Review Article

Current Trends in Ophthalmology Navigating Challenges after Xen

Vera V^{1,*}, Shah M², Smith T³, Pinto LA⁴ and Reitsamer H⁵

¹Department of Glaucoma, Unidad Oftalmologica de Caracas, Caracas, Venezuela

²Kellogg Eye Center, University of Michigan, United States

³Glaucoma Associates of Texas, United States

⁴Faculty of Medicine of Lisbon University, Portugal

⁵University of Salzburg, Austria

*Correspondence: Vanessa Vera, Department of Glaucoma, Unidad Oftalmologica de Caracas, Caracas, Venezuela; E-mail: vanessaveramd@gmail.com

Received date: Jan 19, 2021; Accepted date: Mar 12, 2021; Published date: Mar 17, 2021

Abstract

The XEN Gel Stent is a surgical implant for the treatment of glaucoma unresponsive to maximum tolerated medical therapy, with higher predictability and fewer sight-threatening complications than trabeculectomy or tube shunts. While complications following XEN implantation may be less common than in other glaucoma procedures, they are not completely avoidable. This paper elaborates the most commonly reported complications following XEN implantation with an aim to mitigate their occurrence by understanding the pathophysiology behind them. In addition, the authors provide insights from the literature and their own experience and make recommendations for management when complications do occur.

Keywords: Glaucoma, Glaucoma filtering surgery, Glaucoma gel stent, Bleb revision, Hypotony

Introduction

Glaucoma is the leading cause of irreversible blindness globally, and 58% of cases are believed to be primary open-angle glaucoma (POAG) [1]. While glaucoma is a complex pathology that is not entirely understood, the only means of treating it is to lower intraocular pressure (IOP). The options for lowering IOP are varied, and determining which method is best for an individual patient requires careful consideration of the benefits and risks.

Trabeculectomy and tube shunt surgeries have been the most frequently performed subconjunctival outflow incisional procedures for the management of glaucoma [2], and numerous studies have evaluated the efficacy and risks associated with these procedures. In the Tube Versus Trabeculectomy Study (TVT Study) the efficacy and safety of the two procedures were evaluated in eyes with prior ocular surgery. The study investigators

found that both procedures are viable surgical options for treating medically uncontrolled glaucoma [2] and that the outcomes supported the expanding use of tube shunts beyond refractory glaucoma [3].

Many of the same investigators then applied a similar study design to eyes that had not undergone previous ocular surgery. In the Primary Tube Versus Trabeculectomy Study (PTVT Study), investigators again found both procedures to be worthwhile for glaucoma patients, even with a cumulative probability of failure during the first year of 17.3% in the tube group and 7.9% in the trabeculectomy group [4]. The lower rate of failure in the trabeculectomy group was offset by a higher rate of complications.

The Collaborative Initial Glaucoma Treatment Study

(CIGTS) was a landmark study that was designed to determine whether patients with newly diagnosed POAG are better served by topical medications, with their lower rate of complications, or by immediate trabeculectomy [5]. The results appear to support early surgical intervention, in spite of the increased risks that come with surgery [6].

The most common complications from all three studies can be seen in table 1.

While trabeculectomy and tube shunt surgeries remain very popular due to their efficacy, there have been significant resources devoted to finding options that have the potential to be as efficacious but with reduced associated risks. The XEN Gel Stent (Allergan, an AbbVie company) is one such option. The XEN Gel Stent is a surgical implant that was approved by the United States Food and Drug Administration (FDA) in November 2016 for patients with refractory glaucoma who failed previous surgical treatment or in patients with POAG, pseudoexfoliative, or pigmentary glaucoma with open angles that are unresponsive to maximum tolerated medical therapy [9].

The XEN Gel Stent is a hydrophilic tube 6-mm long that drains aqueous humor from the anterior chamber (AC) to the subconjunctival space (Figure 1) without the need to open the conjunctiva, thereby allowing for higher predictability and fewer sight-threatening complications than trabeculectomy [10,11]. The surgical technique and approaches to XEN have evolved significantly, currently allowing ab interno and ab externo approaches with and without conjunctival dissection, all of which enable surgeons to better optimize results upon consideration of individual patient needs and surgeon preference [12,13]. The ab interno procedure without conjunctival dissection has been shown to provide safe and sustainable reduction of IOP [10,14]. While complications following gel stent implantation may be less common than in other glaucoma procedures, they are still a reality.

Hengerer and colleagues performed a retrospective analysis of 242 eyes of 146 patients that underwent XEN implantation and found a very low rate of complications [15]. While needling was required in 27.7% of eyes to enhance outflow, only 2 eyes (0.8%) required intervention for hypotony. Transient hyphema was observed in 4 eyes (1.7%), and conjunctival bleeding was observed in 12 eyes (5.0%). Conjunctival cysts were observed in 29 eyes (12.0%) up to 3 months postoperatively.

A study by Mansouri and colleagues of 149 eyes that underwent XEN implantation reported that 22 eyes (14.7%) experienced one or more adverse events. These included bleb revision (3.4%), loss of >2 lines of best-corrected visual acuity (2%), damaged XEN device during needling (2%), or visual loss due to retinal detachment or secondary hypotony maculopathy (1.3%). Reitsamer and colleagues performed a prospective, non-randomized study of 218 eyes with XEN implantation either as a standalone procedure or in conjunction with cataract surgery [16]. Intraoperative complications were reported in 10 eyes (4.6%), and postoperative ocular adverse events were reported in a total of 65 eyes (29.8%). The most frequent were glaucoma-related secondary intervention due to uncontrolled IOP (6.4%) and hyphema (4.6%). No eyes had persistent hypotony, and there were no clinical hypotony-related complications. Other complications include device fracture (2.8%), IOP increase (2.8%), choroidal effusion (1.8%), and conjunctival erosion (1.8%).

Figure 1: Diagram showing XEN Gel Stent connecting the anterior chamber to the subconjunctival space (A) and anterior segment OCT image showing final placement of the stent (B). OCT image courtesy of Arsham Sheybani, MD.

In a retrospective comparison of the XEN Gel Stent to trabeculectomy, Schlenker and colleagues evaluated 354 eyes (185 XEN Gel Stent and 169 trabeculectomy) of 293 patients [11]. The study excluded eyes that had undergone previous incisional glaucoma surgery. They found that the gel stent group required more postoperative needling (43.2% vs 30.8%), but overall, a larger percentage of the trabeculectomy group (97.6%) required postoperative interventions (such as laser suture lysis, bleb revision,

Table 1: Most common intraoperative and postoperative complications rates reported after trabeculectomy and tube shunt implantations.

