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XEN gel stent ® in the management of glaucoma: preliminary results of a tertiary center

Rita Vieira, Ana Figueiredo, Rita Reis, Isabel Sampaio, Maria João Menéres

Centro Hospitalar Universitário do Porto (CHUP);

Oporto (Portugal)

Purpose: *To analyze the efficacy and safety of a MIGS device (XEN gel stent ®) in the management of glaucoma in our tertiary center.*

Methods: *Retrospective analysis of patients submitted to XEN ® implant alone or combined with cataract surgery. Patients with previous filtering surgeries were included. Intraocular pressure (IOP) was evaluated at 1st week, 1st, 3rd, 6th and 12th months after surgery. BCVA, RNFL thickness and number of antiglaucoma medications were evaluated 1 year after surgery. Early and late complications and need for an additional glaucoma surgery were recorded.*

Results: *Thirty-four eyes from 28 patients were included. The main diagnosis was primary open angle glaucoma (POAG) (58.8%).*

IOP decreased from 20.5±4.9 mmHg to 15.4±4.1 mmHg 1 year after surgery ($p<0.001$). There was also a decrease in the number of antiglaucoma medications, from 3.6±0.6 to 0.6±0.7 ($p<0.001$). BCVA increased from 0.57±0.30 to 0.87±0.18 in the combined surgery group ($p=0.03$). RNFL thickness remained stable ($p=0.558$).

Hypotony occurred in 2 eyes (5.9%). Two eyes (5.9%) needed another glaucoma surgery in the 1st year of follow-up.

Conclusion: *According to our results, XEN® alone or combined with phacoemulsification showed to be effective in IOP reduction, with few complications, as a primary surgery or even in eyes with previous filtering surgeries.*

Keywords:

XEN ® gel stent, XEN45 ® gel stent, glaucoma, MIGS

Introduction

Glaucoma is a chronic, progressive optic neuropathy most of the times associated with elevated intraocular pressure. It is considered one of the leading causes of blindness worldwide, affecting nearly 76 million people. Untreated cases or uncontrolled intraocular pressure (IOP) usually results in severe vision loss. [1, 2].

The main goal of glaucoma treatment is IOP lowering, which can be reached by hypotensive topical drugs and surgery. Although the hypotensive eyedrops are highly effective, glaucoma surgery is indicated when ocular pressure is uncontrolled with maximum topical medication, progression of glaucoma even with controlled IOP or intolerance to hypotensive eyedrops. [1, 3].

The most frequently performed glaucoma surgery worldwide is Trabeculectomy, although in recent years a lot of other techniques had gain protagonism, like non-penetrating deep Sclerectomy, ExPRESS® implant, Canuloplasty, tubes, various techniques of minimal invasive surgery and others. Filtering surgeries create a bypass of aqueous humor flow from the anterior chamber to the subconjunctival space, which is achieved after creating a scleral flap that led posteriorly to the development of a filtration bleb. These procedures are associated with a considerable rate of complications including cataract development, conjunctival scarring and hypotony with uveal effusion, which is higher in Trabeculectomy according to several studies. [1-4].

In the past few years, minimally invasive glaucoma surgery (MIGS) has gained popularity due to its effective reduction of intraocular pressure, showing lower rates of complications, minimal tissue disruption, ab interno insertion and shorter surgical time when compared to filtering surgeries. MIGS devices can be divided in trabecular, suprachoroidal and subconjunctival. XEN gel stent® is one of the subconjunctival MIGS devices, which creates an alternative outflow pathway of the aqueous humor to the subconjunctival space. [5]. Figures 1A and 1B presents a XEN gel stent captured by an automated gonioscope (GS-1, Nidek®).

This technique is recommended essentially as a primary intention surgery in mild to moderate primary and secondary open angle-glaucoma and ocular hypertension in the low-twenties. Nevertheless, some reports were published related to XEN implant in eyes previously submitted to filtration surgeries, showing promising outcomes. [6, 16]

It has shown to be effective and safe in numerous studies worldwide, although few data are available in Portugal.

