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CASE SERIES

Case Series of Combined XEN Implantation and Phacoemulsification in Chinese Eyes: One-Year Outcomes

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ABSTRACT

Purpose: The outcome of XEN implantation in Chinese eyes has not been previously reported. The purpose of our study is to evaluate the efficacy and safety of combined cataract surgery and XEN implantation in Chinese eyes with glaucoma.

Methods: We conducted a prospective study of 31 consecutive Chinese patients who underwent combined phacoemulsification and XEN implantation at the National University Hospital (Singapore) in this study. Patients were assessed preoperatively and postoperatively on days 1 and 7, and months 1, 3, 6, and 12. The intraocular pressure (IOP), glaucoma medication use, Snellen visual acuity (VA), and complications were assessed at each visit. The Wilcoxon signed rank test for non-parametric data was used for the analysis of IOP and glaucoma medications at baseline versus 12 months after the procedure.

Results: The mean age of the patients was 70 ± 7.9 years and 48.4% were male. Twelve patients (38.7%) were diagnosed with primary open angle glaucoma and 19 patients (61.3%) were diagnosed with primary angle closure glaucoma. There was a significant decrease in IOP at 12 months (12.1 ± 2.6 mmHg) compared with preoperative medicated (15.6 ± 2.7 mmHg, $p < 0.0001$) and unmedicated IOP (22.1 ± 3.6 mmHg, $p < 0.001$). as well as a significant reduction in the number of glaucoma medications (1.4 ± 0.6 vs 0.1 ± 0.4, $p < 0.0001$). The most common complications were transient hypotony (12.9%) and ptosis (12.9%) and there were no sight-threatening intraoperative or postoperative complications. One patient required additional glaucoma surgery for uncontrolled IOP at 8 months after combined phacoemulsification and XEN implantation.

Conclusion: Combined XEN implantation with cataract surgery was effective in lowering the IOP and the number of glaucoma medications in Chinese eyes for at least 12 months, with a favorable safety profile.

Keywords: Glaucoma; Glaucoma surgery; Minimally invasive surgery

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INTRODUCTION

The XEN gel implant is a hydrophilic implant comprising porcine cross-linked gelatin. It is a minimally invasive glaucoma surgical device which is inserted *ab interno*, draining aqueous from the anterior chamber to the subconjunctival space. The XEN gel implant is 6 mm in length and has an internal lumen diameter of 45 μm, with the size and length of the implant conferring approximately 6–8 mmHg pressure resistance according to the Hagen–Poiseuille equation, hence protecting against hypotony [1]. A prospective multicenter study of the XEN gel implant in predominantly Caucasian eyes with medically uncontrolled primary open angle glaucoma (POAG) showed that it effectively decreased intraocular pressure (IOP) ($-$ 6.2 $\pm$ 4.9 mmHg, $p < 0.001$) and medication count ($-$ 1.5 $\pm$ 1.4, $p < 0.001$) at 24 months compared with baseline, with an acceptable safety profile [2].

East Asians account for approximately half of all glaucoma sufferers globally [3] but the outcome of XEN implantation has not been reported in East Asian eyes, in particular Chinese eyes. The success rates of unaugmented and augmented trabeculectomy are reported to be poorer in Chinese persons than Caucasians, with higher complication rates reported [4–6]. Keloid scarring in the skin of Chinese persons has been shown to be more significant than that of darker-skinned Malays [7], which may indicate a higher predisposition to conjunctival scarring after glaucoma filtration surgery as the healing mechanism in skin and conjunctiva is thought to be similar [8]. Chinese persons also have a higher prevalence of primary angle closure glaucoma (PACG) [1] and myopia (and hence thinner sclera) than Caucasian persons [9], which may predispose to a higher rate of surgical complications after conjunctival filtration surgery [10, 11].

Hence, the aim of this study was to determine the safety and efficacy of combined XEN implantation and cataract surgery in Chinese eyes with primary glaucoma.