	TVT Study[2] n=105 (%)	PTVT[7] n=242 (%)	CIGTS[8] n=465(%)
Intraop complications	17 (16.1%)	8 (3.3%)	55 (12%)
Postop complications shallow or flat AC	10%	12%	13%
Wound leak	11%	6%	6%
Choroidal effusion	17%	6%	11%
AC bleeding	8%	5%	10%
Bleb leak	6%	-	-
Encapsulated bleb	6%	15%	12%
Suprachoroidal hemorrhage	3%	-	0.70%
Endophthalmitis/blebitis	5%	-	0%

TVT: Tube vs Trabeculectomy Study; PTVT: Primary Tube vs Trabeculectomy Study; CIGTS: Collaborative Initial Glaucoma Treatment Study; AC: Anterior Chamber; intraop: intraoperative; postop: postoperative.

and conjunctival suturing) than the gel stent group (63.2%). Overall, 18 eyes (9.7%) in the gel stent group and 27 eyes (16.0%) in the trabeculectomy group experienced a treatable complication-usually a leak/dehiscence that was resolved with conservative measures.

Recent articles have elaborated on the best techniques for preoperative assessment, surgical maneuvers, postoperative follow-up, and bleb management [17]. Complications will happen when glaucoma surgical procedures are performed, and the rate of occurrence is sometimes related to the level of experience of the individual surgeon. Thus, we find it worthwhile to elaborate on some of the most common complications after XEN implantation to help prevent or mitigate their occurrence by enhancing understanding of the mechanism of development.

Prominent and/or Nasal blebs

Ideal long-term bleb morphology following gel stent surgery is a low-lying and diffuse bleb with minimal vascularity. Symptomatic blebs may present with a variety of issues and usually create varying degrees of discomfort for patients. Bleb dysesthesia may manifest with a large, elevated bleb with steep walls that encroaches into the intra-palpebral area [18]. Symptoms may include ocular pain, discomfort, burning, foreign body sensation, and tearing [19]. Bleb dysesthesia may also interfere with lid closure, prohibiting proper tear film distribution and thus may cause surface irregularities including desiccation, epithelial defects, and dellen formation [20].

The most common cause of dysaesthetic blebs following trabeculectomy is a nasal location [21], with

Cur Tre Ophthal, 4(1): 210-226 (2021)

additional identified risk factors including young age and poor lid coverage [19]. These same risk factors apply with the gel stent (Figure 2 and 3).

Figure 2: Slit lamp image showing prominent bleb extending nasally. Image courtesy of Luis Abegão Pinto, MD.

Figure 3: Slit lamp image showing prominent nasal bleb with corneal dellen. Image courtesy of Herbert Reitsamer, MD.

Prevention

Nasal blebs can largely be avoided with careful placement and surgical technique:

- Aim to place the gel stent as close to 12 o'clock as possible during implantation (Figure 4).
- Create a 2-3 mm scleral tunnel to avoid side flow around implant (which will create uncontrolled and anterior outflow).
- Adjust the implant as needed to ensure that 1 mm of the implant lies in the anterior chamber, 2 mm in the sclera, and 3 mm in the subconjunctival space in order to allow the most posterior flow possible.
- If an implant is inadvertently too nasal, consider removing and re-implanting such that the distal end of the stent in the subconjunctival portion lies within 1 clock hour of the 12-o'clock position.
- Avoid anterior and errant migration of antimetabolite by using low volumes and utilizing cotton-tip applicators or Weck-Cell sponges to apply pressure on the limbal conjunctiva (preventing contact of antimetabolite with limbus) and pushing the antimetabolite in a posterior direction.

Figure 4: Illustration showing stent placement on a right eye with a temporal main incision at 9-o'clock. When the needle enters the angle at the 12-o'clock position, the outflow through the distal end of the implant will create a bleb at approximately the 12:45 position, the preferred position. When the needle enters the angle at the 1-o'clock position or lower, the outflow through the distal end of the implant will create a bleb at approximately the 1:30 position, thus increasing the risk of nasal bleb formation.

Management recommendations

When a prominent or nasal bleb is present, strategies for management are focused on getting a more favorable bleb morphology. Early intervention is key to success,

so temporary eye patching and/or large diameter bandage contact lens should be considered early in the postoperative period. In the intermediate postoperative course, aqueous suppressants could help by reducing the outflow of aqueous, which allows remodeling of the bleb morphology. In addition, adding lubricant eye drops will prevent ocular surface problems and discomfort.

When early measures do not succeed in improving bleb morphology, more invasive treatments are recommended. These include placing compression sutures (Figure 5, 6 and 7) as described by Palmberg and Zacchei [21], injection of autologous blood, fibrin glue sealant (Video 1), or electrocautery in the area of unwanted filtration to help migrate the bleb to a more superior and/or posterior direction. An understanding of the morphology of the bleb, with attention to the presumed areas of resistance to flow, can guide management. For example, if a bleb is becoming high walled and nasally biased due to fibrosis found in the areas posterior and temporal to the implant, then a needling procedure to lyse this fibrosis combined with antimetabolite injection may enable a more favorable morphology with posterior and diffuse aqueous outflow. A combination of the prior described procedures may be required in some cases (Video 2).

Additionally, the success rates of these techniques are equivocal, and patients should be informed that a salvage intervention may cause a higher IOP than before due to new inflammation and fibrosis, thus requiring additional IOP-lowering medications afterwards. Surgical bleb revision should be the last resource to rescue problematic blebs and should be considered after less invasive methods. Sekaran and colleagues reported success in managing cases of hypertrophic dysaesthetic blebs after XEN with the following protocol: observation with topical NSAIDS and lubrication to see if it self-resolves, slit-lamp lancing to drain the bleb followed by bandage contact lens compression, delineating conjunctival cryotherapy to create an anatomical border, and finally, 'redirect' surgical revision [22]. They assessed that a nasal location appeared to be linked to dysaesthesia and recommended targeting placement as superiorly as possible. Fundamentally, care for these patients should be individualized based on the severity of symptoms as well as the mechanism of aberrant bleb formation and aqueous flow.

Figure 5: Slit lamp image showing a prominent nasal and inferior bleb right eye (A). Intraoperative placement of scleral-conjunctival sutures (B). Final surgical view of nasal compression sutures (C). Images courtesy of Herbert Reitsamer, MD.

Figure 6: Slit lamp image showing prominent inferior nasal bleb (A and B). Immediate postoperative result after bleb revision with needling and nasal compression sutures (C). Long-term postoperative outcome with a diffuse, posterior, and low-lying bleb present (D). Images courtesy of Tosin Smith, MD.

Figure 7: Surgical steps for bleb revision. Intraoperative view of supero-nasal bleb (A), compression suture with Vicryl 7-0 (B), injection of fibrin glue sealant (C), tissue compression (D), needling of the bleb (E), and injection of mitomycin c (MMC) (F). Image courtesy of Manjool Shah, MD.

Avascular Blebs

Avascular blebs are pale and thin and may cause pain or discomfort. These blebs are prone to leaks/oozing that may lead to bleb related infections (Figure 8 and 9).

Prevention

Excessive use of antifibrotic agents seems to be the most significant contributing factor for avascular blebs.

