Case Reports in Ophthalmology

Case Rep Ophthalmol 2018;9:61–69

DOI: 10.1159/000479363
Published online: January 23, 2018

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Case Report

Clinical Efficacy and Safety of the EX-PRESS Filtration Device in Patients with Advanced Neovascular Glaucoma and Proliferative Diabetic Retinopathy

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Keywords
EX-PRESS device · Neovascular glaucoma · Proliferative diabetic retinopathy

Abstract
Background: The prognosis of conventional filtration surgery in eyes with neovascular glaucoma (NVG) is limited due to increased fibrovascular proliferation or bleeding. This study aims to evaluate the safety and efficacy of the EX-PRESS filtration device in the management of NVG associated with proliferative diabetic retinopathy (PDR). ***Methods:*** In this retrospective case series, we reviewed the medical records of patients diagnosed as having NVG associated with PDR who underwent EX-PRESS filtration surgery. The main outcome measures were: postoperative intraocular pressure (IOP), the percent of IOP drop, the number of glaucoma medications, visual acuity, and complications of surgery. Successful surgery was de-

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fined as an IOP <22 mm Hg and >5 mm Hg with or without additional glaucoma surgery, and no loss of light perception or less than a 2-line decrease on the Snellen chart of the best corrected visual acuity (BCVA). ***Results:*** Five patients (5 eyes) were included in this study. The mean preoperative IOP was 33.4 ± 5.9 mm Hg compared to an IOP of 17.0 ± 3.0 mm Hg at the last follow-up (p = 0.003). The mean number of preoperative anti-glaucoma medications was 3.8 ± 0.4 compared to 2.2 ± 1.5 (p = 0.06) at the last follow-up visit. Final visual acuity improved or stabilized within 1 Snellen line in all 5 patients. Three patients had a "hypertensive phase" (defined as an IOP >21 mm Hg during the first 6 postoperative months) which resolved within 2 months. Two patients developed a hyphema that resolved spontaneously. None of the patients experienced any serious complications. ***Conclusion:*** EX-PRESS filtration device has a good IOP-lowering effect and a low rate of complications in patients with advanced NVG associated with PDR. In addition, there was no loss of light perception or no line decrease of the BCVA.

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Introduction

Neovascular glaucoma (NVG) is a refractory disease. It has been reported to occur in over 40 ocular diseases, most commonly, diabetes mellitus, central retinal vein occlusion, and ocular ischemic syndrome [1, 2]. Fibrovascular proliferation in the anterior segment may obstruct the trabecular meshwork and cause peripheral anterior synechiae, progressively closing the anterior chamber angle and leading to an intractable elevation of the intraocular pressure (IOP). Ischemia triggers the release of vascular endothelial growth factor (VEGF), interleukin, and other angiogenic factors that can diffuse into the anterior segment, causing neovascularization of the iris and anterior chamber angle [3–5]. IOP control in NVG patients often necessitates surgical treatment, since medical management alone, such as IOP-lowering medications and anti-VEGF injections, together with panretinal photocoagulation (PRP) are often inadequate. However, conventional filtration surgery carries a guarded prognosis in eyes with NVG due to increased fibrovascular proliferation or bleeding. Allen et al. [6] reported that trabeculectomy surgeries had a 67% success rate after a mean follow-up of 22 months. Glaucoma drainage implants, such as the Ahmed glaucoma valve (AGV; New World Medical, Rancho Cucamonga, CA, USA), especially in combination with mitomycin C (MMC), have been used for the treatment of NVG in patients with proliferative diabetic retinopathy (PDR), forming an alternate aqueous pathway that promotes bleb formation far from the limbus. Although the AGV implant is successful in providing early and intermediate IOP control, it fails to achieve control of IOP in patients with NVG in the long term (5 years) [7–12].

