JOJ Ophthalmology
ISSN: 2473-5477

Juniper Publishers
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Mini Review
Volume 3 Issue 4 - June 2017
DOI: 10.19080/JOJO.2017.03.555617

JOJ Ophthal

A Review of the Data on the Recently Approved Xen Surgical Gel Stent in the Management of Glaucoma

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Submission: April 12 , 2017; **Published:** June 30, 2017

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Abstract

The cornerstone of glaucoma surgery includes trabeculectomy and tube shunting procedures, which utilize an ab externo approach to divert aqueous humor from the anterior chamber to the sub conjunctival space. The XEN Gel Stent is a 6.0mm tube consisting of porcine-derived collagen that similarly creates a non-physiologic shunt but through an ab interno approach. The XEN gel stent has the potential to effectively lower intraocular pressure and medication use with lower complication rates than traditional glaucoma surgery. This mini-review surveys the data of the XEN implant in current literature.

Introduction

Glaucoma maintains a significant disease burden worldwide. It is the most common cause of irreversible blindness, affecting over 64 million individuals [1]. Therapy is focused on lowering intraocular pressure (IOP) by a variety of methods, including topical medications, laser, and incisional surgeries. These surgical interventions-traditionally trabeculectomy or tube shunt surgery-rely on creating an additional subconjunctival reservoir for aqueous humor (AH) drainage and subsequent resorption. However, the three-year results of the Tube Versus Trabeculectomy Study found failure rates of 15 and 28 percent, respectively. Serious postoperative complications such as persistent corneal edema, endophthalmitis, and chronic or recurrent iritis were also reported [2].

There has been a recent proliferation in procedures and medical devices that provide similar IOP-lowering effects to trabeculectomy or tube shunt surgery with fewer complications. One such product is the XEN Glaucoma Treatment System (Allergan, Inc., Irvine, CA, USA), which consists of the XEN Gel Stent and XEN Injector. The XEN stent is derived from porcine collagen, measuring 6.0mm long with inner diameters of 140μm, 63μm, or 45μm, although the 45μm stent is currently recommended. Previous studies in animal models have demonstrated no significant inflammatory response to implantation and no signs of degradation of the stent itself [3]. It was recently approved by the United States FDA in November 2016 for use in refractory glaucoma, including those with a history of failed prior surgical treatment, primary open-angle glaucoma (POAG), and pseudoexfoliative glaucoma with open angles that are inadequately controlled on maximal medical therapy.

The XEN stent is inserted into the angle through the scleral spur via an ab interno approach with its disposable injector. Ideally, the device should extend 3.0mm posteriorly from the limbus and into the subconjunctival space and 2.0mm anteriorly into the anterior chamber (AC). Once placed in an aqueous environment, the device hydrates, becoming soft and flexible, helping to maintain its position. By taking advantage of the resistance to flow in a cylinder as determined by the Hagen-Poiseuille equation, the XEN45 produces a pressure gradient 7.56mm Hg at the physiologic flow rate of AH within the AC, at 2.5 microliters/minute [4]. Thus, this stent can theoretically reduce the risk of hypotony seen in IOP-lowering surgeries despite being a valve less device. The fact that it is inserted ab interno obviates the need from conjunctival dissection, theoretically reducing the potential for conjunctival fibrosis and leaving the ophthalmologist with the option to perform ab externo surgeries if necessary in the future.

XEN Gel Stent in the Literature

Several studies were performed evaluating the XEN Gel Stent with multiple inner diameters. Sheybani, Dick, and Ahmed reported on the results of 49 eyes of 49 patients treated with the XEN140 stent (140um internal diameter) without the use of mitomycin C (MMC) [5]. Of the 49 patients, 22 (45%) had

received previous glaucoma surgery, and nine (18%) had a prior laser trabeculoplasty. Complete success was defined as an IOP <18mm Hg and a greater than 20% reduction of IOP at the primary endpoint of 12 months without glaucoma medications. Criteria for treatment failure included visual acuity less than or equal to light perception, need for additional glaucoma surgery, or a less than 20% reduction of IOP at 12 months. This study revealed that the mean IOP reduced from 23.1±4.1mm Hg preoperatively to 14.7±3.7mm Hg at 12 months, a 36.4% decrease. In all, 40% met the criteria for complete success and 88.9% for partial success. Three patients (6%) failed the study criteria and required additional surgery. The most common complication was needling (47%), with nearly half of the cases occurring within the first month.

Another early study by Sheybani and Ahmed used the XEN140 and XEN63 stent (63um internal diameter) without MMC in patients undergoing phacoemulsification [6]. Of the 37 eyes, 47.1% were considered complete successes while 85.3% were qualified successes. Mean IOP significantly decreased from 22.4±4.2mm Hg preoperatively to 15.4±3.0mm Hg at 12 months, and mean medications were significantly reduced from 2.5±1.4 to 0.9±1.0.

One of the first reports involving the exclusive use of the XEN45 stent (45um internal diameter) involved 31 eyes receiving phacoemulsification and MMC treatment at the time of implantation. Mean IOP and medication use were reduced significantly from 20.8±4.6mm Hg to 13.1±3.6mmHg at 12 months and 2.7±1 to 0.9±1.1 at 12 months, respectively, and without significant complications [7].