Cur Tre Ophthal, 4(1): 210-226 (2021)

The dosage of Mitomycin-C (MMC) or fluorouracil (5-FU) could be too high for the wound-healing propensity of the patient, too high based on the health of the conjunctiva, cumulatively too high following intra- and postoperative use or concentrated to one area due to presence of surrounding conjunctival fibrosis. Exposure of antimetabolites to the limbus is also considered an important risk factor (Figure 10).

Figure 8: Slit lamp image showing avascular bleb with central ooze or sweating. Image courtesy of Vanessa Vera, MD.

Figure 9: Slit lamp image showing a prominent bleb with avascular conjunctiva. Image courtesy of Luis Abegão Pinto, MD.

Figure 10: Slit lamp image showing patient with bilateral XEN Gel Stent implantation with normal conjunctival vascularity OD after ab interno implantation and avascular 360° conjunctiva OS after ab interno XEN air implantation (A). Right eye, bleb present with some vascularity (B). Left eye, bleb present with 360° avascular perilimbal area and 2+ vascularity (C). Images courtesy of Tosin Smith, MD.

- Avoid high doses and volumes of MMC. Most published literature reports an injection of 20-40 ug of MMC (0.2 to 0.4 mg/ml in 0.1 cc) at time of XEN implantation [18]. Low volumes are easier to manage and keep in the intended area of injection. Higher doses should be reserved only for cases with a very high risk of fibrosis.
- Avoid contact and pooling of antimetabolite at the limbal area. Injection should be performed at least 7 mm from the limbus, and a wet cotton swab or Weck-cell is usually very helpful to keep fluid away from limbus.
- Consider spreading the antimetabolite content posteriorly in a wider area.
- Ensure the conjunctiva is healthy and mobile before injecting antimetabolites.
- Stop or taper steroids quickly upon first signs of conjunctival avascularity.

Management recommendations

If a patient presents with an avascular bleb but with good IOP control and no leakage, they can be carefully monitored. Topical lubricants and artificial tears should be used, especially if the patient is experiencing discomfort or ocular surface abnormalities [23]. A short course of steroids (e.g. Loteprednol qds) can also help improve symptoms. In cases where there is a risk of blebitis, consider surgical excision of the avascular zone and placing healthy autologous conjunctiva over the bleb using either advancement of the conjunctiva or suturing a free conjunctival patch/amniotic membrane graft (Figure 11 and Video 3).

Leakage/Erosion

Bleb leaks have been reported as a complication following gel stent implantation in various case reports and are a predisposing factor for infections [24,25].

Figure 11: Surgical steps for avascular bleb revision. View of superonasal avascular bleb area (A). Peritomy cut (B). Conjunctival dissection (C). Removal of avascular tissue (D). Final result after conjunctival advancement (E). Images courtesy of Herbert Reitsamer, MD.

Figure 12: Slit lamp image showing implant erosion. Notice short < 1mm subconjunctival implant segment (A) and short scleral tunnel < 1mm making the stent lift up at the scleral exit and eventually eroding (B). Images courtesy of Vanessa Vera, MD.

Thus, clinicians should specifically inspect for leaks postoperatively and treat immediately if present. If a patient has a low IOP or is experiencing epiphora, a Seidel test should be administered to rule out a bleb leak. This is done by placing a fluorescein strip gently over the bleb and then examining the eye using cobalt blue illumination. Occasionally, a persistent bleb leak may be observed after transconjunctival ab externo gel stent placement if the conjunctival needle entry point in the conjunctiva is not posterior enough.

Prevention

Early bleb leaks are most likely to happen after open conjunctival stent implantation (incision leak) or after transconjunctival stent implantation (closed

conjunctiva, ab externo implantation needle entry point). Implant erosions and subsequent bleb leaks are linked to persistent contact or rubbing of the stent with the conjunctiva. Many factors have been described that may increase the risk of erosion, leading to bleb leaks:

- Implant placement too nasally or fully exposed between the eyelids
- Implant placement on eyelid margin
- Improper gel stent implantation, <2 mm on subconjunctival space, < 2 mm scleral tunnel or the combination of both (Figure 12)
- Curling of the implant, causing tenting of the conjunctiva (Video 4)
- Conjunctival status too thin [24] or scarred down with

superficial implant placement

- Perforation of conjunctiva with injector needle during ab interno placement
- Needle entry too anterior during ab externo transconjunctival placement
- Needling procedures (Video 4)
- High doses or repeated use of anti-metabolites
- Eye rubbing

With careful placement of the gel stent and by avoiding the factors described above, the risk of erosion and leakage should be reduced.

Management recommendations

When erosion and/or leakage do occur, steroids should be tapered and topical antibiotics started. Further management will depend on if the implant is exposed through the conjunctival defect. Attempts to keep the implant in place should be made in cases where the surrounding tissue is vascular and healthy and there is no concern for infection. For small defects without implant exposure, the use of vitamin A eye ointment and an aqueous suppressant medication may further facilitate resolution [26]. For small defects with implant exposure, lifting up the conjunctiva to replace the implant

under it and trimming or amputating the distal end of implant to displace the drainage location will allow small defects to heal without the mechanical presence of the stent. Larger defects will need to be sutured and can be done using the same strategy as that used to suture a buttonhole defect following trabeculectomy. The use of aqueous suppressants in combination with any of the described procedures may be helpful in cases where temporarily reducing outflow through the implant may aid with healing. If the conjunctiva is fragile or the defect is particularly large, it may be necessary to consider revising the bleb and dissecting surrounding tissue to ensure the defect closes fully with suturing. In some cases, repositioning of the stent prior to suturing the bleb may be beneficial [27].

In cases of recurrence, improper stent location, or persistent conjunctival defect, it is recommended to remove the implant and plan for a new surgery, using topical IOP medications as needed in the interim. Removal of the implant is a simple procedure that can be done at the slit lamp by simply grabbing the exposed portion of the gel stent and carefully pulling it out. A stitch may be required if there is persistent leakage from the wound (Figure 13).

Figure 13: Slit lamp images showing implant erosion and resolution over time. Postoperative day 1 (A) showing bleb and implant under the conjunctiva. Postoperative week 3 (B) showing conjunctival thinning over implant area. Postoperative week 6 (C) showing implant tip exposure through avascular conjunctiva; implant was pulled out using toothed forceps. Postoperative week 6 (D) showing conjunctival stitch where opening was located. Postoperative month 3 (E) showing seidel negative. IOP was controlled by adding back topical medications. Images courtesy of Vanessa Vera, MD.

Infection/Endophthalmitis

The incidence of endophthalmitis after filtering surgery with MMC has been reported to be from 2.1% to 2.6% and may occur from the first few days after surgery to decades later [28,29]. Endophthalmitis following XEN Gel Stent implantation is rare, but various cases have been published [16,24,25,30-33].

The use of antifibrotics during filtering surgery is a known risk factor for bleb-related infections, and it is thought this is because they cause thinner, cystic, and

Cur Tre Ophthal, 4(1): 210-226 (2021)

avascular blebs that may be more susceptible to the transconjunctival migration of bacteria through the bleb [34]. Bleb leaks and blebs located at the inferior limbus are also risk factors [35].