METHODS

This was a prospective single-center case series of consecutive Chinese patients who underwent combined phacoemulsification with XEN implantation at the National University Hospital in Singapore. Approval was obtained from the National Healthcare Group Domain Specific Review Board and the study was conducted in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients prior to surgery.

Study Subjects

Subjects with POAG and PACG who required 1–4 glaucoma medications and who were phakic in the same eye were included in this study. PACG was defined as eyes in which the posterior trabecular meshwork was visible for more than 180° on gonioscopy in the primary position and glaucomatous optic neuropathy as defined by Foster et al. [12]. PACG was defined as eyes in which the posterior trabecular meshwork was not visible for at least 180° on gonioscopy in the primary position, elevated IOP (greater than 21 mmHg) with or without peripheral anterior synechiae (PAS), and glaucomatous optic neuropathy [13]. All subjects had healthy, free, and mobile conjunctiva in the target quadrant, were at least 21 years of age, and were able to provide informed consent.

Exclusion criteria included advanced glaucoma (as defined as cup–disc ratio of at least 0.9 and/or a visual field defect within central 10° of fixation) [14]; diagnosis of glaucoma other than POAG and PACG (including uveitic, neovascular, traumatic glaucoma, or glaucoma secondary to raised episcleral venous pressure); prior incisional glaucoma surgery or cataract surgery; presence of scarring, prior surgery, or other conjunctival pathologies in the target quadrant; presence of vitreous in the anterior chamber; presence of intraocular silicone oil; clinically significant inflammation or infection in the study eye within 30 days before the preoperative visit; known or suspected allergy or sensitivity to drugs required for the surgery (including anesthesia) or any of the device

components (e.g., porcine products and glutaraldehyde); and any corneal, choroidal, retinal, or orbital disease which may interfere with cataract surgery or XEN implantation.

Perioperative and Operative Procedures

All subjects were prescribed topically administered prednisolone acetate 1% eyedrop (Pred Forte®, Allergan, Dublin, Ireland) four times daily in the study eye 1 week before surgery. Topical glaucoma medications in the study eye were stopped on the day of the surgery. Combined phacoemulsification and XEN implantation was performed under peribulbar anesthesia by an experienced surgeon who has performed more than 100 XEN surgeries (CCAS). Intra-Tenon's injection of 0.1 ml mitomycin C (0.2 mg/ml) at least 5 mm from the limbus was performed at the start of the surgery, ensuring that the mitomycin C does not spread anteriorly to the limbal conjunctiva. Phacoemulsification was performed via a standard clear corneal incision with acrylic intraocular lens implantation. The XEN implant was inserted only if cataract surgery was successful and uncomplicated. The surgical steps for XEN implantation were creation of main and side port corneal incisions; injection of cohesive viscoelastic (Healon GV®, Florida, USA) into the anterior chamber; insertion of the injector through the main incision across the anterior chamber towards the superior-nasal quadrant; advancement of the injector needle through the sclera using a second instrument at the side port to provide stabilization and counter-traction; injection of the implant into the subconjunctival space by moving the slider on the injector handle anteriorly; removal of the injector and viscoelastic; pressurization of the eye with balanced salt solution and creation of a subconjunctival bleb. All corneal incisions were hydrated at the end of the surgery. Ideal placement of the XEN implant was 1 mm in the anterior chamber, 2 mm in the scleral tunnel, and 3 mm in the subconjunctival space [2].

After surgery, all glaucoma medications were discontinued in the study eye and all patients were prescribed topically administered levofloxacin (Cravit 1.5%, Santen, Osaka, Japan) four times daily for 1 month and topically administered prednisolone acetate 1% (Pred Forte®, Allergan Ltd, Dublin, Ireland) for at least 6 months. The frequency of topical steroid therapy was initially three hourly and tapered according to the severity of conjunctival injection around the bleb.

