Intraocular pressure reduction in neovascular glaucoma using Ex-PRESS implantation

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Abstract:

Purpose: evaluation of the role of the Ex-PRESS device implantation in IOP reduction of neovascular glaucoma.

Design: non-comparative case series study.

Patients and methods: 5 eyes with neovascular glaucoma scheduled to undergo Ex-PRESS glaucoma filtration device. Each study patient underwent a complete ophthalmic examination preoperatively including full clinical history taking, VA measurement, autorefraction examination, slit lamp biomicroscopy of the anterior segment, IOP measurement using Goldmann applanation tonometer, gonioscopic examination to evaluate of the angle of AC, and ophthalmoscopy of the posterior segment using a direct ophthalmoscopy. All patients included were having neovascular OAG (angle grade 3 and 4 on Shaffer classification). Patients were excluded if they were under 18 years old. All eyes underwent Ex-PRESS device implantation performed by the same surgeon for consistency, using the standardized technique for the procedure. A complete ophthalmologic follow-up examination included IOP measurement using Goldmann applanation tonometry, number of drugs required to attain IOP control and any associated complications was carried out postoperatively at the 1st and 3rd days, the end of 1st week, every month till the end of the 6th month and the end of 1st year. Best-corrected visual acuity (BCVA) was tested using Snellen chart, which was converted to LogMAR for statistical analysis. Criteria for success were defined as follows; Absolute success: IOP ≤21 mmHg without any medication, qualified success: IOP ≤21 mmHg with ocular hypotensive medications.

Results: all cases (100%) showed qualified success. There is a statistically significant reduction in IOP 1, 3, 6 months and one year postoperatively (P<0.001) with the most reduction in IOP observed at 6 months after surgery due to controlling all cases with IOP >21 mmHg using anti-glaucoma medications by this time. There is a statistically significant improvement of postoperative BCVA (P=0.002). Moreover, there is a statistically significant reduction of number of anti-glaucoma medications used postoperatively (P<0.001).

Conclusion: Ex-PRESS is preferable for neovascular glaucoma.

Introduction:

NVG is an aggressive type of glaucoma, which often results in poor visual outcomes. Neovascularization (NV) occurs as a result of angiogenic stimuli, including the vascular endothelial growth factor (VEGF).[1] Most NVG patients have severe underlying systemic and ocular pathology which causes NVG as a late presentation of their primary systemic and/or ocular disease. These patients present with elevated IOP, NVI and NVA, often with hyphema and other ocular findings, such as ectropion uveae. The fibrovascular scaffolding of these vessels cross the angle and IOP becomes markedly elevated, though the angle may still be gonioscopically open. Ultimately, in the absence of definitive treatment, these fibrovascular membranes contract and produce synechial angle closure and ectropion uveae with intractable elevation of IOP and damage to the optic nerve with subsequent vision loss.[2] The management of NVG has

two main components. The first component is reduction of the IOP by both medical and surgical means. The second component, which is arguably the most critical for effective long-term treatment outcomes, is reduction of the ischemic drive that induces formation of new blood vessels. The mainstay of this treatment component is panretinal photocoagulation (PRP).[2]

One of the surgical treatments for pseudohakic glaucoma is glaucoma drainage device (GDD) implantation such as Ex-PRESS device as their success is less dependent on control of intraocular inflammation.[3] The Ex-PRESS miniature glaucoma implant (Alcon Laboratories Inc., Fort Worth, TX) is a biocompatible, non-valved stainless steel tube. The Ex-PRESS is currently implanted under a partial thickness sclera flap, as first suggested by Dahan and Carmicheal.[4] the procedure is similar to standard trabeculectomy, and includes creation of scleral flap and a conjunctival filtration bleb, but no peripheral iridectomy is required. Modulating the wound healing process to lessen scar formation around the scleral flap plays a crucial role in the success of glaucoma filtering surgery. Current studies have shown evidence of reduced bleb failure after subconjunctival injections of bevacizumab as an anti-VEGF.[5-6] The application of bevacizumab at the time of surgery could temporarily block the postoperative increased VEGF concentration and its level of up-regulation in the AH.[7]

Herein, we evaluate the role of the Ex-PRESS device implantation in IOP reduction of neovascular glaucoma.