Prevention

Standard bacterial prophylaxis involves preoperative antibiotic, intraoperative aseptic technique, and postoperative antibiotics. As a majority of the causative organisms in acute postoperative endophthalmitis come from the patient's own periocular flora [36], preparation of

the eye at the time of surgery is critical. The surface of the eye can be treated with 5% povidone-iodine to the cornea, conjunctival sac, and periocular skin for a minimum of 3 minutes prior to surgery [37]. If the patient has a true allergy to povidone iodine, aqueous chlorhexidine 0.05% may be used. In addition, it is advised that the eyelid margin and lashes be isolated from the surgical field. There is little conclusive evidence that prophylactic antibiotics prevent early endophthalmitis. Nevertheless, they are considered the standard of care [38,39]. All of the previously mentioned factors to avoid erosion of the gel stent or conjunctival leak will also reduce the risk of infections that could lead to endophthalmitis. Limiting the period of steroid administration postoperatively has been shown to reduce the occurrence of thin, cystic blebs, which are correlated with infection risk [40].

Blebitis is thought to be prodromal to endophthalmitis, thus patients with blebitis should be observed closely to identify extension into the vitreous cavity. Aggressive antimicrobial therapy, which may include oral quinolones, is warranted, as are intravitreal antibiotics should the blebitis move to the vitreous cavity [34].

Management recommendations

Patients should be educated about early symptoms of infection as they should be treated swiftly and aggressively. Infections are likely to respond to intensive treatment with both topical and systemic antibiotics. Corticosteroids may also be required to treat the inflammation. Endophthalmitis will need aggressive intravitreal injections and vitrectomy. Removal of the stent may be necessary, and simultaneous management of high IOP will also likely be required.

Clinical Hypotony

Hypotony is a term meant to describe IOP that is so low it can result in visual loss from choroidal effusion, maculopathy, optic neuropathy, and cataract [41]. It is necessary to differentiate numerical hypotony (IOP <5 mm Hg without clinical signs of hypotony) from clinical hypotony (manifestations of choroidal effusion, maculopathy, optic neuropathy, and cataract, irrespective of IOP) [42].

It is well known and expected to have numerical hypotony after XEN implantation in the early postoperative days. There have been cases of numerical hypotony following XEN reported in the literature [43,44]. In most cases, this hypotony is transient and self-resolving, but occasionally it becomes clinical hypotony. Hypotony maculopathy is characterized by choroidal effusion/

Cur Tre Ophthal, 4(1): 210-226 (2021)

detachment, a shallow anterior chamber, and choroidal folds (Figure 14). Rarely, hypotony may result in more serious complications, such as suprachoroidal bleeding [45], suprachoroidal hemorrhage, rhegmatogenous retinal detachment [46], or malignant glaucoma.

Prevention

The XEN Gel Stent was carefully designed following the Hagen-Poiseuille law, restricting aqueous humor outflow through the lumen of the implant so that hypotony is prevented as long as the average rate of aqueous humor production is maintained at 2.5 $\mu\text{L}/\text{min}$ and all the outflow goes through the lumen. However, hypotony may occur under certain circumstances such as: unregulated outflow around the implant (side flow or paraflow), reduced aqueous humor production (from ciliary body shut down, continuation, or washout effect of glaucoma drops), inadvertent clefts, incision leaks, etc. The following practices can help to avoid hypotony:

- Avoid a “down flick” of the injector needle. Poor surgical technique or challenging cases may inadvertently create a cyclodialysis cleft, usually as a result of a downward flick during implantation. Ensure that you relax and loosen any force, traction, or torsion you have before deploying the implant and maintain a slight forward bias during implantation to help reduce flicks or sudden movements of the injector (Figure 15).
- Be aware of high-risk patients. Reported risk factors are similar to those for persistent hypotony following trabeculectomy, including young age and high myopia [47,48]. Also, patients who previously underwent a cyclodestructive procedure and thus have low aqueous humor production, may be at higher risk. Consider leaving a small amount of dispersive viscoelastic at the end of the case.
- Avoid short scleral tracks or tunnels. This increases the chance for side flow, which eliminates the implant's ability to restrict outflow. A minimum tunnel length of 2 mm has been recommended by the manufacturer.
- Ensure a fully formed and stable AC at the end of the surgery.

Management recommendations

If persistent hypotony occurs, ultrasound biomicroscopy imaging and/or gonioscopic evaluation should be performed to rule out a cyclodialysis cleft. It is common to be unable to visualize a cleft when the AC is shallow or when the eye is soft, so suspect the presence of a cleft in cases of prolonged hypotony that cannot be

Figure 14: Images showing shallow AC (A) and peripheral choroidal detachment (B) in the immediate postoperative period after gel stent implantation. Images courtesy of Vanessa Vera, MD.

explained by bleb overfiltration or morphology. When the patient is still on corticosteroids, these should be tapered quickly and cycloplegia can be initiated if the AC is shallow. Tapering steroids quickly may allow the natural healing response to close any inadvertent clefts and reduce the size of an over-filtering bleb, which will result in elevation of the IOP. Close monitoring is advised.

compression suture technique and a bleb revision [44].

In cases with persistent hypotony, where several attempts have failed to increase IOP, removal of the gel stent should be considered with alternative methods (including a properly placed gel stent) to control the long-term elevated IOP at the same time or on a phased surgical approach.

When a cyclodialysis cleft has been identified and no improvement is seen with medical management, other treatments to consider are:

- **Argon Laser:** Using a 200- μ m spot size and a duration of approximately 0.5 seconds, argon laser can be applied to the sclera at an intensity of 1-1.2 W and to the adjacent choroid at 0.3-0.7 W. Subconjunctival or retrobulbar anaesthesia may be required.
- **Cryo:** The probe is applied about 3 mm posterior to the limbus in the cleft area, and a double- or triple-freeze-thaw technique is utilized.
- **Surgical revision:** While numerous methods of surgical closure of a cyclodialysis cleft have been described, two methods that may be applicable in these smaller and more localized clefts are the direct and indirect closure methods. In the direct approach, a conjunctival peritomy and scleral flap are created overlying the cleft, and a cutdown is made under the flap to access the supraciliary space. Interrupted sutures are used to reapproximate the uveal tissue to the sclera, after which the flap and conjunctiva are closed in a watertight manner. In the indirect approach, a conjunctival peritomy is created over the cleft area, followed by sequentially passing each needle of a double-armed 10-0 polypropylene suture

Figure 15: Gonioscopic image showing cleft next to gel stent angle entry point. Image courtesy of Luis Abegão Pinto, MD.