Study Measures

Study subjects underwent a complete ophthalmic examination by a fellowship-trained glaucoma specialist preoperatively and on day 1, week 1, and months 1, 3, 6, and 12. This included assessment of the best corrected Snellen visual acuity (BCVA) and a detailed slit lamp examination of the anterior and posterior segments. The IOP was measured with Goldmann applanation tonometry using a masked, two-person method [15]: two consecutive measurements were performed, followed by a third if the difference between the first two measurements exceeded 2 mmHg. The average or median IOP was used for analysis, respectively, depending on whether two or three measurements were taken. The IOP was assessed in the morning of each study visit and bleb needling was performed at the slit lamp using a 25G needle without adjunctive antimetabolites if the IOP exceeded the target IOP according to the Canadian Consensus Guidelines [14] in the absence of a subconjunctival filtering bleb. The number of needling procedures was noted for each patient. If there were three prior needling procedures in the study eye, topical glaucoma medications were reintroduced in a stepwise fashion (i.e., one class of medication at a time). Unmedicated IOP was defined as the highest IOP recorded prior to starting glaucoma medications. Anterior segment optical coherence tomography (ASOCT) imaging of the bleb was performed at 6 and 12 months postoperatively, and bleb images were obtained along a line scan that was tangential to the limbus and passed through the point of highest elevation of the bleb (located by a light reflex on the ASOCT video display).

The primary outcome measure was IOP reduction at 12 months compared with baseline unmedicated IOP. Secondary outcomes measures included topical glaucoma medication use at 12 months, the incidence of complications, and failure. Failure was defined as IOP exceeding 21 mmHg or less than 20% decrease from baseline unmedicated IOP on two consecutive visits after 3 months, IOP $\leq$ 5 mmHg on two consecutive visits after 3 months, loss of light perception vision, or reoperation for glaucoma [16]. Postoperative complications were noted at each visit, including hyphema, loss of two or more lines of BCVA, hypotony (defined as IOP $\leq$ 5 mmHg, considered persistent hypotony if not resolved by 3 months), shallow anterior chamber, choroidal detachment, hypotonous maculopathy, implant exposure, implant occlusion, ptosis, strabismus, bleb leak, blebitis, endophthalmitis, cystoid macular edema, persistent cornea edema, and suprachoroidal hemorrhage. Needling was not considered an adverse event or glaucoma-related additional surgical intervention but was documented as a postoperative procedure, which is consistent with other recent studies [2].

Statistical Analysis

Statistical analyses were performed using STATA v 15.0 (StataCorp., College Station, TX, USA) and SPSS v20.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to describe the baseline characteristics of the study subjects. All patients were included in the safety analysis based on the incidence of surgical complications. To assess the efficacy of the XEN implant in all subjects as well as POAG and PACG subjects, postoperative IOP and topical glaucoma medication use at 12 months were compared to preoperative values using the Wilcoxon signed rank test. The IOP reduction at 12 months from preoperative medicated and unmedicated IOP was compared between subjects with POAG and PACG using the Mann–Whitney *U* test. Kaplan–Meier analysis was used to describe the cumulative probabilities of survival in our study cohort. To assess possible factors associated with failure and needling (i.e., age, gender, glaucoma subtype, number of preoperative glaucoma medications, preoperative medicated IOP, preoperative unmedicated IOP), univariate logistic regression analysis was performed. Statistical significance was set at $p < 0.05$.

RESULTS

The baseline characteristics of the study subjects are shown in Table 1. We included 31 eyes of 31 subjects in this study and the XEN implant was

Table 1 Demographic data and baseline characteristics of study participants

Characteristic	Number
Mean age (years)	70 ± 7.9
Gender (*n*, %)	
Male	15 (48.4%)
Female	16 (51.6%)
Glaucoma subtype (*n*, %)	
Primary open angle glaucoma	12 (38.7%)
Primary angle closure glaucoma	19 (61.3%)
Baseline number of topical glaucoma medications, mean ± SD	1.4 ± 0.6
Bseline intraocular pressure (mmHg), mean ± SD	
Medicated	15.5 ± 2.7
Unmedicated	22.7 ± 3.8
Best corrected visual acuity (*n*, %)	
20/20 or better	0 (0%)
20/40 or better	20 (64.5%)
20/100 or better	9 (29.0%)
Worse than 20/100	2 (6.5%)
Baseline visual field mean deviation (dB), mean ± SD	− 10.4 ± 6.1
Baseline visual field pattern standard deviation (dB), mean ± SD	7.2 ± 4.5

SD standard deviation

successfully inserted in all 31 eyes after uneventful phacoemulsification (Fig. 1).