Pérez-Torregrosa et al. [8] were among the first to describe the efficacy of the XEN45 in patients with mild and moderate glaucoma (defined as a mean deviation between 0 and -12dB on Humphrey 24-2 perimetry) [8]. Additionally, subjects included in this study had pressures<30 while being managed on two or more medications. Twelve months after concomitant phacoemulsification and XEN45 implantation, 27 of 30 (90%) subjects met the successful treatment criteria of IOP≤18mm Hg with no glaucoma medications. The authors reported several intra operative complications, including sub conjunctival hemorrhage with MMC instillation (36.6%), and minor hemorrhage intra camerally (86.6%) and at the scleral exit point (90%). A total of six (20%) stents required relocation, and one eye required re-implantation of the device. One subject was excluded from analysis due to extensive subconjunctival hemorrhage after MMC injection and another due to extrusion of the device into the subconjunctival space intra operatively.

Two studies have addressed the effect of simultaneous implantation and phacoemulsification versus the XEN alone. One such study involved 567 eyes, of which 54% underwent XEN implantation only, and 46% the combined implantation and phacoemulsification [9]. There were no inclusion or exclusion criteria regarding the grade of POAG, and data from all three diameters of XEN stents were not separated. The data revealed a mean preoperative IOP of 21.9±4.2mm Hg that was significantly decreased at 12 months (15.7mm Hg), 24 months (15.0mm Hg), and 36 months (13.2mm Hg) of follow-up. Likewise, a significant decrease in medications by 74, 77, and 74 percent from the mean of 2.7 was observed at 12, 24, and 36 months, respectively. The percentage of patients who were converted to another procedure was 4% by 12 months, 5% by 24 months, and 5% by 36 months. After analysis, it was determined that there was no statistical difference in mean IOP or medications between eyes receiving the implant alone and the combination procedure. Likewise, a 75 patient cohort demonstrated no significant difference in IOP reduction between the standalone and combination procedures at 12 months [10]. The most frequent complications from this study were needling (15.4%) and hypotony defined as an IOP <6mm Hg on postoperative day 1 (12.6%).

The most recent article involving the XEN stent evaluated its use in eyes with suboptimal IOP and medication intolerance, medication noncompliance, or maximum therapy with no history of glaucoma surgery [11]. A total of 13 eyes underwent XEN45 implantation in addition to phacoemulsification if previously phakic. At the 12-month end point. 41.7% were complete successes, with a>20% drop in IOP and discontinuation of all glaucoma medications, while an additional 25% met the IOP goal but remained on at least one medication. Among the reported complications, four eyes required needling, two eyes developed choroidal detachment and hypotony requiring systemic steroids and atropine treatment, one implant extruded, and two eyes required subsequent trabeculectomy.

Discussion

The current literature available for the XEN Gel Stent demonstrates its effect on IOP and medication reduction in addition to reducing severe intra operative and postoperative complications. The data also suggests a lower early failure rate than those published from trabeculectomy and tube shunt surgery. There remains little data on long-term outcomes of the XEN stent at this time, inherent with a newly approved procedure. Thanks to its earlier implementation outside the USA, data are available for the XEN from mild to refractory glaucoma. However, this data should be evaluated in light of the fact that some studies were performed using the XEN140 and XEN63 stents, which are no longer recommended by the manufacturer.

Of the complications encountered with the XEN stent, subconjunctival hemorrhage and needling were most common, and extrusion of the device was the most common serious complication. It should be noted that the rates of needling varied widely in the literature, from 15.4% to 47%. This could be due in part to varying degrees of experience with the XEN stent and injector as well as different technical approaches such as the use and dose of anti fibrotic used at the time of implantation.

How to cite this article: Colby A, Shane H. A Review of the Data on the Recently Approved Xen Surgical Gel Stent in the Management of Glaucoma. JOJ Ophthal. 2017; 3(4): 555617. DOI: 10.19080/JOJO.2017.03.555617.

It is well known that cataract extraction provides some improvement in IOP [12]. Thus, the efficacy of the XEN stent may be confounded by those studies in which patients also underwent phacoemulsification. In fact, higher preoperative IOP, older age, and greater anterior chamber depth have all been shown to correlate to the amount of IOP improvement with phacoemulsification in medically managed glaucoma patients [13]. However, two studies with the XEN stent reported no significant difference in IOP reduction and medication use postoperatively between XEN implantation combined with phacoemulsification and XEN implantation alone. Indeed, this is one relationship that will be unlikely to be discerned until more data from more eyes is available for analysis.

Looking forward, several clinical trials in various stages of progress will look to further elucidate the properties of the XEN device and its role in the management of glaucoma. One trial – NCT02036541 – is a Phase 3 trial currently past its primary completion date that will further assess the XEN45 in patients with refractory glaucoma. Another is a parallel assignment, Phase 4 trial for XEN45 in moderate POAG patients (NCT02006693). Yet another study, soon to begin enrollment, will assess the in vivo effects of various interventions on outflow at Schlemm's canal, of which the XEN stent is part of the surgical branch (NCT02807935).

Conclusion

At present, there are multiple surgical options available for effective glaucoma management. The XEN Gel Stent is one such intervention that provides advantages over traditional glaucoma surgery and newer minimally invasive glaucoma surgery (MIGS) procedures while lowering IOP and medication dependence. The device is well tolerated by the ocular tissues and can be placed via an ab interno approach but still creates a non-physiologic subconjunctival shunt or bleb to increase aqueous outflow without the use of a valve system. Since it involves little manipulation of the conjunctiva, implantation of the XEN stent does not preclude future conjunctival surgeries if necessary. Questions remain as to what long-term outcomes of the XEN Gel Stent will demonstrate, as well as which types of glaucoma patients stand to benefit the most from the surgery. Larger-scale studies are needed to resolve these questions and confirm the initial optimistic results.

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