, be treated effectively with suitable surgical measures, such as ligating the tube or placing a stent in it. Systems with valves, if correctly implanted, are less likely to cause hypotonia but are associated with somewhat higher intraocular pressure in the long term.

Tube erosion is a relatively rare complication, arising at a reported frequency of 2% to 3%. The tube pierces the conjunctiva at a site where it is often very thin, in the transitional zone between the sclera and the cornea. This happened in 4 of 107 patients participating in the TVT study; it is a serious complication that calls for immediate surgical revision of the system. Unless promptly treated, such a

Figure 4: An Ahmed valve implanted in the upper temporal quadrant of the right eye of a 17-year-old male patient. Markedly abnormal position of the right globe four months after implantation. Pseudostrabismus and pseudotumor under the right upper lid (arrow). The cause of this problem is an excessive wound-healing response to the foreign material of the base plate, as seen in the picture at right—the cornea (dark) is barely visible at the bottom right of the picture. Images reproduced with the permission of the patient

situation can lead to superinfection and potentially organ-threatening endophthalmitis. A further problem that remains unsolved to date is the uncontrolled wound healing that can be so exuberant as to impair the functionality of the implant, causing the intraocular pressure to rise once again (*Figure 4*).

The rates of encapsulation reported in the literature vary widely, ranging from 4% to 30%. The fibrovascular capsule that arises as a reaction of Tenon's capsule to the silicone foreign body has been well studied clinically and histologically (20). Essentially, Tenon's capsule fibroblasts begin to differentiate and turn into contractile myofibroblasts. Increased amounts of collagen and extracellular matrix have been observed, as has the formation of an epithelial layer, oriented toward the implant, which is impermeable to aqueous humor. The aqueous humor that finds its way into this cyst is not adequately resorbed and therefore builds up, causing the intraocular pressure to rise again. The predisposing factors for encapsulation are known to include the following:

- prior surgery,
- patient age,
- the time at which the cyst/base plate makes contact with aqueous humor,
- the concentration of growth factors in the aqueous humor of the individual patient,
- the eye surgeon's experience with the implanted system.

A further reason for encapsulation that has not attracted much attention to date is the nature of the base-plate surface itself (21). Depending on the manufacturer and model, surface roughness may promote the adhesion of Tenon fibroblasts after implantation. Shear stress due to movements of Tenon's capsule over the base plate when the eye moves may play a role as well, along with other factors (22).

The control of wound healing remains elusive. Future anti-glaucoma drainage systems will have to overcome the problem of encapsulation (*Figure 4*). Glaucoma may be present for many years, or indeed many decades, in the case of childhood-onset glaucoma; thus, long-term success is required of implantable drainage systems and other surgical methods used to treat the disease. Current research centers on using the base plate itself (a component of the system that must be implanted anyway in all cases) as a tool to control wound healing. Special modifications of its surface might make this possible (23). Two approaches are now being tested:

- Altered surface topography: Many of the base plates in use today have a very smooth surface. When capsules are surgically removed, there is generally no visible adherence of the base plate to the cyst wall. The surface must still be as flat and smooth as possible. Even today, some models (particularly those with valves) still have a high profile and a relatively rough sur-

face. This might be improved by a chemical modification of the silicone used to make the base plate. The optimal composition of silicone for this purpose is still unknown.

- Coating the base plate: The base plate might be covered with an antiproliferative or anti-adhesive coating. Laboratory research in this area involves a combination of cell-culture techniques and materials science. Preliminary data suggest that paclitaxel, an antiproliferative substance used to coat coronary stents, might be useful here as well (24).

The four decades since Molteno introduced the basic model of an implantable anti-glaucoma drainage system in 1969 have seen continual improvements yielding a wide variety of models and materials. In parallel, microsurgical methods have been refined and optimized. The development of implantable anti-glaucoma drainage systems is not yet at an end; these can be expected to evolve further, just as intraocular lenses did. The ultimate goal of current research is the development of an anti-glaucoma implant that can modulate wound healing and prevent the development of severe fibrovascular encapsulation. This would be particularly useful in the treatment of medically intractable childhood glaucomas.

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Conflict of interest statement

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KEY MESSAGES

- Glaucoma is treated by reduction of the intraocular pressure, either with drugs or, when these are ineffective, with surgery.
- Primary open-angle glaucoma is a common cause of blindness. A classic disease of old age, it is expected to become more common in the coming decades.
- The clinical benefit of glaucoma surgery is limited by excessive wound-healing reactions.
- Anti-glaucoma drainage systems are a further mode of surgical treatment of glaucoma.
- Studies have shown that the implantation of anti-glaucoma drainage systems yields clinical results comparable to those of the standard operation, trabeculectomy.

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