Thirty eyes (96.8%) did not require further glaucoma surgery during the 12 months of follow-up, while one eye (3.2%) with POAG required Ahmed aqueous shunt implantation at 8 months because of uncontrolled IOP (24 mmHg) despite maximum tolerated glaucoma medications ($n = 3$). At the 12-month visit, 30 eyes were available for efficacy evaluation, after excluding the eye which required further glaucoma surgery. In a paired analysis of these 30 eyes, the mean IOP at 12 months was significantly decreased compared with preoperated medicated and unmedicated IOP, with a significant reduction in the mean number of topical ocular hypotensive medications. Results were similar when this analysis was performed separately for eyes with POAG and PACG (Table 2). There was no significant difference between eyes with POAG and PACG in the IOP reduction at 12 months

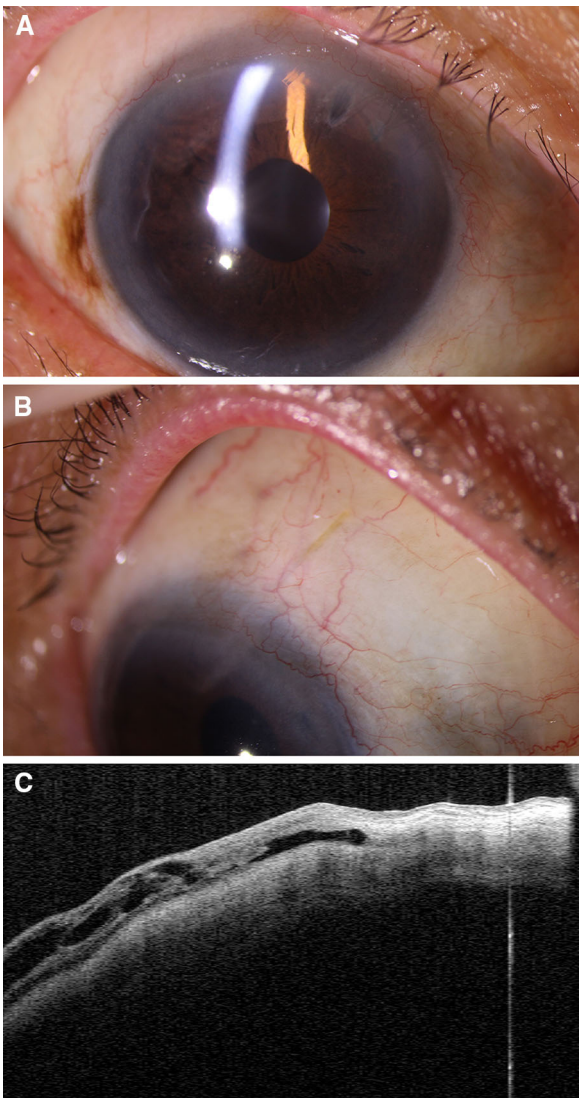

Fig. 1 Anterior segment photographs showing a XEN implant in the anterior chamber (**a**) and the subconjunctival space (**b**) of a Chinese eye at postoperative month 12. An anterior segment optical coherence tomography image of the associated bleb (**c**)

Table 2 Mean intraocular pressure and mean number of glaucoma medications at 12 months compared with baseline in all subjects and those with primary open angle glaucoma and primary angle closure glaucoma