The EX-PRESS filtration device is a small non-valved device consisting of a stainless steel, magnetic resonance imaging-compatible implant. It has a 50-μm and a 200-μm lumen that lowers IOP by shunting aqueous humor from the anterior chamber into the subconjunctival area near the limbus [13, 14]. To the best of our knowledge, there are no reports on the safety and efficacy of the EX-PRESS filtration device in the management of NVG in eyes with a history of PDR. The purpose of this study is to report our experience and the out-

comes of EX-PRESS filtration device surgery with the addition of MMC application in patients with NVG.

Methods

This retrospective case series included 5 eyes of 5 consecutive advanced glaucoma patients diagnosed as having NVG due to PDR who underwent EX-PRESS filtration device surgery between September 2011 and May 2014. An indication for surgery was failed maximal glaucoma medication treatment in advanced NVG patients (defined by a progression of retinal nerve fiber layer thinning on 3 successive visits). The diagnosis of NVG was made by a glaucoma specialist (B.T.) and defined as neovascularization of the iris and/or iridocorneal angle (the latter diagnosed by gonioscopy), with an IOP >21 mm Hg. Advanced glaucoma was defined according to ICD-9 staging codes, which include elevated IOP, optic nerve abnormalities consistent with glaucoma, glaucomatous visual field abnormalities in both hemifields, and/or loss within 5 degrees of fixation in at least 1 hemifield [15]. Exclusion criteria were patients younger than 18 years, and those with a history of cyclodestructive procedures, the presence of other retinal diseases, and a follow-up of <12 months.

The study was approved by the Hillel Yaffe Medical Center's Institutional Review Board, and it was carried out in accordance with The World Medical Association's Declaration of Helsinki. All EX-PRESS surgeries were performed by a single surgeon (B.T.). Two patients underwent EX-PRESS 50-μm implantation and 3 patients underwent EX-PRESS 200-μm implantation. One patient also underwent cataract extraction at the time of surgery. One patient had undergone trabeculectomy 2 years before the EX-PRESS surgery.

All 5 patients underwent PRP prior to surgery. Two patients underwent vitrectomy surgery because of vitreous hemorrhage and a retained nucleus in the vitreous after a complicated cataract surgery 3 and 6 months before the index EX-PRESS surgery, respectively. All of the patients received an intravitreal injection of bevacizumab at least 3 months before the EX-PRESS surgery.

The data that were collected during each visit were age, gender, and the results of a complete ophthalmological evaluation, including visual acuity, preoperative IOP, the number of glaucoma medications, previous bevacizumab injections, and previous intraocular surgeries.

The follow-up schedule consisted of visits on the first postoperative day, and at 1 week, 1 month, and every 3–6 months after surgery until a maximal follow-up of 15 months after surgery. A postoperative "hypertensive phase" was defined as an IOP >21 mm Hg during the first 6 postoperative months.

Surgical success was defined as an IOP <22 and >5 mm Hg without additional glaucoma surgery and with no loss of light perception (LP) on at least 2 postoperative visits. Surgical failure was defined as an IOP <5 or >22 mm Hg on at least 2 consecutive follow-up visits, a deterioration of the best corrected visual acuity (BCVA) with loss of LP, or the need for additional glaucoma surgical interventions. Subjects who had a decrease in their BCVA but maintained LP vision or greater were not considered a surgical failure. The definition of hypotony in this study was an IOP of ≤5 mm Hg at 2 consecutive visits.