It is possible to refill the AC with dispersive viscoelastic if the AC is very shallow or the visual acuity is reduced. This procedure can be repeated if necessary. However, a viscoelastic with a high molecular weight (cohesive) is not recommended as it has been shown to create IOP spikes [43]. In cases of over-filtration with prominent blebs present, reports have also been published of successful management with a modified transconjunctival bleb

through a paracentesis, into the ciliary sulcus, and out through the sclera approximately 1 mm posterior to the limbus. The two suture arms are passed to cover the radial extent of the cleft. Knots are tied externally and buried, followed by closure of the conjunctiva. Gonioscopic confirmation of cleft closure is suggested regardless of surgical approach.

It is important to note that most of these suggestions encourage focal inflammation and create scarring and resultant fibrosis, which will most likely result in bleb failure. A careful approach with close monitoring to balance the patient's response is necessary to prevent extreme IOP changes.

Migration or dislocation of the stent

The XEN gel stent is designed to become soft and swell slightly once implanted to reduce the risk of implant migration. Even so, cases of stent displacement have been reported in the literature [49-52]. It is not always understood why a stent may migrate. Attempts to move or straighten a bent tip on a stent, needling, eye rubbing, short scleral tracks, intra-Tenon placement and subsequent fibrosis, and abnormal scleral anatomy (e.g. post cyclophotocoagulation, cryotherapy, episcleritis, etc.) have all been associated as possible causes.

Prevention

- Advise patients not to rub their eyes after surgery, as this may apply exterior pressure that can result in movement.
- If a stent is bent or caught in tissue, it is most likely due to Tenon. Avoid attempting to straighten the stent with a blunt spatula, as this may result in dislocation. Primary needling during surgery or needling at the postoperative visit is recommended to release the tissue around the implant.
- Avoid needling when the stent cannot be visualized under the conjunctiva, as you will be more likely to inadvertently pull, push, or amputate it.
- Create a scleral track or tunnel that is a minimum of 2 mm. A long scleral tunnel will allow appropriate anchoring and friction with the stent.
- Avoid implanting the gel stent in patients with known scleral pathologies or previous transscleral treatments. In such patients, the scleral elasticity necessary to secure the implant in place may be compromised [49].

Management recommendations

Treatment options include observation, stent

repositioning, or stent removal. Determining which action to take will depend on the severity of the displacement and surgeon discretion.

- If the implant has partially migrated from its original placement position-without compromising functionality (stent is still connecting AC to subconjunctival space with IOP under control) or adjacent tissue (touching endothelium, iris, etc) - observing versus repositioning the implant can be considered (Figure 16). When observation has been decided, the current position should be documented, ideally with photographs or AC-OCT, and the patient should be closely monitored to confirm the stability of the new location. When repositioning is the course to be taken, timing is important as early repositioning may make the maneuver easier and less traumatic; this is done by grabbing the subconjunctival portion of the implant at the slit lamp with toothless forceps and attempting to move the stent into a more favorable position.
- If the implant has migrated and the new position is compromising function or adjacent ocular structures (Figure 17), repositioning at the slit lamp can be considered as a first action. If unsuccessful, a surgical revision to attempt better placement should be considered rather than removal and replacement of the device.
- If the implant is dislocated, a surgical approach to remove the implant from the AC is recommended.

In cases where migration or dislocation of the gel stent are suspected to be associated with poor surgical placement or patient-related anomalies, removal of the device should be considered. A new properly placed "XEN Gel Stent" or an alternative glaucoma surgical procedure should be discussed with the patient.

Occlusion or Obstruction

Device obstruction is not a common adverse event following "XEN Gel Stent" implantation. Studies report that both De Gregorio (n=41 eyes) [53] and Schlenker (n=354 eyes) [11] each had one case of stent obstruction. If the stent becomes obstructed the bleb will flatten and IOP will rise. Stents can be occluded due to external causes or poor placement. External causes of stent occlusion may include a fibrin plug or a blood clot obstructing the internal ostium [54]. Occlusion can also happen from small Descemet membrane's detachment, nuclear or cortex remains, viscoelastic, iris pigment (Figure 18), etc [55,56].

Figure 16: Slit lamp images showing gel stent migration into the AC (A and B) following needling at 6 weeks postoperatively. Note the functioning bleb present despite partial migration and no iridocorneal touch. Patient is being closely monitored (C). Images courtesy of Tosin Smith, MD.

Figure 17: Slit lamp image showing implant migration into the AC and touching the cornea. Image courtesy of Vanessa Vera, MD.

Poor positioning of the gel stent at the time of implantation, such as entering the angle too low or too close to the ciliary body, will increase the risk of having the tip of the implant too close to the iris, and/or leaving an implant too long (more than 1 mm) in the anterior chamber. Implant placement too close to the iris or too long in the AC may increase the risk of occlusion (Figure 19 and 20).

Prevention

- Place XEN properly by entering the angle at the nonpigmented portion of the trabecular meshwork and leaving approximately 1 mm of the implant connected in the anterior chamber.
- Ensure the AC portion of the implant is away from the iris and cornea.
- Ensure complete removal of cataract or lens material during combined surgery, viscoelastics, and any loose pigment or blood.

- Identify and stop any intraoperative bleeding to avoid later blood clot or fibrin formation.
- Fibrinogenesis is closely related to the degree of ocular inflammation [57] and may be more likely in patients with known uveitis or diabetes [58]. Taking these facts into account, caution should be taken when combining XEN placement with dense cataract removal or other intraocular surgery as the combined inflammatory response may result in dense fibrous tissue blocking the gel stent [59].

Management recommendations

Depending on the cause, several options have been proposed and used by the authors:

- Frequent digital ocular compression should be recommended when visible particles (pigment or blood) are observed in the subconjunctival lumen portion of the implant to help push or move them out.
- Nd:YAG laser has been a very useful tool in the postoperative period to break, remove, or push away any of the potential agents, such as those discussed above, that can cause blockage of the ostium in the AC portion of the stent. Even when nothing can be visualized by gonioscopy (they may be microparticles), attempting low-power Nd:YAG laser (0.3-0.5 mJ) to the AC lumen of the implant can help shake and displace any potential blockage without fracturing the implant. This last approach has been also recommended after needling when the bleb has not been successfully reestablished [60].
- Argon laser iridoplasty can be used when the iris is blocking the internal lumen of the stent. Standard parameters for iridoplasty (600-800 mW, 0.2 seconds, and around 500-µm spot size) have been successfully used by the authors to “pull away” iris tissue from the implant tip without releasing pigment.

