

Trabeculectomy ab interno with the Trabectome® as a therapeutic option for uveitic secondary glaucoma

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Abstract

Purpose Treatment of secondary glaucoma in uveitis patients is challenging. Owing to the young age of these patients, sufficient lowering of the intraocular pressure (IOP) is essential to prevent progression of visual field loss. However, because of the chronic inflammatory stimulus, filtration surgery has an increased risk of failure, especially in patients who have previously undergone surgery. Therefore, minimally invasive glaucoma surgery is a valuable alternative.

Methods The clinical records of 24 consecutive patients with uveitic secondary glaucoma who underwent trabeculectomy ab interno with the Trabectome® at the Eye Center of the Albert-Ludwigs University of Freiburg between June 2009 and June 2014 (registered in the Freiburg trabectome database) were retrospectively analyzed. The general baseline information for each patient included age, gender, glaucoma type, ocular medication and current IOP. The postoperative IOP and number of antiglaucomatous medications were recorded at each visit. Statistical analyses were performed using the Kaplan-Meier estimator and Dunnett's t-test.

Results The mean IOP before surgery was 31 ± 6.7 mmHg (median 32 mmHg). Both the IOP and the number of medications significantly decreased over the various follow-up intervals after trabeculectomy ab interno with the Trabectome®. Patients with follow-ups continuing past one year showed an IOP-reduction of approximately 40 % and a medication number reduction from 2 to 0.67. The failure rate (necessitating further glaucoma surgery) was $N=3$ (12.5 %) patients.

Conclusions Trabeculectomy ab interno with the Trabectome® is a minimally invasive and effective method for controlling IOP in uveitic secondary glaucoma.

Keywords Uveitic glaucoma · Trabectome® · Minimal invasive glaucoma surgery · Uveitis

Introduction

Uveitic glaucoma was first described by Joseph Beer in 1813 [1]. The mean age at first diagnosis of uveitis is 39 years [2]. The prevalence of secondary glaucoma in patients with uveitis is approximately 20 % [3]. Owing to the young age of these patients, sufficient control of IOP is necessary for the prevention of progressive visual field deterioration. The success of trabeculectomy ab externo is lower in uveitis patients than in patients with primary open angles glaucoma, as both young age and autoimmune inflammation cause an accelerated and intensified wound-healing response [4, 5]. Glaucoma drainage devices are an alternative for lowering IOP in uveitis patients [6–9], although using these requires a complex surgical intervention.

In uveitic glaucoma, the outflow resistance is primarily increased as a result of alterations in the trabecular meshwork [3, 10, 11]; therefore, removal of the altered meshwork should lead to sufficient IOP reduction. Since 2006, the Trabectome®, a device used to perform an ab interno trabeculectomy, has been used in glaucoma surgery [12, 13]. The trabecular meshwork is removed by electroablation, resulting in an increased aqueous outflow to the opened Schlemm's canal.

In this study, we investigated the effectiveness and safety of surgery with the Trabectome® in uveitic patients.

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Methods

Patient selection

The study protocol was approved by the ethics committee of the Albert Ludwigs University Freiburg (No. 235/10_160678). The study followed the regulations of the Good Clinical Practice (GCP) Guidelines and the Declaration of Helsinki.

The clinical records of consecutive patients who underwent trabeculectomy ab interno with the Trabectome® at the University Eye Hospital Freiburg between June 2009 and June 2014 (registered in the Freiburger Trabectome database) were retrospectively analyzed. All patients with uveitis and a follow-up >60 days were included. A total of 24 eyes from 24 patients with anterior or intermediate uveitis were included. Indication for glaucoma surgery was based on clinical observation. All patients suffered from elevated IOP under maximal tolerated antiglaucomatous therapy and showed an open angle. In 11 of the 24 patients a preoperative visual field examination was available. The mean defect (MD) was 4.92 ± 4.69 (mean \pm standard deviation). Surgery was performed by three experienced glaucoma surgeons (JJ, MN, AA).

Evaluation of outcomes

Baseline information for each patient included age, gender, glaucoma type, antiglaucomatous and other ocular medication, and current IOP level.

