Capsule excision and Ologen™ implantation for revision after glaucoma drainage device surgery

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Abstract

Background There is little information available about surgical management after failed glaucoma drainage device (GDD) surgery. We present the outcome of capsule excision after failed GDD surgery compared to capsule excision with additional use of a biodegradable implant (Ologen™, version 2) as a placeholder.

Methods In an observational comparative case series of 19 patients undergoing excision of the GDD capsule, ten prospectively observed consecutive patients were treated by excision of the capsule, topical mitomycin C application, and implantation of an 10×10×2 mm-sized Ologen™ implant (group A) while 9 retrospectively observed consecutive patients were treated by excision of the capsule and topical mitomycin C application alone (group B).

Results Mean preoperative IOP was 29.4 mmHg for group A and 27.6 mmHg for group B, while mean postoperative IOP at the last follow-up (mean follow-up 11.2 (group A) and 8.6 (group B) months) was 17.3 mmHg for group A and 19.3 mmHg for group B (p>0.05). Follow-up of the two groups demonstrated a significant difference in success rate (log-rank test, p=0.04) in favor of group A. No further pressure-reducing surgery was necessary in any of the patients in group A, but it was needed in three of nine patients in group B.

Conclusions Although our study has the limitations of small sample size and observational study design, it shows that further investigation is warranted into the potential of Ologen™ in revision surgery after GDD implantation.

Keywords Glaucoma drainage device · Biodegradable implant · Ologen™ implant · Capsule excision

Introduction

Episceral glaucoma drainage devices have recently proven efficacious in large-scale studies. Recurrent failure of conventional filtrating surgery is the main reason for the use of the glaucoma drainage device (GDD). Other indications include situations in which the formation of a filtering bleb seems unpromising because of extensive conjunctival scarring. Furthermore, GDDs offer a better chance of successful glaucoma control in the first 2 years of life in infantile glaucoma compared to trabeculectomy with MMC [1]. Surgical success rates of glaucoma drainage devices range between 60 and 90% in a period of 12–27 months after surgery, with a yearly failure rate of 10% in subsequent years almost regardless of the type of implant used [2–5].

A tube-specific complication is the development of a bleb encapsulation in the natural course of secondary wound healing following glaucoma implant surgery [6]. If bleb encapsulation has occurred in a primarily working glaucoma implant and IOP cannot be controlled any longer by topical or systemic medication or digital massage capsule needling [7], injection of 5-fluorouracil [7, 8],...
additional implantation of a GDD or surgical excision of the capsule around the glaucoma implant has been proposed [9], although there is a lack of evidence that these “enhancing” secondary interventions have any long-term benefit.

Recently, tissue-engineered biodegradable implants have been created as an alternative augmentation in glaucoma surgery. It has been proposed that a porous collagen-glycosaminoglycan matrix (Ologen™, version 1) will favor the development of remarkably normal tissue instead of a scar postoperatively [10, 11]. The collagen-glycosaminoglycan matrix will reduce conjunctival contraction and promote formation of an almost normal subconjunctival stroma [12]. Furthermore, this implant should prevent the collapse of the subconjunctival space. In animal studies, randomized collagen deposition and microcyst formation after penetrating antiglaucomatous surgery have been shown following the use of Ologen™ [10, 11]. Recently, a new version of the Ologen™ implant (version 2) has been created. This implant consists of atelocollagen instead of collagen and promises a lower immunogenicity and better compatibility than the former version [13].

In an observational comparative case series with two interventional groups we investigated the effect of capsule excision and the additional use of an Ologen™ implant (version 2) as a placeholder in the event of malfunction after GDD surgery. Our study focused on postoperative IOP, antiglaucomatous medication, and postoperative complications.

Methods

Patients and preoperative examination

In an observational comparative case series we compared two study groups undergoing revision surgery after GDD surgery. Group A comprised ten prospectively observed consecutive patients who were treated by excision of the capsule around the GDD and implantation of an 10×10×2 mm-sized Ologen™ implant (version 2) on top of the GDD. Group B comprised nine retrospectively observed consecutive patients treated only by excision of the capsule (group B). Possible alternatives, beneficial effects, and potential complications of the surgical procedures were explained in detail to all patients. Written informed consent was obtained from all participants. Before surgical intervention, all patients underwent a baseline examination, which included measurement of best-corrected visual acuity (ETDRS charts, Lighthouse, Long Island, USA), visual field examination (30-2, Humphrey field analyzer, Humphrey Instruments, Munich), biomicroscopy, gonioscopy, and Goldmann applanation tonometry.

Ologen™ implant

The Ologen™ implant, version 2, (Aeon Astron Corporation, Taipei, Taiwan) is a porous implant comprising >90% lyophilized porcine atelocollagen and <10% lyophilized porcine glycosaminoglycan with a pore size of 10–300 µm. In our study, we used a cylindrical (10 mm in diameter) implant of 2 mm in height.