- Intracameral injection of tissue plasminogen activator or TPA (10 to 25 μ g in 0.1 cc) has been successfully used to help remove or reduce blood clots or fibrin blocking the stent. Caution should be taken in patients using anticoagulant oral therapy.
- In cases where the AC portion of the implant was left too long, repositioning at the slit lamp in the immediate postoperative period has been successfully used to move the implant away from iris.
- In rare situations where the implant is too long in the AC and obstructed by the iris, higher energy Nd:YAG laser (1.5-1.8 mJ) can be considered to purposely fracture the internal tip of the implant, thus creating a new unobstructed inner ostium.
- Furthermore, if there is concern for obstruction at the distal lumen of the stent, the needle can be used to amputate the distal tip of the implant when performing needling.
- When the above attempts are unsuccessful, or when a surgical revision is deemed necessary, the surgeon can assess the patency of the XEN Gel Stent by injecting dyes such as Vision Blue (Dutch Ophthalmic Research Center) into the AC and verifying if the bluish color reaches the subconjunctival space (Video 5). If an open conjunctival approach is chosen, verify outflow at the distal tip of the implant (with a surgical sponge to visualize beading of aqueous humor) after dissecting surrounding tissue. If flow cannot be confirmed, using a small 27-gauge canula to flush balanced salt solution through the implant or using a 9-0 Ethilon (Johnson & Johnson Vision) or nylon suture to canulate the lumen of the implant will help dislodge possible particles and re-establish flow (Video 6). Using microforceps via ab interno with direct lens visualization can be helpful to remove a particle or the stent if necessary.

Figure 18: Slit lamp images showing pigment inside the lumen at postoperative month 4 with IOP 10 mm Hg (A) and at month 6 with IOP 7 mm Hg (B). Digital ocular massage was recommended to encourage outflow and prevent lumen obstruction. Images courtesy of Vanessa Vera, MD.

Figure 19: Gonioscopic image showing implant entering angle too low and creating the "V" sign on the iris. Image courtesy of Herbert Reitsamer, MD.

Figure 20: Slit lamp images showing pigment outflow in the bleb area, most likely through side flow around the implant, which subsided and did not compromise the internal lumen of the stent. Images at postoperative day 1 (A), week 1 (B), month 1 (C), month 6 (D), and month 9 (E). Images courtesy of Vanessa Vera, MD.

Conclusion

Complications are unavoidable when surgeries are performed. The best means to reduce the rate or risk of complications is to learn about the most commonly reported ones and try to understand the physiopathology behind them. This might give us some insight into why they happen and, in some instances, how can they be prevented.

In this paper, authors who have significant experience with XEN Gel Stent offer their best understanding of complications they have experienced and those commonly reported in the literature. They provide insight into potential causes with an aim to aid surgeons in preventing them, as well as describe management options gathered from the literature or their personal experience.

Declarations

Ethics Compliance: This review paper does not include new data from studies on human participants or animals.

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article. All names authors take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

Disclosure: All of the authors are consultants to Allergan, an AbbVie company.

The authors were not provided honoraria for any time spent developing, reviewing, or editing the manuscript, or for contributing images or videos.

The authors acknowledge Iqbal Ike K. Ahmed, MD, FRCSC; Dan Lindfield, MD; Ingeborg Stalmans, MD; and Daniel Krivoy, MD, for their contributions on this paper.

Medical writing and editorial assistance in the preparation of this article was provided by Adrienne Resek, MA. Support for this assistance was funded by Allergan, an AbbVie Company.

References

1. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*. 2014;121(11):2081-2090. Doi: <https://www.doi.org/10.1016/j.ophtha.2014.05.013>
2. Gedde SJ, Schiffman JC, Feuer WJ, et al. Treatment outcomes in the Tube Versus Trabeculectomy (Tvt) study after five years of follow-up. *Am J Ophthalmol*. 2012;153(5):789-803.e2. Doi: <https://www.doi.org/10.1016/j.ajo.2011.10.026>
3. Gedde SJ, Singh K, Schiffman JC, Feuer WJ. The Tube Versus Trabeculectomy Study: interpretation of results and application to clinical practice. *Current Opinion in Ophthalmology*. 2012;23(2):118-126. Doi: <https://www.doi.org/10.1097/ICU.0b013e32834ff2d1>
4. Gedde SJ, Feuer WJ, Shi W, et al. Treatment outcomes in the primary tube versus trabeculectomy study after 1 year of follow-up. *Ophthalmology*. 2018;125(5):650-663. Doi: <https://www.doi.org/10.1016/j.ophtha.2018.02.003>
5. Musch DC, Lichter PR, Guire KE, Standardi CL. The Collaborative Initial Glaucoma Treatment Study: study design, methods, and baseline characteristics of enrolled patients. *Ophthalmology*. 1999;106(4):653-662. Doi: [https://www.doi.org/10.1016/s0161-6420\(99\)90147-1](https://www.doi.org/10.1016/s0161-6420(99)90147-1)
6. Musch DC, Gillespie BW, Lichter PR, Niziol LM, Janz NK, CIGTS Study Investigators. Visual field progression in the Collaborative Initial Glaucoma Treatment Study the impact of treatment and other baseline factors. *Ophthalmology*. 2009;116(2):200-207. Doi: <https://www.doi.org/10.1016/j.ophtha.2009.01.013>