Materials and methods

This study was conducted in accordance with the tenets of the Declaration of Helsinki (1964) and its latest amendment (Brazil, 2013). A retrospective, single center study was performed, including all patients submitted to XEN gel stent® (Allergan) implant alone or combined with phacoemulsification.

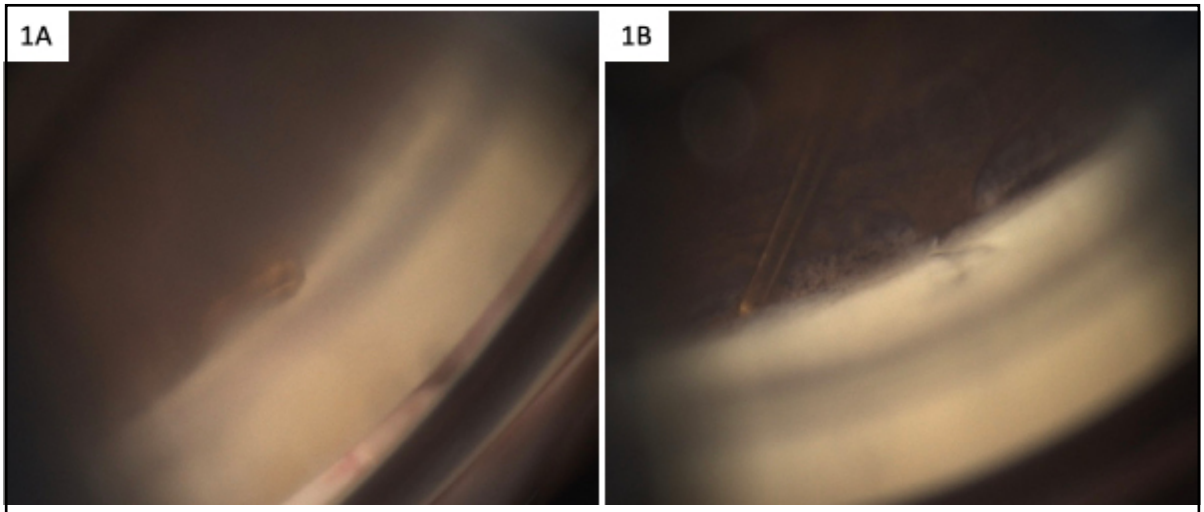

Fig. 1A and 1B. Automated gonioscopy (GS1, Nidek®) showing XEN implant emerging at anterior chamber through iridocorneal angle. Captured at Ophthalmology department of CHUP.

Surgical technique. The surgeries were performed by four different and experienced glaucoma surgeons, using the same technique. All surgeries were performed under topical anesthesia with oxybuprocaine and intracamerular lidocaine. After sterile measures and placing of an eyelid speculum, the superior-nasal conjunctiva is marked 3mm from the limbus, in the planned exit point of the stent. Then, a subconjunctival injection of 0.1 mL of 0.02% diluted MMC with a 30-gauge needle and a posterior massage of this area using cellulose sponges, keeping it away from the limbus, is done. Main incision is performed temporally, 180 degrees from the exit point and a side port is placed in-between the main incision and exit point; viscoelastic is placed in the AC. The preloaded injector passes through the temporal incision in the direction of superior-nasal quadrant, passing through the angle, and when the injectors' needle is observed subconjunctivally, the implant can be injected. When necessary, an intraoperative gonioscopy is performed to confirm the implant placement in AC. [1-3].

Collected data and analysis. Demographic and clinical data were collected at baseline including age and gender, previous glaucoma surgeries, type of glaucoma, central corneal thickness, retinal nerve fiber layer thickness (RNFL), best corrected visual acuity (BCVA), intraocular pressure (IOP) and number of antiglaucoma medications. All patients submitted to XEN implant as first surgery presented mild glaucoma, according to Hodapp classification. Eyes with previous filtering surgeries had moderate glaucoma.