Atelocollagen is a highly purified pepsin-treated type I collagen. A collagen molecule has an amino acid sequence, known as a telopeptide, at both N- and C-terminals, which confers most of the collagen's antigenicity. Atelocollagen obtained by pepsin treatment is low in immunogenicity because it is free of telopeptides [13].

Surgical technique and follow-up

The surgical procedure was performed under general anesthesia in every case. Operations were performed as follows: The procedure commenced with an incision of the conjunctiva above the GDD distant to the limbus. The capsule was carefully prepared in both groups, after which the top of the capsule was excised and the reservoir of aqueous humour opened. For maintenance of the anterior chamber, balanced salt solution was injected through a paracentesis into the anterior chamber. Mitomycin C (concentration 0.2 mg/ml) was applied in a sponge in both groups for 2 min on top of the implant. In group A, a 10×10×2 mm-sized Ologen™ implant was positioned on top of the GDD. Finally, the conjunctiva was closed with a 9-0 polyglactin suture (Vicryl, Ethicon Limited, Edinburgh, UK). The standard postoperative regimen consisted of topical ofloxacin three times a day and dexamethasone five times a day in a preservative-free preparation.

Postoperative examinations were performed on a daily basis during hospitalization. Follow-up visits were arranged at 1 week, and 1, 3, 6, and 12 months after surgery. At each follow-up visit, all the aforementioned examinations except for visual field testing and gonioscopy were repeated. Visual field examination was repeated 6 and 12 months after surgery. Side-effects and complications were recorded during postoperative visits. Complications were defined as follows: encapsulated filtering bleb, shallow anterior chamber, hyphema, ablation of the choroidals, persistent leakage, hypotony, macular edema, corneal complications, allergy, suprachoroidal hemorrhage, and blebitis/endothphalmitis.

Statistics

Qualified success was defined as an IOP lower than 21 mmHg and a relative reduction of IOP of 20% or more with or without additional topical medication. Absolute success was defined as an IOP lower than 21 mmHg and a...
relative reduction of IOP of 20% or more without any additional topical medication. Particular attention was paid to postoperative complications. Pre- and postoperative antiglaucomatous medication was classified according to a medication score [14]. If an additional surgical procedure was necessary for IOP-control in a patient, no further data was collected and the patient was defined as a dropout.

Statistical analysis was performed using Prism software (version 2, GraphPad software). Qualified success was compared using the log-rank test and survival curves (Kaplan–Meier curves). Differences between preoperative and postoperative IOP and medication were compared by the nonparametric t test (Mann-Whitney test, two-tailed) and p values of less than 0.05 were considered statistically significant.

Results

Nineteen (10/9) patients, ten women and nine men, participated in the study. The mean age was 44.5 (SD 20.6) years. Eighteen patients were of Caucasian ancestry and one of African. In all cases, Baerveldt drainage devices with a surface area of 350 mm² were primarily used for glaucoma drainage device surgery (BG-101-350; Pharmacia Groningen, Netherlands). Mean time between primary glaucoma drainage device surgery and revision was 17 months (SD 17.5) (18 months (SD 20.6) for group A and 15.1 months (SD 11.7) for group B; p=0.71). Mean time of last follow-up was 11.2 months (SD 1.7) in group A, and 8.6 months (SD 4.4) in group B (p=0.84). In group A, six patients had primary open-angle glaucoma, one patient had a congenital glaucoma, two patients had an ICE syndrome, and one had aphakic glaucoma. In group B, four patients had primary open-angle glaucoma, three patients had a congenital glaucoma, and two patients had a secondary open-angle glaucoma. The mean preoperative intraocular pressure was 28.5 (SD 7.2) mmHg for all patients enrolled. No difference in mean preoperative IOP was observed between the two groups (p=0.59), nor was any difference in preoperative medication score noted (p=0.43). Summarized information about the two groups is given in Table 1.

Table 1 Comparison of the two study groups. Mean values and standard deviation are given

<table>
<thead>
<tr>
<th></th>
<th>Excision+Ologen™ (group A)</th>
<th>Only excision (group B)</th>
<th>p value (t test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.9 (13.6)</td>
<td>47.2 (17.7)</td>
<td>0.83</td>
</tr>
<tr>
<td>Previous antiglaucomatous, surgical procedures</td>
<td>4.2 (1.5)</td>
<td>4.0 (0.8)</td>
<td>0.75</td>
</tr>
<tr>
<td>Preoperative IOP (mmHg)</td>
<td>29.4 (6.1)</td>
<td>27.6 (8.5)</td>
<td>0.59</td>
</tr>
<tr>
<td>Preoperative medication score</td>
<td>5.3 (1.6)</td>
<td>4.6 (2.4)</td>
<td>0.43</td>
</tr>
<tr>
<td>Period between GDD insertion and revision (months)</td>
<td>18.0 (20.6)</td>
<td>15.1 (11.7)</td>
<td>0.71</td>
</tr>
</tbody>
</table>