Patients and methods:

This is a non-comparative case series study of 5 eyes with neovascular glaucoma that were scheduled to undergo Ex-PRESS glaucoma filtration device. All patients' data were collected between November 2016 and July 2018 (the patients are operated between November 2016 to April 2017 and then followed up for one year) at Ophthalmology department - Sohag University hospital. The research adhered to the tenets of the Declaration of Helsinki. Written informed consent was taken from each patient. Each study patient underwent a complete ophthalmic examination preoperatively including full clinical history taking, VA measurement, autorefraction examination, slit lamp biomicroscopy of the anterior segment, IOP measurement using Goldmann applanation tonometer, gonioscopic examination to evaluate of the angle of AC, and ophthalmoscopy of the posterior segment using a direct ophthalmoscopy. All patients included were having neovascular OAG (angle grade 3 and 4 on Shaffer classification). Patients were excluded if they were under 18 years old.

Surgical technique: All eyes underwent Ex-PRESS device implantation performed by the same surgeon for consistency, using the standardized technique for the procedure. All the procedures were performed in the superior conjunctival area. After retrobulbar local anesthesia, superior rectus bridle suture was taken. A fornix-based conjunctival flap was created with a relaxing incision on one side (Figure 1). Next, a 50% thickness rectangular scleral flap (5x5mm) was constructed and advanced anteriorly into the clear cornea using Alcon crescent knife (Saint Crescent, angled, bevel up) (Figure 2). Paracentesis was done temporally using a 20G micro-vitreoretinal (MVR) blade. As the scleral flap was lifted, care was taken to identify the center of the “blue line” adjacent to the clear cornea, which corresponds to the location of the TM.

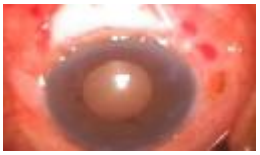

Figure 1:
Conjunctival dissection

Figure 2:
Creating scleral flap using crescent knife

A 25G needle (Ex-PRESS entry system) was inserted into the AC through the center of the "blue line" at an angle parallel to the iris plane to create a path for the Ex-PRESS (model P-50) and then removed gently to avoid lateral movement that may extend the channel and cause aqueous humor to leak around the shunt (Figure 3). The Ex-PRESS shunt is preloaded on an injector (Figure 4).

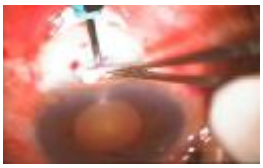

Figure 3:
25G trocher inserted into the AC

Figure 4:
Preloaded Ex-PRESS on an injector

The shunt is introduced into the AC exclusively through the ostium created by the needle (Figure 5) and released by applying pressure to the shaft of the inserter. The tip of the device was confirmed to be in the AC in the iris plane away from the cornea and without any iris obstruction.

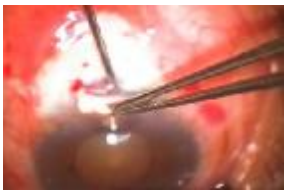

Figure 5:
Introduction of the shunt into AC

The scleral flap is then sutured with interrupted 10-0 Nylon (Figure 6). Two to three sutures were typically required with the tightness adjusted depending on the resultant flow during inflation of the AC with balanced salt solution using a 27G needle through the temporal paracentesis to restrict flow to a "slow trickle" while the AC remains well maintained. Finally, the conjunctival incision was closed water tight fashion using an interrupted 10-0 Nylon (Figure 7).

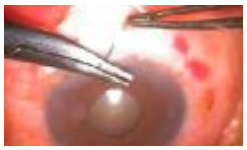

Figure 15:
Suturing scleral flap

Figure 16:
Closing conjunctival incision

We confirmed that there was no leakage from the blebs. All patients received similar postoperative topical medications: 0.5% moxifloxacin five times daily for 3 weeks and 0.1% prednisolone acetate five times daily for 3 week without tapering after operation.