	Baseline	Month 12	*P*
All subjects ($n = 30$)			
Intraocular pressure/mmHg			
Medicated	15.6 ± 2.7	12.1 ± 2.6	< 0.001
Unmedicated	22.1 ± 3.6		< 0.001
Number of glaucoma medications	1.4 ± 0.6	0.1 ± 0.4	< 0.001
POAG ($n = 11$)			
Intraocular pressure/mmHg			
Medicated	16.1 ± 2.0	12.6 ± 1.7	0.004
Unmedicated	23.1 ± 3.3		0.003
Number of glaucoma medications	1.4 ± 0.5	0.0 ± 0.0	0.003
PACG ($n = 19$)			
Intraocular pressure/mmHg			
Medicated	15.2 ± 3.0	11.7 ± 3.0	< 0.001
Unmedicated	21.7 ± 3.7		< 0.001
Number of glaucoma medications	1.4 ± 0.7	0.2 ± 0.5	< 0.001

Data are presented as mean ± standard deviation

compared with preoperative medicated (− 4.5 ± 4.0 vs − 3.4 ± 3.1 mmHg, $p = 0.503$) and unmedicated IOP (− 11.5 ± 5.4 vs − 10.0 ± 4.1 mmHg, $p = 0.516$), or in the decrease in the number of topical glaucoma medications (− 1.4 ± 0.5 vs − 1.2 ± 0.5, $p = 0.332$). A total of 28 eyes (90.3%) did not require any topical glaucoma medications 12 months after XEN implantation. Glaucoma medications were required in two eyes at 12 months, of which one eye required one medication and one eye required two medications (Fig. 2).

Bleb needling at the slit lamp (Fig. 3) was performed in 11 eyes, with 8 eyes requiring needling within the first 3 months, 2 eyes requiring needling between 3 and 6 months, and 1 eye requiring needling after 6 months. Five eyes underwent one needling procedure, four eyes underwent two needling procedures, and two eyes underwent three needling procedures.

The 12-month cumulative Kaplan–Meier survival probability was 80.6% (Fig. 4). On univariate logistic regression analysis, we did not find a significant predictive factor for failure [age ($p = 0.83$), gender ($p = 0.96$), glaucoma subtype ($p = 0.90$), number of preoperative glaucoma medications ($p = 1.00$), preoperative medicated IOP ($p = 0.76$), preoperative unmedicated IOP ($p = 0.61$)] or the requirement for bleb needling [age ($p = 0.43$), gender ($p = 0.32$), glaucoma subtype ($p = 0.66$), number of preoperative glaucoma medications ($p = 0.34$), preoperative medicated IOP ($p = 0.88$), preoperative unmedicated IOP ($p = 0.76$)].

There were no sight-threatening intraoperative complications. Intraoperative hyphema occurred in two eyes (6.5%), and implant malposition requiring removal of the malpositioned implant and insertion of a second XEN implant occurred in two eyes (6.5%). The postoperative complications are shown in Table 3, with the most common postoperative complications being transient hypotony (12.9%) and ptosis (12.9%). Postoperative hypotony resolved spontaneously within 3 weeks in all the affected eyes. Of these, one eye (3.2%) had hypotony in association with a shallow anterior chamber which resolved spontaneously within 2 weeks after reducing the frequency of topically administered prednisolone acetate 1% to twice a day. None of the eyes developed persistent hypotony. One eye developed cystoid macular edema 1 month after combined phacoemulsification and XEN implantation, which resolved within a month after treatment with topically administered ketorolac tromethamine 0.5% (Acular®, Allergan Ltd, Dublin, Ireland) and topically administered prednisolone acetate 1% four times a day. Implant occlusion with iris occurred in one eye (3.2%) with PACG 1 week after combined phacoemulsification and XEN implantation, which resolved after laser iridoplasty (Fig. 5). Postoperative hyphema occurred in one eye (3.2%), with the blood occupying