Intraocular pressure and medication

One day after surgery the mean postoperative IOP was 7.0 (SD 5.1) mmHg for the Ologen™/excision group (A) (p<0.01 compared to preoperative IOP) and 10.0 (SD 7.6) mmHg for the excision group (B) (p<0.01 compared to preoperative IOP), respectively. One week after surgery, the IOP in group A remained at a low level (6.2 (SD 3.6) mmHg), though IOP in group B increased to a mean value of 19.0 (SD 12.4) mmHg (p<0.01). One month after surgery, the IOP was quite similar in the two groups. The intraocular pressure in both groups remained stable over follow-up after surgery (see Table 1 and Fig. 1). Mean IOP at the last follow-up in group A was 17.3 mmHg (SD 4.0 mmHg) at a mean follow-up of 11.2 months. In group B, the mean IOP at the last follow-up was 19.3 mmHg (SD 7.7 mmHg) at a mean follow-up of 8.6 months (p=0.45).

Immediately and 1 week after surgery no pressure-reducing medication at all was applied in any of the patients. After 1 month IOP-reducing medication was necessary in three cases of group A (medication score 1.1 (SD 1.8)) and in five cases of group B (medication score 2.0 (SD 2.4)). Three months after surgery a mean medication score of 2.9 was necessary for IOP control in both groups. The medication score in both groups still remained stable from 3 months to 12 months of follow-up after surgery (see Table 2).

Ultrasound biomicroscopy (50 MHz)

One month postoperatively, an aqueous humour reservoir surrounding the glaucoma drainage device was detectable in both groups in ultrasound biomicroscopy (Fig. 2). At this timepoint, the Ologen™ implant was no longer detectable in ultrasound biomicroscopy in the observed cases.

Postoperative complications

During postoperative follow-up visits we could not detect any possible Ologen™ specific side-effects such as allergy or translocation of the implant. No severe postoperative complications, such as suprachoroidal hemorrhage, were
detected at follow-up. A significant difference for slight postoperative complications was not determined.

In group A (capsule excision and Ologen™ implantation) no further revision was necessary. Otherwise, in three cases of group B (only capsule excision) further pressure-reducing surgery was necessary due to insufficient IOP control. In one patient, an additional trabeculectomy was conducted 15 days after revision surgery for IOP control. Cyclophotocoagulation was necessary in two cases, one at 3 months and the other at 9 months after surgery.

In all 19 cases observed, the visual acuity remained stable until the last follow-up. The visual field also remained stable in all cases.

Qualified success and Kaplan–Meier chart

Follow-up of both groups demonstrated a significant difference in the qualified success rate (log-rank test, *p* = 0.04) in favor of group A (Fig. 3). The absolute success rates in both groups was low. In only one patient of group A the IOP was controlled for a period of 12 months after surgery without

Table 2 Mean intraocular pressure (IOP) and mean medication score during the postoperative period after capsule excision w/wo Ologen™-implantation on top of the GDD. SD standard deviation; med. score medication score

<table>
<thead>
<tr>
<th></th>
<th>Excision+Ologen™</th>
<th>Only excision</th>
<th></th>
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<th></th>
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<tbody>
<tr>
<td></td>
<td>Mean IOP (mmHg)</td>
<td>Mean med. score</td>
<td>Mean IOP (mmHg)</td>
<td>Mean med. score</td>
<td>p value (t test)</td>
<td></td>
</tr>
<tr>
<td>Preop</td>
<td>29.4 (6.1)</td>
<td>5.3 (1.6)</td>
<td>27.6 (8.5)</td>
<td>4.6 (2.4)</td>
<td>0.59</td>
<td>0.43</td>
</tr>
<tr>
<td>1 d</td>
<td>7.0 (5.1)</td>
<td>0.0 (0.0)</td>
<td>10.0 (7.6)</td>
<td>0.0 (0.0)</td>
<td>0.34</td>
<td>–</td>
</tr>
<tr>
<td>7 d</td>
<td>6.2 (3.6)</td>
<td>0.0 (0.0)</td>
<td>19.0 (12.4)</td>
<td>0.0 (0.0)</td>
<td>0.01</td>
<td>–</td>
</tr>
<tr>
<td>1 mo</td>
<td>15.3 (4.7)</td>
<td>1.1 (1.8)</td>
<td>15.3 (5.1)</td>
<td>2.0 (2.4)</td>
<td>0.98</td>
<td>0.37</td>
</tr>
<tr>
<td>3 mo</td>
<td>16.6 (3.0)</td>
<td>2.9 (1.9)</td>
<td>19.7 (6.3)</td>
<td>2.9 (2.4)</td>
<td>0.18</td>
<td>0.97</td>
</tr>
<tr>
<td>6 mo</td>
<td>16.7 (3.6)</td>
<td>3.0 (1.6)</td>
<td>16.3 (3.7)</td>
<td>3.5 (2.1)</td>
<td>0.84</td>
<td>0.59</td>
</tr>
<tr>
<td>12 mo</td>
<td>17.9 (4.7)</td>
<td>3.4 (2.4)</td>
<td>16.8 (4.8)</td>
<td>4.0 (2.1)</td>
<td>0.70</td>
<td>0.48</td>
</tr>
</tbody>
</table>
medication. In all other cases, topical antiglaucomatous medication was necessary for IOP control sometime in the observed time course.