The surgical technique consisted of a fornix-based conjunctival incision with subconjunctival anesthesia. A wound-modulating agent (MMC 0.02%; Kyowa Hakko Kirin Co. Ltd., Japan) was applied under the conjunctiva for 1 min and copiously irrigated with balanced salt solution. A half-thickness trapezoidal scleral flap of 4 × 4 mm was constructed and advanced anteriorly into the cornea. A 25-gauge needle was used to penetrate the anterior chamber, and the EX-PRESS glaucoma device was inserted into the anterior chamber through this entrance. The corneoscleral flap was sutured at its 2 corners using a 10-0 nylon suture. The conjunctival flap was advanced and sutured by a continuous 10-0 nylon suture. Cefuroxime sodium (Zinacef 750 mg/50 mL; GlaxoSmithKline, Italy) was injected into the anterior chamber at the end of the procedure. Following surgery, all patients received the topical antibiotic ofloxacin 0.3% (Oflox; Allergan, Ireland) 5 times daily for 1 week. Steroid eye drops were prescribed 5 times daily for 4 weeks, followed by tapering down over 1 month. They consisted of a combined ophthalmic suspension containing dexamethasone 0.1%, neomycin sulfate 3,500 IU/mL, and polymyxin B sulfate 6,000 IU/mL (Maxitrol; Alcon-Couvreur, Belgium).

Statistics

The values are presented as means ± standard deviation (SD) and percentages. The differences between the groups were compared using the one-way ANOVA test. A p value of <0.05 was considered to be statistically significant. The statistical analysis was carried out using the SPSS-23 statistical software (IBM Corp, Armonk, NY, USA).

Results

The demographic data and preoperative information of the 5 study patients are listed in Table 1. The postsurgical follow-up period was 12–15 months. One patient who had a follow-up visit 2 months after surgery, and another follow-up visit 15 months after surgery was included. All patients were under individualized maximal therapy before surgery. The mean preoperative IOP was 33.4 ± 5.9 mm Hg (range 26–40 mm Hg), and it decreased to 17.0 ± 3.0 mm Hg (12–20 mm Hg) (p = 0.003). There was a mean of 3.8 ± 0.4 glaucoma medications before surgery which dropped to 2.2 ± 1.1 postoperatively (p = 0.06) (Table 2). Final visual acuity improved or stabilized within 1 Snellen line in all 5 patients.

The IOP was lowered in all of the patients on the first postoperative day, with the mean IOP measuring 10.8 ± 5.2 mm Hg without additional glaucoma medications (p = 0.001). None of the patients developed postoperative hypotony. Three patients had a "hypertensive phase" that gradually stabilized over 2 months: their IOP was controlled with glaucoma medications during that period. Surgical success was achieved in all of the patients at the last follow-up (Fig. 1). Figure 2 shows the IOP measurements for each patient until final follow-up.

Two patients developed intraoperative hyphema that resolved spontaneously within the first week of follow-up. There were no major intraoperative, early, or late postoperative complications.

Discussion

The purpose of this study was to analyze the clinical outcome of EX-PRESS filtration surgery in patients with NVG associated with PDR. There are only a few reports in the literature on glaucoma drainage devices for the treatment of NVG [7–12]. Glaucoma drainage implants, especially the AGV, in combination with an injection of bevacizumab are gaining wide acceptance as a primary procedure for patients with NVG. Variable success rates for IOP control have been reported: Mahdy et al. [16] reported a 95% success rate (complete and qualified) using AGV surgery for NVG when intravitreal bevacizumab injection and PRP were followed by implantation of an AGV. Ma et al. [17] reported a 70% success rate 1 year after AGV implantation combined with an intraoperative bevacizumab injection. A recent study reported a success rate of 79% after 1 year and of 56% after 2 years using the Baerveldt implant for treating NVG [18]. The success rates when using the Molteno tube were reported to be 37–72% and 29–60% after 1 and 2 years, respectively [8, 19, 20].

The EX-PRESS glaucoma implant is a well-tolerated miniature glaucoma device aimed at lowering IOP. Previous publications have reported on the device's efficacy and relatively low rates of postoperative complications [21, 22]. Our results show that the control of IOP was achieved up to the final follow-up visit in all of our patients with NVG associated with PDR, although 4 of them still required glaucoma medications. The overall mean number of glaucoma medications for the group, however, was reduced (Table 2). There was only 1 intraoperative minor and transient complication (mild hyphema) in 2 patients, and no postoperative complications in any patient.