Main outcomes. IOP was evaluated at the 1st week, at 1st, 3rd, 6th months and 1 year after implant. BCVA, RNFL thickness and number of antiglaucoma medications were evaluated 1 year after surgery. Surgical complications, such as hypotony and hyphema were recorded.

Surgical success was defined as: absolute success if IOP≤18 mmHg, one year after surgery with no need of antiglaucoma medications; partial success: IOP≤18 mmHg one year after surgery with the need of antiglaucoma medications; surgical failure was defined as uncontrolled IOP that needed additional glaucoma surgery.

A comparative analysis was performed considering two groups, the patients who underwent XEN gel stent implantation alone and the patients with device implantation combined with phacoemulsification. A sub-analysis of patients with previous glaucoma surgeries was also undertaken.

Statistical analysis. Statistical analysis was performed with SPSS® version 27.0 and a significance value of 0.05 was considered. A repeated measures ANOVA was performed to IOP analysis. The other continuous variables, such as number of antiglaucoma medications, BCVA and RNFL were analyzed using a T-test.

Results

Baseline. Thirty-four eyes from 28 patients were included. Mean age was 66.2±15.3 years-old and 15 were female (44.1%). Eighteen eyes (52.9%) underwent XEN implant alone and 16 (47.1%) XEN combined with phacoemulsification. Mean follow-up was 23.1±3.7 months. Seven eyes (20.6%) had been submitted to previous glaucoma surgeries. Four eyes were submitted to XEN® implant not for uncontrolled IOP, but because of drops' intolerance.

Primary open angle glaucoma (POAG) was the most frequent, happening in 20 eyes (58.8%), followed by Pseudoexfoliative glaucoma in 7 eyes (20.6%), Glaucoma secondary to intravitreal steroids in 5 eyes (14.7%), Juvenile glaucoma in one eye (2.9%) and narrowed angle glaucoma in one eye (2.9%). In this last patient a XEN combined with phacoemulsification was performed.

Mean central corneal thickness was 517.9±40.2 μm.

Mean Intraocular pressure (IOP) was 20.5±4.9 mm Hg at baseline, with no differences between XEN® alone or combined with phacoemulsification (p=0.104). Mean antiglaucoma topical medications was 3.6±0.6, being slightly higher in the XEN alone group versus XEN+Phacoemulsification

Table 1. Baseline characteristics

Number of patients / eyes	28 patients 34 eyes	
Age (mean±SD)	66.2±15.3 years-old	
Gender	15 Female (53.6%) 13 Male (46.4%)	
Type of glaucoma	POAG: 20 eyes (58.8%) PEX: 7 eyes (20.6%) Secondary to steroid intravitreal implants: 5 eyes (14.7%) PCAG: 1 eye (2.9%) Juvenile Glaucoma: 1 eye (2.9%)	
Previous glaucoma surgeries	7 eyes (20.6%)	
Central corneal thickness (CCT)	517.9±40.2 μ	
Follow-up (months)	23.1±3.7 months	
Baseline IOP (mmHg)	20.5±4.9 mmHg.	P=0.104
Antiglaucoma topical medications	3.6±0.6 XEN group: 3.83±0.4 XEN+Phaco: 3.38±0.7	**P=0.033**
RNFL central thickness	64.5±27.7	P=0.886
BCVA (decimal)	Total: 0.57±0.30 XEN group: 0.64±0.32 XEN+Phaco: 0.47±0.22	P=0.076

Legend: SD: standard deviation; IOP: intraocular pressure; RNFL: Retinal Nerve Fiber Layer; BCVA: Best Corrected Visual Acuity.

(3.83±0.4 vs 3.38±0.7, respectively, p=0.033). Mean central RNFL thickness was 64.5±27.7 μm, with no differences between groups (p=0.886). Mean BCVA (decimal scale) in the XEN alone group was 0.64±0.32 and 0.47±0.22 in the XEN+phaco group, although no statistical difference was found (p=0.076). Baseline data is summarized in table 1.