Surgical procedure Surgery was performed using the Trabectome® system, including the Trabectome single-use handpiece including an irrigation-aspiration (I/A) system (Neomedix Inc., Tustin, USA). After topical anaesthesia a 1.7 mm clear cornea tunnel was made; local anaesthesia was instilled into the anterior chamber. Surgery was performed under gonioscopic control using the modified Swan-Jacob-Lens. The trabecular meshwork was removed over 90 to 120° (described in detail by Jordan et al. [14]). None of the eyes had active inflammation for at least 6 weeks at the time of surgery. At the end of surgery, dexamethasone 4 mg was applied intracamerally.

Postoperative management

All patients received steroid eye drops (prednisolone 1 %) every hour for the first few days. The dosage was adapted to the individual intraocular inflammation level. To prevent anterior synechia, pilocarpine (2 %) was administered to all eyes 3 times a day for the first 6 weeks after surgery, and twice a day thereafter for 6 more weeks. IOP-lowering medication was given topically or systemically according to the individual's postoperative IOP levels. No change in basic therapy

was done. All patients went on taking their individual immunosuppressive basic therapy including steroids, if needed.

Statistics

Time points of follow-up visits were clustered in follow-up intervals. The IOP and the number of antiglaucomatous medications were analyzed at each follow-up: follow-up interval 1, 1–30 days post-operatively ($n=10$); follow-up interval 2, 31–90 days post-operatively ($n=12$); follow-up interval 3, 91–180 days post-operatively ($n=10$); follow-up interval 4, 181–365 days post-operatively ($n=8$); and follow-up interval 5, 366–1046 days post-operatively ($n=9$).

Statistical analysis was performed using the Kaplan-Maier estimator [15] and Dunnett's t-test [16, 17] for multiple comparisons.

Results

A total of 24 eyes from 24 patients were included. Baseline data for the patients are shown in Table 1. During follow up time no relaps of uveitic inflammation was seen in any of the patients (Mean 394 ± 341 days, range 60 – 1046 days).

The baseline mean IOP was 31 ± 6.7 mmHg (median 32 mmHg). The mean individual postoperative IOP at the last documented visit was 20 ± 11.4 mmHg (median 16 mmHg). The mean postoperative IOP in follow-up interval 1 was 26 ± 18.4 mmHg (median=16 mmHg); in follow-up interval 2, 15 ± 2.9 mmHg (median=16 mmHg); in follow-up interval 3, 16 ± 4.1 mmHg (median=17 mmHg); in follow-up interval 4, 20 ± 12.7 mmHg (median=18 mmHg); and in follow-up interval 5, 18 ± 6.6 mmHg (median=16 mmHg). The IOP results during follow-up are presented in Fig. 1. Figure 2 shows the IOP results at the final documented visit compared to baseline for each patient. Dunnett's t-test confirmed a significant difference between baseline and follow-up (significance level $p < 0.05$).

The mean number of glaucoma medications at the preoperative visit was 2 ± 1.4 (range=0–4, median=2). The mean number of postoperative medications was 1 ± 0.82 in follow-

Table 1 Baseline data

Characteristic	Value
Number (eyes)	24
Gender (male: female)	10:14
Age (years, mean \pm SD)	52 \pm 18.4, range 14–77
Follow-up (days, mean \pm SD)	423.2 \pm 359, range 60–1046
Type of uveitis	
Anterior uveitis	17
Intermediate uveitis	7