Follow up: A complete ophthalmologic follow-up examination included IOP measurement using Goldmann applanation tonometry, number of drugs required to attain IOP control and any associated complications was carried out postoperatively at the 1st and 3rd days, the end of 1st week, every month till the end of the 6th month and the end of 1st year. Best-corrected visual acuity (BCVA) was tested using Snellen chart, which was converted to LogMAR for statistical analysis. Criteria for success were defined as follows; Absolute success: IOP ≤21 mmHg without any medication, qualified success: IOP ≤21 mmHg with ocular hypotensive medications.

Results:

One case had an intraoperative complication in the form of opening of the AC during scleral flap advancement and the procedure was completed as a conventional trabeculectomy, which was excluded from the results.

Patients included 2 males and 2 females. Studied patients' demographics and ocular characteristics preoperatively are summarized in tables 1. The ocular characteristics one year postoperative are summarized in tables 2. Comparisons between pre- and post-operative data are summarized in tables 3 and 4. all cases (100%) showed qualified success (IOP <21 mmHg with anti-glaucoma medical treatment)

Table 1: Preoperative demographics and ocular characteristics of studied patients

Variable	Mean	Std. Deviation
Age	55.40	7.34
IOP	36.76	9.14
BCVA	1.64	0.46
NO. of Medications	3.66	0.41

Table 2: Postoperative ocular characteristics of studied patients

Variable	Mean	Std. Deviation
IOP after 1 month	21.84	2.83
IOP after 3 months	20.96	5.41
IOP after 6 months	17.92	3.80
IOP after 1 year	18.20	1.82
BCVA	1.53	0.45
NO. of Medications	0.93	1.18
Time to Re-enter Medications	3.03	0.96

Table 3: Comparison of preoperative IOP and IOP 1, 3, 6 months and 1 year postoperatively

	Postoperative IOP	*P* value
Preoperative IOP (36.76±9.14)	1 Month (21.84±2.83)	<0.001
	3 Months (20.96±5.41)	
	6 Months (17.92±3.80)	
	1 Year (18.20±1.82)	

Table 4: Comparisons between data preoperatively and one year postoperative

Variable	Preoperative (mean±sd)	Postoperative (mean±sd)	*P* value
BCVA	1.64±0.46	1.53±0.45	0.002
NO. of Medications	3.66±0.41	0.93±1.18	<0.001

Discussion:

Glaucoma is the leading cause of irreversible blindness worldwide and represents a significant public health concern.[8] The Ex-Press GDD is a new method for standardizing trabeculectomy with outcomes quite similar to trabeculectomy reported in the literature. Trabeculectomy and other filtering surgeries are moderately successful in the long term in patients with NVG. The success of trabeculectomy surgery is limited by the severe inflammation encountered with NVG eyes. In contrast with trabeculectomy, Ex-PRESS implantation is less invasive and causes fewer complications, subsequent inflammation, less IOP variance and faster recovery during the early postoperative period.[9-10] GDDs have gained popularity in the surgical treatment of NVG, as their success is less dependent on control of

intraocular inflammation and the failure of a filtering bleb.[3]

Our study revealed that all patients with NVG had qualified success 1 year after Ex-PRESS implantation. In a previous study by YU et al,[11] a significant mean IOP reduction was observed in the first postoperative week after Ex-PRESS implantation in NVG, but 3out of 4 patients had failed blebs and recurrent NVG afterward. However, IOP of 2 of these 3 patients remained <21 mmHg without medication after shunt reposition. At the last follow-up, IOP control <21 mmHg without anti-glaucoma agents was shown in 3 cases out of 4 patients (75.0%). As for the final Snellen BCVA, 2 out of 4 patients (50%) in that study demonstrated improvement, though 1 patient reflected the same level of no light perception, as in the preoperative condition, and another patient had deterioration due to macula-off RD. Before RD, the BCVA of that patient was actually better than his preoperative BCVA. Compared to other interventions, 40% of NVG patients had improved BCVA after trabrculectomy with MMC, whereas 46.7% of patients experienced deteriorated BCVA.[12]