Main outcomes. IOP decreased from 20.5±4.9 mmHg at baseline to 9.6±7.5 mmHg at 1st week, 14.1±4.6 mmHg at 1st month, 15.6±4.1 mmHg at 3rd month, 15.4±3.1 mmHg at 6th month and to 15.4±4.1 mmHg 1 year after surgery (Repeated measures ANOVA with in-between subjects: $F(2.5; 38.1)=10.27$, $p<0.001$), with no differences between XEN alone or combined with cataract surgery (p=0.824). This reflects a reduction of 24.9% in IOP, comparing the results of one year follow up and baseline. The variation of IOP is presented in figure 2.

Antiglaucoma medications decreased from 3.6±0.6 to 0.6±0.7 one year after surgery ($p<0.001$), with no differences between groups (p=0.478)- figure 3. BCVA increased from 0.57±0.30 to 0.87±0.18 in the combined surgery group (p=0.03), with no changes in the Xen alone group- figure 4. RNFL thickness did not show differences from baseline to 1 year follow up in both groups (p=0.558).

Surgical success and complications. Absolute success was achieved in 17 eyes (50%) and relative success in 15 eyes (44.1%). Two eyes (5.9%) needed another glaucoma surgery in the 1st year of follow-up, and both were submitted to ExPRESS® implant, showing controlled IOP until the last follow-up, although with the need of antiglaucoma eyedrops in both cases.

In the immediate post-surgical time, transient uncomplicated hypotony occurred in 2 eyes (5.9%), without register of hypotonic maculopathy or need to perform needling of the bleb.

Eyes with previous glaucoma surgeries. Seven eyes (20.6%) had been previously submitted to glaucoma surgery: 4 eyes to a Trabeculectomy, one eye to a Deep Sclerectomy and one eye had two previous glaucoma surgeries, an ExPRESS® implant combined with phacoemulsification and a cyclophotocoagulation.

In this group of eyes, absolute success was achieved in 3 eyes (42.9%), relative success in 3 eyes (42.9%) and one eye (14.3%) needed an additional glaucoma surgery in the first year. This last patient was submitted to ExPRESS® and has controlled IOP until last follow-up, with the need of antiglaucoma eyedrops.

Discussion

The XEN45® gel stent consists of a collagen tube with 6 mm length and 45 μm of inner lumen that is injected via ab-interno though the trabecular meshwork. This device provides a moderate decrease in IOP through a subconjunctival drainage, without the need of conjunctival dissection. During device development, 45 μm was found to be the ideal diameter to prevent hypotony whereas maintaining aqueous outflow for IOP control. Currently, this procedure is indicated alone or in combination with cataract surgery for mild to moderate glaucoma that is uncontrolled with topical medications or in patients that shows pharmacological intolerance. This device was approved by FDA in 2016 and since then several studies have been published worldwide. However, in Portugal only a few studies were published. [1, 2, 7].

This minimally invasive glaucoma surgery (MIGS) has been associated with fewer complications comparing to other filtrating surgeries. Theillac V. et al studied two equivalent groups of eyes submitted to XEN gel stent or non-penetrating deep sclerectomy (NPDS), both combined with phacoemulsification. They concluded that XEN implant combined with phacoemulsification is capable of significantly lower IOP and the number of antiglaucoma medications, with shorter operating time. In this cohort, only one patient in the group of NPDS presented hypotony with choroidal detachment; the surgical failure with the need of other glaucoma surgery was the same in both groups (2 eyes). [4]. Stoner A. et al in their study aimed to compare the efficacy and safety of two similar groups of eyes that underwent implant of XEN or ExPRESS devices, concluding that XEN group was associated with fewer hospital visits and fewer complications, more specifically less hypotony and choroidal effusions (1 eye in