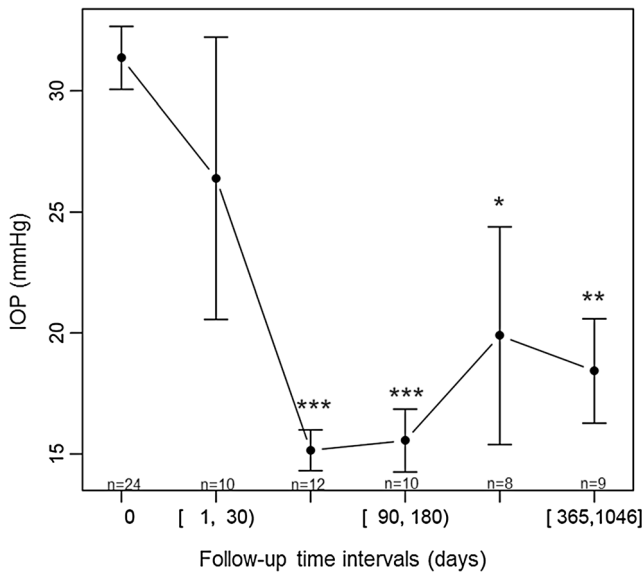
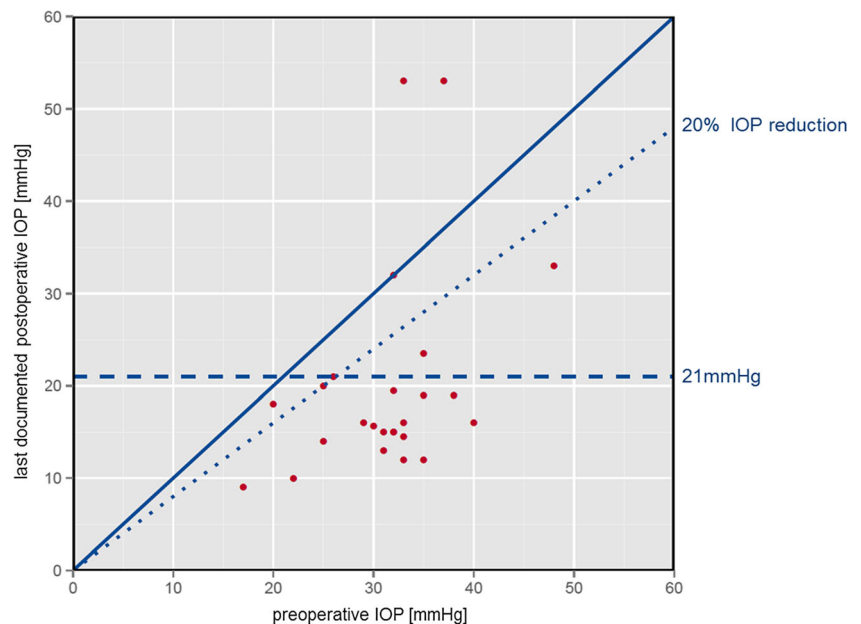


Fig. 1 Mean intraocular pressure was significantly lower during follow-up than before surgery. The ordinate indicates IOP [mmHg], whereas the abscissa is the time after surgery in days. Significance level: *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$. Follow up visits were grouped by time after surgery to compensate for inhomogeneous timepoints of follow up. If a single patient was seen several times during a defined timeframe, mean IOP values for this patient and timeframe were calculated first. During the first follow-up interval (1–30 days) ten patients showed up for one follow up visit. During the second follow-up interval (31–89 days) a total of twelve patients showed up for follow up visit. Nine of these patients showed up for one visit, one patient for two visits and two patients for three visits. During the third follow-up interval (90–180 days) a total of ten patients showed up for follow up visit. Nine of these patients showed up for one visit and one patient for two visits. During the fourth follow up interval (181–364 days) a total of eight patients showed up for follow up visit. Five of these patients for one visit, two patients for two visits and one patient for three visits. During the fifth follow-up interval (365 – 1046 days) a total of nine patients showed up for follow up visit. Six of these patients showed up for one visit and three patients for two visits

Fig. 2 IOP reduction between baseline and the last visit. Scatter plot of preoperative IOP on the abscissa compared to postoperative IOP on the ordinate at the last documented visit. Each dot indicates a patient. Points below the oblique line define a lower postoperative IOP than baseline. The dotted line represents a 20 % reduction of the IOP from baseline



up interval 1; 1.1 ± 0.37 in follow-up interval 2; 1.1 ± 0.88 in follow-up interval 3; 0.92 ± 0.85 in follow-up interval 4; and 0.67 ± 0.83 in follow-up interval 5. The mean number of medications during follow-up is presented in Fig. 3.

In 87.5 % (21 of 24) of the eyes, the IOP was controlled after trabeculectomy ab interno with the Trabectome® (20 % IOP reduction and IOP < 21 mmHg) with additional medication (relative success). None of the patients achieved absolute success (20 % IOP reduction and IOP < 21 mmHg without additional medication). Three eyes, or 12.5 %, needed further glaucoma surgery for IOP control. One eye received a Baerveldt device at day 7. In 2 eyes, we performed a trabeculectomy with mitomycin C: 1 at day 11 and 1 at day 389. Qualified success, defined as sufficient IOP lowering using antiglaucomatous medications, is demonstrated in the Kaplan-Meier survival plot in Fig. 4.