A period of transient elevation of IOP ("hypertensive phase") was described after glaucoma drainage implant surgery by Ayyala et al. [9]. Those authors reported that 83.5% of their patients with advanced uncontrolled glaucoma that underwent AGV implantation experienced a "hypertensive phase" compared to 43.5% of the patients that underwent double-plate Molteno implantation [23]. Three of our 5 patients also developed a transient "hypertensive phase".

Many reports have shown the efficacy of anti-VEGF application in treating NVG [24, 25]. Intravitreal and intracameral bevacizumab injections have been reported to be a safe and effective adjuvant for glaucoma drainage devices in the setting of NVG [16, 17]. In the current study, all 5 patients received an intravitreal bevacizumab injection within 1 month before surgery.

The limitations of this study include its small sample size as well as its retrospective nature, and the lack of a control group. In addition, although all of the patients showed surgical success, we could not properly evaluate the effect of the bevacizumab injection alone because of the small sample size. The study size also prevented a comparison of the surgical results between the 50-μm lumen EX-PRESS device and the 200-μm lumen EX-PRESS device, and there are no studies comparing the efficacy of 50-μm versus 200-μm EX-PRESS device in humans. In our study, both devices were equally beneficial.

In conclusion, our experience indicates that the EX-PRESS filtration device has a good and long-lasting IOP-lowering effect with a low rate of mild and transient complications in patients with NVG due to PDR.

Statement of Ethics

The study was approved by the Hillel Yaffe Medical Center's Institutional Review Board.

Disclosure Statement

The authors report no conflict of interest with this work.

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Drs. Hanna and Tiosano contributed equally to this study.