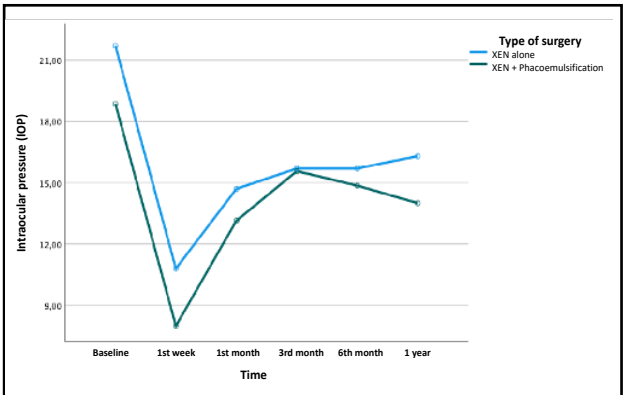

Fig. 2. IOP during follow up.

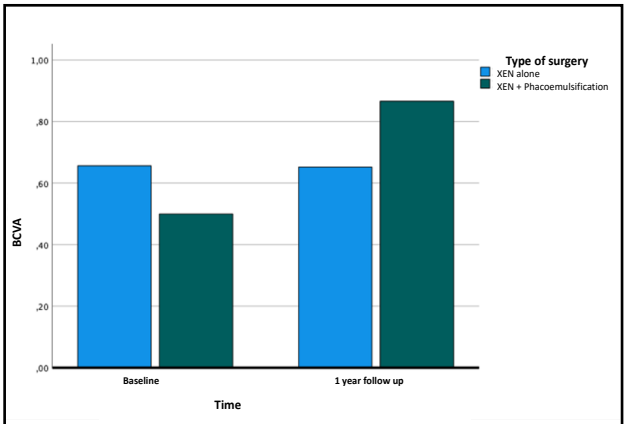

Fig. 4. BCVA during follow-up.

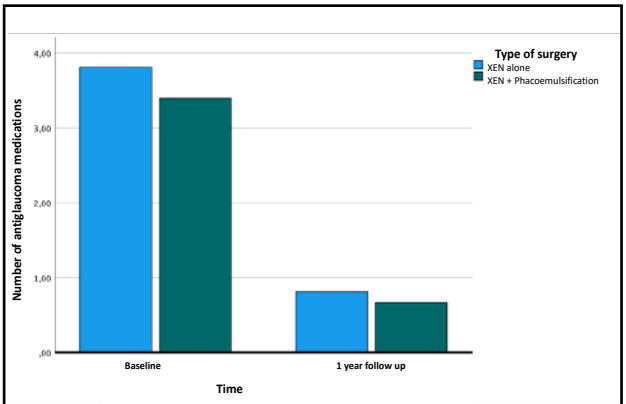

Fig. 3. Number of antiglaucoma medications.

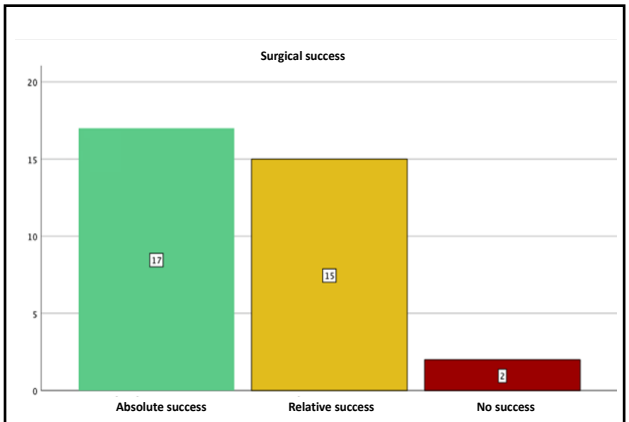

Fig. 5. Surgical success.