One patient had a significant anterior chamber hemorrhage postoperatively (although this patient was not on anticoagulative medication); thus, it was necessary to perform an anterior chamber lavage. No eyes showed endophthalmitis or uveitis reactivation following surgery with the Trabectome®.

Discussion

In this retrospective, noncomparative study, surgery with the Trabectome® seems to be an effective, minimally invasive method for lowering the IOP in uveitic glaucoma. The IOP-lowering effect is approximately 40 %, with a simultaneous significant reduction in antiglaucomatous medication use. No serious side effects were seen.

The pathophysiology of secondary IOP elevation in patients with uveitis is multifactorial and is not completely

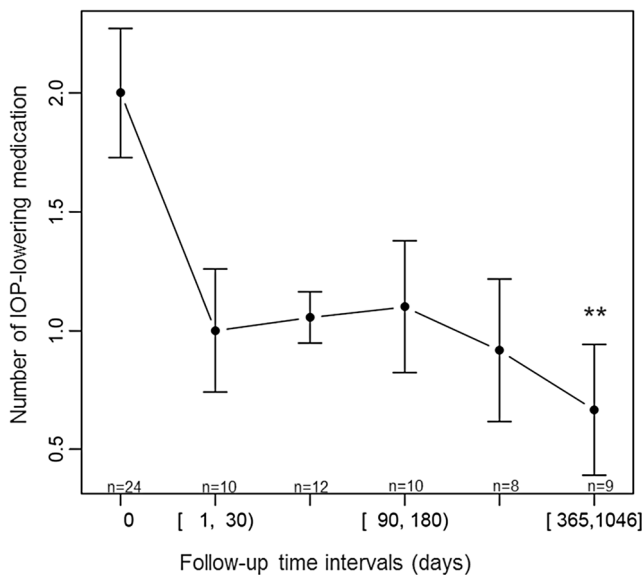


Fig. 3 The mean number of medications was lower during the whole follow-up than before surgery. The ordinate indicates the number of antiglaucomatous substances, whereas the abscissa is the time after surgery in days. Significance level: $**p < 0.01$. Same timeframes as in Fig. 1 were used

understood [10]. Chronic or long-term use of topical steroids leads to a steroid-induced alteration of the trabecular meshwork in one-third of uveitis patients [11]. In particular, young age seems to be a risk factor for steroid-induced glaucoma [18, 19]. Furthermore, in uveitis patients, cell debris causes mechanical obstruction and reduced aqueous outflow during acute inflammation. Additionally, the trabecular meshwork

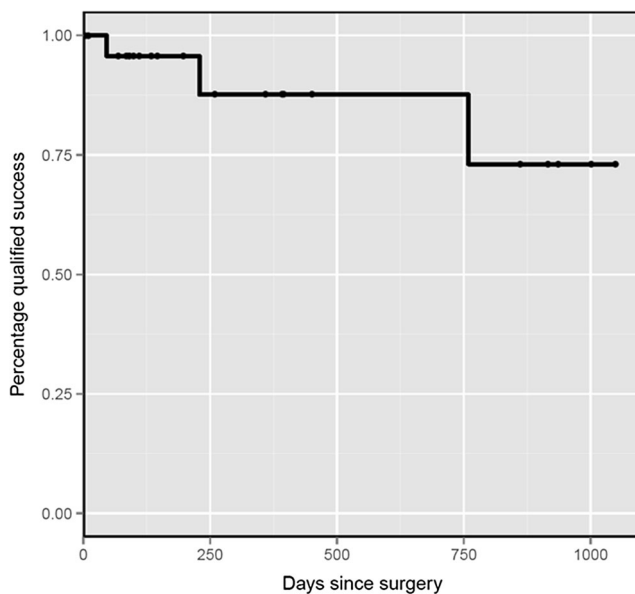


Fig. 4 Kaplan-Meier survival plot for probability of qualified success. Qualified success was defined as a 20 % IOP reduction and an IOP < 21 mmHg with antiglaucomatous therapy. Failure was assumed when the target criteria (20 % IOP reduction and IOP < 21 mmHg with antiglaucomatous therapy) could not be achieved on two consecutive follow-up visits

swells as result of the acute inflammation; therefore, outflow resistance increases. Secondary scarring due to chronic inflammation in the trabecular meshwork leads to increased outflow resistance and, as a result, the IOP becomes elevated [3]. Therefore, the primary cause of elevated IOP is reduced outflow following alterations in the trabecular meshwork. Initially, the increased IOP should be treated by topical administration of antiglaucomatous drugs [20]. If medical therapy is ineffective, surgical intervention is required. Various surgical options are available to lower the IOP in patients with medically uncontrolled uveitic secondary glaucoma. Irrespective of the method used, intraocular surgery should only be performed in eyes with controlled uveitis, with no signs of acute inflammation [21].