Discussion

Glaucoma drainage devices for episcleral implantation have recently proven efficacious for pressure regulation in various forms of glaucoma. Most widely used in clinical practice are the valved Ahmed (New World Medical, USA) and Krupin (Hood Laboratories, USA) devices and the non-valved Baerveldt (Advanced Medical Optics, USA) and Molteno (Molteno Ophthalmic Ltd, New Zealand) devices. As described above, surgical success rates ranged from 60 to 90% over a period of 12–27 months postoperatively, almost regardless of the type of implant used [2–5].

Little information is available regarding tube failure due to an encapsulation of the aqueous reservoir and the surface of the GDD in a primarily working glaucoma implant only. A few interventional methods are described as case series. Needling revision to the overlying aqueous humour reservoir has been reported to have a qualified success rate of 43% [7]. Furthermore, injection of 5-fluorouracil seems to enhance the outcome after failed GDD surgery [7, 8]. For shunt revision with excision of the capsule, a qualified success rate of 42% has been reported [9]. Another therapeutic approach, having a qualified success rate of 62% [9], is implantation of an additional GDD. Due to the limited information concerning revision after failed glaucoma implant surgery, no recommendation can be given.

Biodegradable implants have recently been tested in animal models. A poly(L-lactide-co-epsilon-caprolactone) film has been shown to work as an adhesion barrier in filtration surgery [15]. A solid hyaluronic acid-carboxymethyl cellulose film significantly inhibited subconjunctival scar formation and prevented adhesions of the conjunctiva and sclera [16]. Furthermore, the use of Seprafilm™ (sodium hyaluronate and carboxymethylcellulose) reduced postoperative conjunctiva-sclera adhesion [17]. A porous collagen-glycosaminoglycan matrix (Ologen™ implant, version 1) has been tested in animal models. This implant was designed to prevent collapse of the subconjunctival space, e.g., the conjunctiva-sclera adhesion. Furthermore, it led to randomized collagen deposition and microcyst formation after penetrating antiglaucomatous surgery in contrast to the negative control and decreased early postoperative scarring [10, 11]. In human subjects, the Ologen™ implant has been tested for augmentation in deep sclerectomy. This study revealed that deep sclerectomy with Ologen™ implantation is an effective and well-tolerated method for reduction of IOP [18]. Furthermore, it has been shown that it serves as a placeholder until it is degraded [10, 11, 18]. In summary, the use of the Ologen™ implant promises to reduce scar formation and should serve as a placeholder in the early postoperative period.

The new Ologen™ implant (version 2) is comprised of atelocollagen instead of collagen and has a very low immunogenicity. Atelocollagen is used for a wide range of purposes, including wound healing, intradermal injection in plastic surgery, and also as a bone cartilage substitute.

The significant difference in IOP in our study 1 week after surgery can be explained by the maintenance of a reservoir by the Ologen™ implant (version 2), which serves as a placeholder. Thus, a collapse of the subconjunctival space is avoided.

Fig. 2 Ultrasound biomicroscopy (50 MHz). Aqueous humour reservoir 1 month after capsule excision and implantation of an Ologen™-implant. Asterisk indicates the aqueous humour reservoir, arrow indicates the Baerveldt drainage device, and crosshairs indicate the edges of the Baerveldt implant

Fig. 3 Kaplan–Meier chart for qualified success (IOP of 21 mmHg or lower and an additional decrease in IOP of at least 20% in comparison to preoperative IOP, without topical antiglaucomatous medication allowed) over 1 year of follow-up
Our study reveals that capsule excision with additional implantation of an Ologen™ implant (version 2) is a safe and powerful method for revision of failed GDD surgery due to encapsulation of a primary working implant. Although our study has the limitations of small sample size and observational study design, it shows that further investigation of the potential of Ologen™ in revision surgery after GDD implantation is warranted.

References