www.doi.org/10.1016/j.opthta.2008.08.051

7. FDA approves Xen gel stent for glaucoma. American Academy of Ophthalmology. <https://www.aao.org/headline/fda-approves-xen-gel-stent-glaucoma>. Published November 28, 2016.
8. Mansouri K, Guidotti J, Rao HL, et al. Prospective evaluation of standalone xen gel implant and combined phacoemulsification-xen gel implant surgery: 1-year results. *J Glaucoma*. 2018;27(2):140-147. Doi: <https://www.doi.org/10.1097/IJG.0000000000000858>
9. Schlenker MB, Gulamhusein H, Conrad-Hengerer I, et al. Efficacy, safety, and risk factors for failure of standalone ab interno gelatin microstent implantation versus standalone trabeculectomy. *Ophthalmology*. 2017;124(11):1579-1588. Doi: <https://www.doi.org/10.1016/j.opthta.2017.05.004>
10. Vera V, Gagne S, Myers JS, Ahmed IK. Surgical approaches for implanting xen gel stent without conjunctival dissection. *Clinical Ophthalmology*. Doi: <https://www.doi.org/10.2147/OPHT.S265695>
11. Panarelli JF, Yan DB, Francis B, Craven ER. Xen gel stent open conjunctiva technique: a practical approach paper. *Adv Ther*. 2020;37(5):2538-2549. Doi: <https://www.doi.org/10.1007/s12325-020-01278-1>
12. Buffault J, Baudouin C, Labbé A. XEN® Gel Stent for management of chronic open angle glaucoma: A review of the literature. *J Fr Ophtalmol*. 2019;42(2):e37-e46. Doi: <https://www.doi.org/10.1016/j.jfo.2018.12.002>
13. Hengerer FH, Kohnen T, Mueller M, Conrad-Hengerer I. Ab interno gel implant for the treatment of glaucoma patients with or without prior glaucoma surgery: 1-year results. *Journal of Glaucoma*. 2017;26(12):1130-1136. Doi: <https://www.doi.org/10.1097/IJG.0000000000000803>
14. Reitsamer H, Sng C, Vera V, et al. Two-year results of a multicenter study of the ab interno gelatin implant in medically uncontrolled primary open-angle glaucoma. *Graefes Arch Clin Exp Ophthalmol*. 2019;257(5):983-996. Doi: <https://www.doi.org/10.1007/s00417-019-04251-z>
15. Vera V, Department of Ophthalmology, Unidad Oftalmológica de Caracas, Venezuela, Ahmed I Ike K, et al. Gel stent implantation recommendations for preoperative assessment, surgical technique, and postoperative management. *US Ophthalmic Review*. 2018;11(1):38. Doi: <https://www.doi.org/10.17925/USOR.2018.11.1.38>
16. Fernández-García A, Romero C, Garzón N. Dry Lake technique for the treatment of hypertrophic bleb following XEN® Gel Stent placement. *Arch Soc Esp Oftalmol*. 2015;90(11):536-538. Doi: <https://www.doi.org/10.1016/j.oftal.2015.03.003>
17. Budenz DL, Hoffman K, Zacchei A. Glaucoma filtering bleb dysesthesia. *Am J Ophthalmol*. 2001;131(5):626-630. Doi: [https://www.doi.org/10.1016/s0002-9394\(00\)00901-6](https://www.doi.org/10.1016/s0002-9394(00)00901-6)
18. Anis S, Ritch R, Shihadeh W, Liebmann J. Surgical reduction of symptomatic, circumferential, filtering blebs. *Arch Ophthalmol*. 2006;124(6):890-894. Doi: <https://www.doi.org/10.1001/archopht.124.6.890>
19. Palmberg P, Zacchei AC. Compression sutures - A new treatment for leaking or painful filtering blebs. *INVESTOPHTHALVISUAL SCI*. 1996;37(3). <https://miami.pure.elsevier.com/en/publications/compression-sutures-a-new-treatment-for-leaking-or-painful-filter>.
20. Sekaran A, Karimi A, Lindfield D. Hypertrophic dysaesthetic blebs following ab-interno gel stent (Xen) glaucoma surgery: management and "redirect" revision surgery. *Clin Exp Ophthalmol*. 2018;46(9):1093-1095. Doi: <https://www.doi.org/10.1111/ceo.13335>
21. Vijaya L, Manish P, Ronnie G, Shantha B. Management of complications in glaucoma surgery. *Indian J Ophthalmol*. 2011;59(Suppl1):S131-S140. Doi: <https://www.doi.org/10.4103/0301-4738.73689>
22. Karri B, Gupta C, Mathews D. Endophthalmitis following xen stent exposure. *J Glaucoma*. 2018;27(10):931-933. Doi: <https://www.doi.org/10.1097/IJG.0000000000001012>
23. Kerr NM, Wang J, Sandhu A, Harasymowycz PJ, Barton K. Ab interno gel implant-associated bleb-related infection. *Am J Ophthalmol*. 2018;189:96-101. Doi: <https://www.doi.org/10.1016/j.ajo.2018.02.014>
24. Salinas L, Chaudhary A, Guidotti J, Mermoud A, Mansouri K. Revision of a leaking bleb with xen gel stent replacement. *J Glaucoma*. 2018;27(1):e11-e13. Doi: <https://www.doi.org/10.1097/IJG.0000000000000811>
25. Santamaría-Álvarez JF, Lillo-Sopena J, Sanz-Moreno S, Caminal-Mitjana JM. Management of conjunctival perforation and xen gel stent exposure by stent repositioning through the anterior chamber. *J Glaucoma*. 2019;28(2):e24-e26. Doi: <https://www.doi.org/10.1097/IJG.0000000000001109>
26. Higginbotham EJ, Stevens RK, Musch DC, et al. Bleb-related endophthalmitis after trabeculectomy with mitomycin C. *Ophthalmology*. 1996;103(4):650-656. Doi: [https://www.doi.org/10.1016/s0161-6420\(96\)30639-8](https://www.doi.org/10.1016/s0161-6420(96)30639-8)

27. Greenfield DS, Suñer IJ, Miller MP, Kangas TA, Palmberg PF, Flynn HW. Endophthalmitis after filtering surgery with mitomycin. *Arch Ophthalmol*. 1996;114(8):943-949. Doi: <https://www.doi.org/10.1001/archophth.1996.01100140151007>
28. Lapira M, Cronbach N, Shaikh A. Extrusion and breakage of xen gel stent resulting in endophthalmitis: *Journal of Glaucoma*. 2018;27(10):934-935. Doi: <https://www.doi.org/10.1097/IJG.0000000000001058>
29. Olgun A, Imamoğlu S, Karapapak M, Düzgün E, Kaçar H. Endophthalmitis after xen gel stent implantation: 2 cases. *J Glaucoma*. 2018;27(12):e191-e194. Doi: <https://www.doi.org/10.1097/IJG.0000000000001076>
30. Gillmann K, Bravetti GE, Rao HL, Mermoud A, Mansouri K. Bilateral xen stent implantation: a long-term prospective study of the difference in outcomes between first-operated and fellow eyes. *J Glaucoma*. 2020;29(7):536-541. Doi: <https://www.doi.org/10.1097/IJG.0000000000001520>
31. Napoli L, Riva I, Oddone F, Michelessi M, Quaranta L. A rare case of endophthalmitis after bleb needle revision for glaucoma Xen® gel stent. *Eur J Ophthalmol*. 2021;31(1):NP9-NP12. Doi: <https://www.doi.org/10.1177/1120672119878016>
32. Ciulla TA, Beck AD, Topping TM, Baker AS. Blebitis, early endophthalmitis, and late endophthalmitis after glaucoma-filtering surgery. *Ophthalmology*. 1997;104(6):986-995. Doi: [https://www.doi.org/10.1016/s0161-6420\(97\)30196-1](https://www.doi.org/10.1016/s0161-6420(97)30196-1)
33. Lehmann OJ, Bunce C, Matheson MM, et al. Risk factors for development of post-trabeculectomy endophthalmitis. *Br J Ophthalmol*. 2000;84(12):1349-1353. Doi: <https://www.doi.org/10.1136/bjo.84.12.1349>
34. Bannerman TL, Rhoden DL, McAllister SK, Miller JM, Wilson LA. The source of coagulase-negative staphylococci in the Endophthalmitis Vitrectomy Study. A comparison of eyelid and intraocular isolates using pulsed-field gel electrophoresis. *Arch Ophthalmol*. 1997;115(3):357-361. Doi: <https://www.doi.org/10.1001/archophth.1997.01100150359008>
35. Wu PC, Li M, Chang SJ, et al. Risk of endophthalmitis after cataract surgery using different protocols for povidone- iodine preoperative disinfection. *J Ocul Pharmacol Ther*. 2006;22(1):54-61. Doi: <https://www.doi.org/10.1089/jop.2006.22.54>
36. Zheng C, Quigley H. Prophylactic antibiotics after glaucoma surgery: where is the evidence? *Ophthalmol Glaucoma*. 2018;1(2):83-84. Doi: <https://www.doi.org/10.1016/j.ogla.2018.05.001>
37. Azuara-Blanco A, Katz LJ. Dysfunctional filtering blebs. *Surv Ophthalmol*. 1998;43(2):93-126. Doi: [https://www.doi.org/10.1016/s0039-6257\(98\)00025-3](https://www.doi.org/10.1016/s0039-6257(98)00025-3)
38. Sagara H, Yamamoto T, Imaizumi K, Sekiryu T. Impact of topically administered steroids, antibiotics, and sodium hyaluronate on bleb-related infection onset: the japan glaucoma society survey of bleb-related infection report 4. *J Ophthalmol*. 2017;2017:7062565. Doi: <https://www.doi.org/10.1155/2017/7062565>
39. Stein JD, McCoy AN, Asrani S, et al. Surgical management of hypotony owing to overfiltration in eyes receiving glaucoma drainage devices. *J Glaucoma*. 2009;18(8):638-641. Doi: <https://www.doi.org/10.1097/IJG.0b013e31819aa4e0>
40. Abbas A, Agrawal P, King AJ. Exploring literature-based definitions of hypotony following glaucoma filtration surgery and the impact on clinical outcomes. *Acta Ophthalmol*. 2018;96(3):e285-e289. Doi: <https://www.doi.org/10.1111/aos.13601>
41. Bruynseels A, Sii F, Masood I, Shah P. Severe intraocular pressure elevation after intracameral healon 5 viscoelastic support for postoperative hypotony after xen gel stent insertion. *J Glaucoma*. 2018;27(4):e75-e76. Doi: <https://www.doi.org/10.1097/IJG.0000000000000883>
42. Karaconji T, Naqvi S, Mercieca K. Transconjunctival compression sutures for an overfiltering bleb following subconjunctival gel stent insertion for glaucoma. *J Glaucoma*. 2019;28(3):e41-e43. Doi: <https://www.doi.org/10.1097/IJG.0000000000001140>
43. Prokosch-Willing V, Vossmerbaeumer U, Hoffmann E, Pfeiffer N. Suprachoroidal bleeding after xen gel implantation. *J Glaucoma*. 2017;26(12):e261-e263. Doi: <https://www.doi.org/10.1097/IJG.0000000000000795>
44. Rooney DM, Shadid HR, Siegel LI, et al. Postoperative complications of ab interno gelatin microstent. *J Glaucoma*. 2019;28(5):e77-e81. Doi: <https://www.doi.org/10.1097/IJG.0000000000001194>
45. Stamper RL, McMenemy MG, Lieberman MF. Hypotonous maculopathy after trabeculectomy with subconjunctival 5-fluorouracil. *Am J Ophthalmol*. 1992;114(5):544-553. Doi: [https://www.doi.org/10.1016/s0002-9394\(14\)74481-2](https://www.doi.org/10.1016/s0002-9394(14)74481-2)
46. Cohen SM, Flynn HW, Palmberg PF, Gass JD, Grajewski AL, Parrish RK. Treatment of hypotony maculopathy after trabeculectomy. *Ophthalmic Surg Lasers*. 1995;26(5):435-441. <https://pubmed.ncbi.nlm.nih.gov/8963858/>