Trabeculectomy ab externo has been described as more effective when using additional an antimetabolite medication such as Mitomycin C or 5-Fluorouracil [4, 22–24]. The results for trabeculectomy with an antimetabolite medication in uveitic glaucoma seem to be comparable to those for primary open angle glaucoma, in cases of inactive uveitis without previous surgery [25]. However, in patients who have previously undergone surgery, the risk of failure through conjunctival scarring increases. Drainage valves are an alternative option. Previous studies describe success rates of up to 90 % [7, 26–28], with the best results for Baerveldt-devices [7]. However, drainage implantation is a complex surgical procedure with a risk of serious, vision-threatening complications [29, 30].

Goniotomy, or opening of the altered trabecular meshwork, has been reported to lower the IOP in young uveitis patients, with a success rate of up to 75 % and few complications [31]. Classic goniotomy, as described in the past, uses the same surgical access as the Trabectome[®], but it is inferior because of overlapping wound edges, which could lead to secondary scarring. In contrast, trabeculectomy ab interno with the Trabectome[®] requires the removal of the trabecular meshwork by electroablation such that no overlapping wound edges exist. In particular, considering the chronic inflammation process, this approach could result in even better success rates than goniotomy. Following these pathophysiological considerations, we investigated the results of trabeculectomy ab interno with the Trabectome[®]. In our study, we showed sufficient IOP lowering and reduction of medication use, with a failure rate of 17 %. Owing to the use of clear cornea incisions, the patients' conjunctivas were not affected; thus, later trabeculectomy ab externo [32] or drainage implantation procedures were possible. This method is therefore an option to delay cyclodestruction. The early postoperative results could be influenced by the steroid therapy. However, considering that the trabecular meshwork which contributes to outflow resistance in steroid-response glaucoma is removed during surgery, the influence of steroid induced IOP variations in the early postoperative period seems so be negligible.

The achievable target pressure following trabeculectomy ab interno with the Trabectome® is limited because of the outflow resistance across the collector channels and because of the complex downstream draining and vascular system [14]. Therefore, very low target pressures are not obtainable. However, the Trabectome® is a good option for early surgery in eyes with moderate optic disc damage. Minimally invasive glaucoma surgery shows an advantageous risk profile, and the postoperative treatment is less complex than that for fistulating surgery (trabeculectomy/drainage tubes) [33, 34]. Compared with other minimally invasive glaucoma surgeries (trabecular microbypass stent, Schlemm's canal scaffold or suprachoroidal microstent), trabeculectomy ab interno with a Trabectome® does not require any device implantation. Because the implantation of extraneous material can lead to prolonged intraocular inflammation even in non-uveitic eyes [35, 36], this is another advantage of this particular method. Furthermore, small devices with a small lumen, such as the iStent®, CyPass® or Hydrus scaffold®, could be obstructed by inflammatory cell debris. However, there are no controlled studies testing the effectiveness of minimally invasive glaucoma surgery in patients suffering from secondary glaucoma due to uveitis.

Typically, miotics are avoided in therapy for uveitic glaucoma as they can induce posterior synechia, exacerbate the symptoms of inflammation caused by ciliary spasm and worsen inflammation by disrupting the blood aqueous barrier [21]. Furthermore, it is known that miotics cause postoperative inflammation [37]. However, to avoid anterior synechia in the area of the trabecular meshwork ablation, we administered pilocarpine 2 % in all patients for a minimum of 6 weeks postoperatively. In no patients did we see a reactivation of the uveitis.

This study has the limitations of a retrospective study. Furthermore, the number of cases included was too small to create subgroups for different types of uveitis.

Because of its minimally invasive character, favorable perioperative risk profile and uncomplicated post-surgical treatment, trabeculectomy ab interno with the Trabectome® seems to be an effective and feasible method for glaucoma surgery in patients with secondary uveitic glaucoma.

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