the XEN group versus 9 in the ExPRESS), but less efficacy in lowering IOP. [8]. Wagner FM et al. compared the XEN implant with trabeculectomy and realized that 6 months after surgery the Trabeculectomy showed higher rates of either absolute or qualified success (with the need of antiglaucoma medications), but one year after surgery XEN implant showed similar rates of qualified success, maintaining lower rates of absolute success; XEN showed higher safety, yet only 2 eyes experienced hypotony versus 6 eyes in the trabeculectomy group. [9]. Similarly, Theilig T. et al, showed lower rates of hypotony in the XEN group comparing to Trabeculectomy and similar efficacy in IOP reduction. [10]. Also Marcos Parra MT. et al in their study concluded that XEN implant, either alone or in combination with phacoemulsification, significantly reduces both IOP and the number of antiglaucoma medications to a similar rate than trabeculectomy, but with a better safety profile. [11]. Analyzing the results of those publications and many others we conclude that there is no consensus of how effective is XEN, but this is a procedure gaining popularity. An important factor to take in account is the baseline IOP, since all these studies presented baseline IOP below 30 mmHg. A metanalysis conducted by Wang, B. et al compared XEN with Trabeculectomy and realized that the XEN is effective, but not as much as Trabeculectomy; however, both procedures were equally effective in reducing antiglaucoma medications and less rates of hypotony were observed at XEN group. Nevertheless, in this metanalysis the mean baseline IOP was 26 mmHg, as the previous studies discussed, so it remains unclear the effectiveness of XEN in higher baseline levels of IOP. [12].

Ibáñez-Muñoz et al studied the efficacy of XEN gel stent in a 12 month follow up in primary and secondary open angle glaucoma, reporting rates of IOP decrease of 28.4%, which is close to our results. Also, they conclude that XEN is a safe procedure and is able to significantly reduce IOP and antiglaucoma medications, without differences if it is performed alone or with phacoemulsification. [13]. Although higher rates of IOP reduction had been reported in literature, it is been studied that lowering IOP by 25% or more seems to delay the progression of POAG. [14].

Other factor that is important to point out is the learning curve for XEN device: this procedure is usually faster and easier, especially because it avoids the conjunctival dissection and the creation of a scleral flap. In a study conducted in a tertiary Portuguese center, Marques R. et al concluded that XEN is associated with a fast-learning curve for both experienced surgeons and ophthalmology residents, and after six implants the rate of complications

and time of surgery dropped significantly in all surgeons evaluated. [15].

Although it has been widely studied for initial to moderate glaucoma, refractory glaucoma with previous surgeries can also be an indication for XEN implant, but there is a lack of literature regarding this theme. In fact, eyes that previously underwent filtration surgeries may have severe conjunctival scarring despite the use of antimetabolites intraoperatively. The surgical procedure of XEN device implant doesn't need conjunctival dissection, and it is usually placed in the superior-nasal quadrant, differently from the valves (which most of the times are placed temporally) and from the other filtration surgeries, that generally are performed at 12 o'clock. Karimi A. et al retrospectively reviewed 259 eyes that underwent XEN implantation, where 18 eyes had been previously submitted to a glaucoma surgery (11 to a trabeculectomy and 7 to Ahmed Valve) and found a similar efficacy in IOP reduction, no difference in the number of antiglaucoma medications after 12 months and similar rates of complications and bleb needling. [16]. Heidinger A. et al also reviewed 199 eyes from 160 patients who underwent XEN implantation, where 29 eyes had previous open glaucoma surgeries (28 trabeculectomy and 1 goniotomy), and did not report different results from this sub-group.

In conclusion, XEN implant alone or combined with phacoemulsification appears to be a promising procedure at glaucoma surgery, although its place in higher levels of IOP, moderate to severe glaucoma and refractory glaucoma with previous surgeries remains to be clarified, and the indication must be individualized. Our single-center study is in accordance to published literature, once XEN was capable of reducing IOP and number of antiglaucoma medications with a good safety profile in POAG, Pseudoexfoliative glaucoma and other types of glaucoma.

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Disclosures

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Corresponding author: *Rita Vieira – anarita.vieira1693@gmail.com.*

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