47. Boese EA, Shah M. Late spontaneous dislocation of an ab interno gelatin microstent. *J Glaucoma*. 2018;27(4):e84-e86. Doi: <https://www.doi.org/10.1097/IJG.0000000000000897>
48. Atalay K, Nacaroglu SA, Kirgiz A. Complication of microbypass stenting: the anterior chamber displacement of a Xen implant. *Arq Bras Oftalmol*. 2018;81(6):514-516. Doi: <https://www.doi.org/10.5935/0004-2749.20180098>
49. Derveniz N, Mikropoulou AM, Derveniz P, Lewis A. Dislocation of a previously successful XEN glaucoma implant into the anterior chamber: a case report. *BMC Ophthalmology*. 2017;17(1):148. Doi: <https://www.doi.org/10.1186/s12886-017-0540-1>
50. Gillmann K, Bravetti GE, Mermoud A, Mansouri K. Anterior chamber xen gel stent movements: the impact on corneal endothelial cell density. *J Glaucoma*. 2019;28(6):e93-e95. Doi: <https://www.doi.org/10.1097/IJG.0000000000001200>
51. De Gregorio A, Pedrotti E, Russo L, Morselli S. Minimally invasive combined glaucoma and cataract surgery: clinical results of the smallest ab interno gel stent. *Int Ophthalmol*. 2018;38(3):1129-1134. Doi: <https://www.doi.org/10.1007/s10792-017-0571-x>
52. Pinto Ferreira N, Abegão Pinto L, Marques-Neves C. Xen gel stent internal ostium occlusion: ab-interno revision. *J Glaucoma*. 2017;26(4):e150-e152. Doi: <https://www.doi.org/10.1097/IJG.0000000000000625>
53. Lee GA, Shah P. Yag laser xen stent truncation. *Ophthalmol Glaucoma*. 2020;3(5):359. Doi: <https://www.doi.org/10.1016/j.ogla.2020.05.002>
54. Razeghinejad R. Xen luminal obstruction. *Ophthalmol Glaucoma*. 2020;3(5):376. Doi: <https://www.doi.org/10.1016/j.ogla.2020.04.010>
55. Sebestyen JG. Fibrinoid syndrome: a severe complication of vitrectomy surgery in diabetics. *Ann Ophthalmol*. 1982;14(9):853-856. <https://pubmed.ncbi.nlm.nih.gov/7181348/>
56. Cunha LP, Costa-Cunha LVF, Costa CF, Bastos RR, Prata T dos S, Monteiro MLR. Predictive factors for anterior chamber fibrin formation after vitreoretinal surgery. *Revista Brasileira de Oftalmologia*. 2014;73(2). Doi: <https://www.doi.org/10.5935/0034-7280.20140021>
57. Gillmann K, Mansouri K, Bravetti GE, Mermoud A. Chronic intraocular inflammation as a risk factor for xen gel stent occlusion: a case of microscopic examination of a fibrin-obstructed xen stent. *J Glaucoma*. 2018;27(8):739-741. Doi: <https://www.doi.org/10.1097/IJG.0000000000001002>
58. Vera V, Sheybani A, Lindfield D, Stalmans I, Ahmed IIK. Recommendations for the management of elevated intraocular pressure due to bleb fibrosis after XEN gel stent implantation. *Clin Ophthalmol*. 2019;13:685-694. Doi: <https://www.doi.org/10.2147/OPTH.S195457>
59. Gillmann K, Mansouri K, Bravetti GE, Mermoud A. Chronic intraocular inflammation as a risk factor for xen gel stent occlusion: a case of microscopic examination of a fibrin-obstructed xen stent. *J Glaucoma*. 2018;27(8):739-741. Doi: <https://www.doi.org/10.1097/IJG.0000000000001002>
60. Vera V, Sheybani A, Lindfield D, Stalmans I, Ahmed IIK. Recommendations for the management of elevated intraocular pressure due to bleb fibrosis after XEN gel stent implantation. *Clin Ophthalmol*. 2019;13:685-694. Doi: <https://www.doi.org/10.2147/OPTH.S195457>

Copyright: © **Vera et al.** This is an Open Access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.