Surgical intervention, such as the placement of a GDD, can also lead to hyphema as a result of iris and globe manipulation during surgery and intraocular trauma to NV.[2] Hyphema can impair visualization during surgery and lead to longer operative times, as well as cause blood clots which can occlude the tube tip of a GDD. In our study, hyphema occurred in one out of four eyes with NVG which resolved spontaneously within the first week. We also injected anti-VEGF subconjunctivally to reduce incidence of hyphema and help regression of NVI.

In a previous study by Choi and Hyung,[13] 50% of NVG patients developed hyphema. All cases were resolved spontaneously during the first week after surgery. In previous studies on NVG, the most common complication of trabeculectomy was hyphema. The incidence was around 30% and 58%, and significantly decreased to the levels around 10% and 33.3% if adjuvant anti-VEGF or peripheral iris cauterization was used.[12,14]

We injected the bevacizumab at the near-limbal location which was close to the NVI. This was based on findings from a previous study that has been suggested that macromolecules may diffuse through the sclera and directly into the iris after subconjunctival injections.[15] In pharmacokinetic studies, bevacizumab was detectable in the AC until one week after subconjunctival injections.[16-17] Therefore, its effect in suppressing anterior segment NV should be transient. Nonetheless, our cases show that it is still useful in preventing the aggravation of the disease during the time window before applying PRP. Moreover, associated decrease of hyphema or corneal edema allows for prompt PRP.

A certain correlation between VEGF expression and the outcome of glaucoma surgery was suggested and the potential usefulness of anti-VEGF therapy was then considered in improving the success rate of glaucoma surgery.[18-19] Kim et al systematically reviewed the effect of subconjunctival or intravitreal injection of bevacizumab in combination with trabeculectomy, and increased bleb survival time was found in their related animal study.[20] Possible explanation is that NVI resolution might be caused by increased aqueous outflow through Ex-PRESS, resulting in a decreased VEGF level in the AC.

In our study, the number of anti-glaucoma medications taken postoperatively (0.93±1.18) was significantly lower than number of medications taken preoperatively (3.66±0.41) (P<0.001). In previous study by Liu et al,[21] the number of glaucoma medications taken postoperatively was lower than the number of glaucoma medications taken pre-operatively (0.94 ± 0.96 vs. 1.18 ± 1.38). In a study comparing Ex-PRESS to trabeculectomy in an African origin population,[22] the number of glaucoma medications used to control IOP postoperatively was reduced from (3.82±0.8) at baseline to (0.86±1.00) (P=0.05) at 12 months for Ex-PRESS group.

VA may improve following surgery or may deteriorate following surgery either as a result of complications of surgery or progression of disease. Our results showed significant improvement of BCVA from (1.64±0.46) LogMAR preoperatively to (1.53±0.45) LogMAR postoperatively (P=0.002). Good and Kahook[23] reported increased visual recovery following surgical intervention in patients undergoing Ex-PRESS surgery.

On the other hand, several investigators have noted a risk of central VA loss after filtration surgery in eyes with advanced glaucoma.[24-25] Wagschal et al[26] found that VA in patients treated with the Ex-PRESS implant did not differ significantly from baseline by 1 month post-operation (P=0.17), and remained stable for all subsequent visits. In another prospective randomized trial by Beltran-Agullo et al,[27] by month 1, VA in the Ex-PRESS group was no longer significantly different from baseline (P=0.23) and remained stable throughout 6 months of follow-up.

In this study, we can conclude that, Ex-PRESS is preferable for neovascular glaucoma. Stable filtration after Ex-PRESS implantation may be expected to show less IOP fluctuation during the intraoperative and early postoperative periods.

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