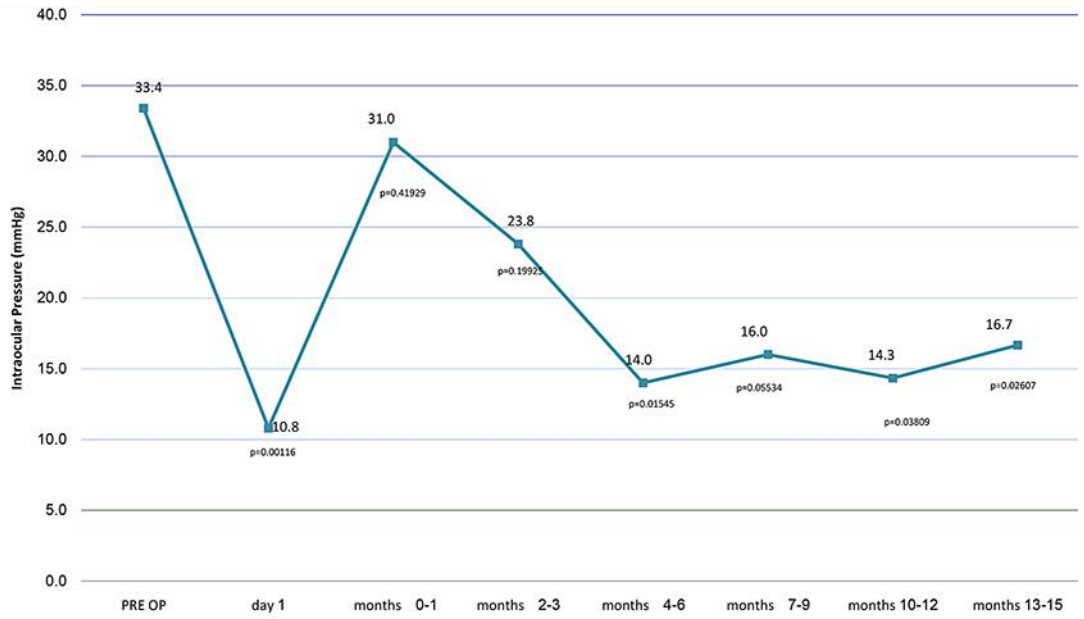
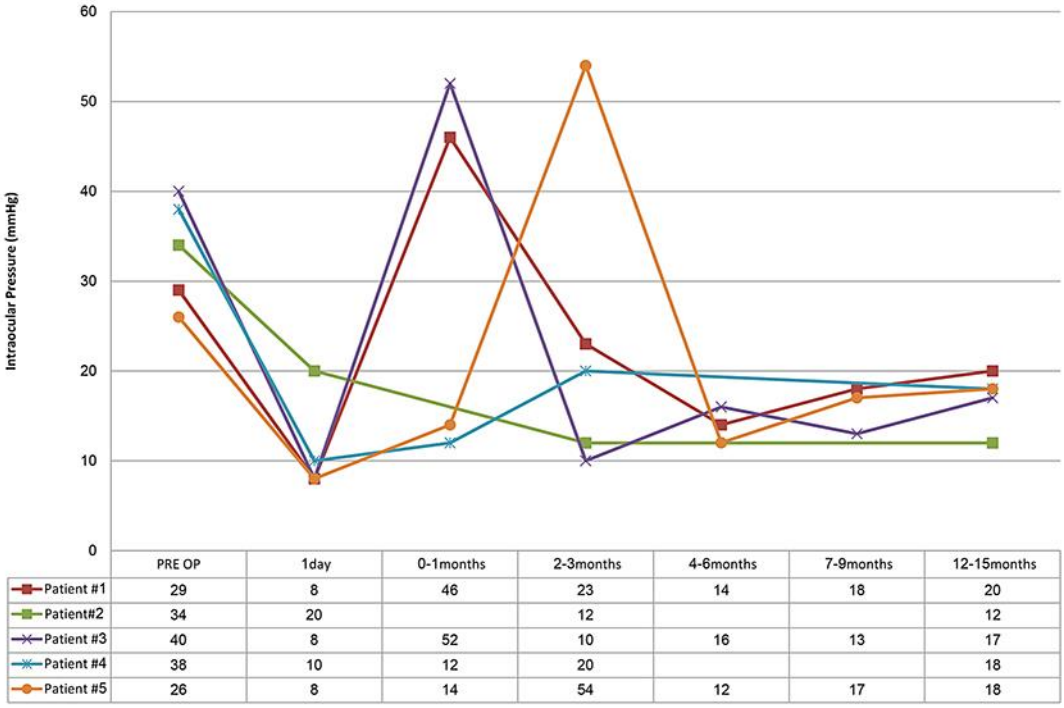


Fig. 1. Surgical outcome at the last follow-up.



	PRE OP	1day	0-1months	2-3months	4-6months	7-9months	12-15months
Patient #1	29	8	46	23	14	18	20
Patient#2	34	20		12			12
Patient #3	40	8	52	10	16	13	17
Patient #4	38	10	12	20			18
Patient #5	26	8	14	54	12	17	18

Fig. 2. Intraocular pressure measurements for each patient until final follow-up.

Table 1. Baseline characteristics of the study group

Male:female	4:1
Mean age ± SD, years	64.6±12.1
Side of operated eye	
Right:left	1:4
Phakia:pseudophakia	1:4
Prior glaucoma surgery	1
Prior vitrectomy	2
Prior PRP laser	5
Prior intravitreal bevacizumab injection	5

PRP, panretinal photocoagulation; SD, standard deviation.

Table 2. Comparison of preoperative and postoperative results with the EX-PRESS glaucoma device in neovascular glaucoma

	Preoperative	Postoperative	*p* value
Mean IOP ± SD, mm Hg	33.4±5.9	17.0±3.0	0.00368
Mean number of glaucoma medications ± SD	3.8±0.4	2.2±1.5	0.06012
Visual acuity, *n* patients			
≥20/200	2	2	
<20/200-CF	2	2	
Hand motion and light perception	1	1	

IOP, intraocular pressure; SD, standard deviation.