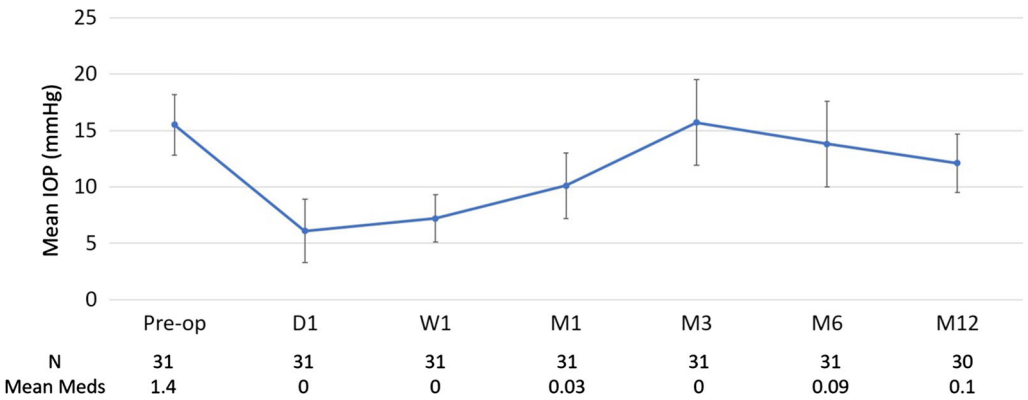

Fig. 2 Mean intraocular pressure and number of topical glaucoma medications from preoperative baseline over time in Chinese eyes. *IOP* intraocular pressure, *Pre-op* preoperative, *D1* day 1, *W1* week 1, *M1* month 1, *M3* month 3, *M6* month 6, *M12* month 12, *N* number, *Meds* medications

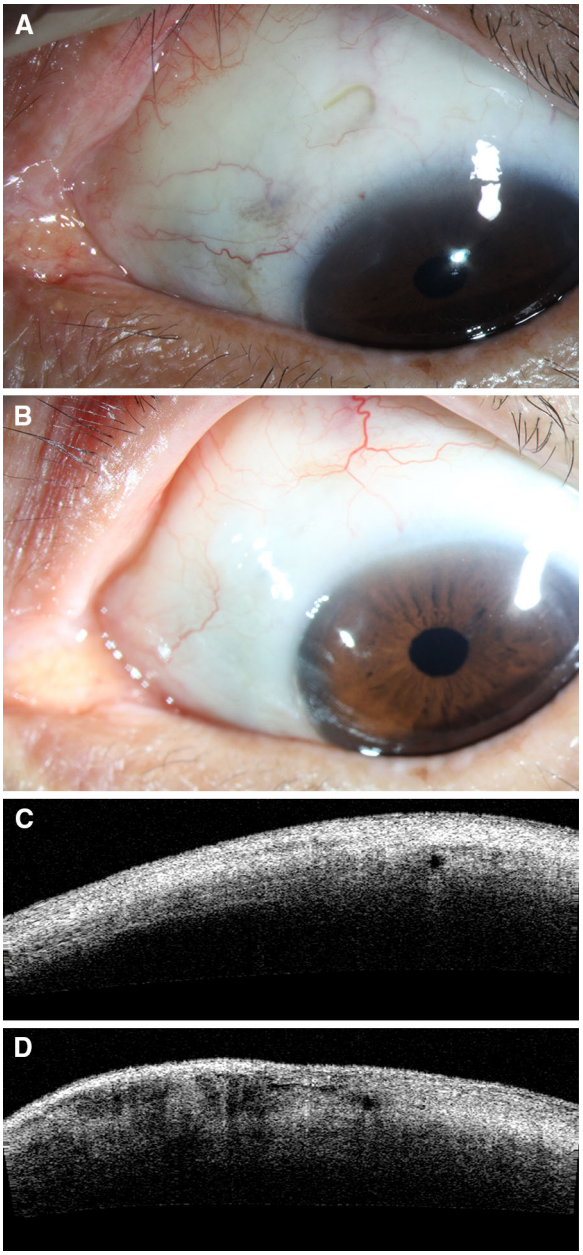

Fig. 3 Bleb needling performed at 6 months after combined phacoemulsification and XEN implantation: anterior segment photographs showing the bleb before (**a**) and after (**b**) bleb needling; anterior segment optical coherence tomography images showing the bleb before (**c**) and after (**d**) bleb needling

less than one-third of the anterior chamber (grade I hyphema), and this resolved spontaneously by the first postoperative week. None of the eyes developed implant exposure, loss of

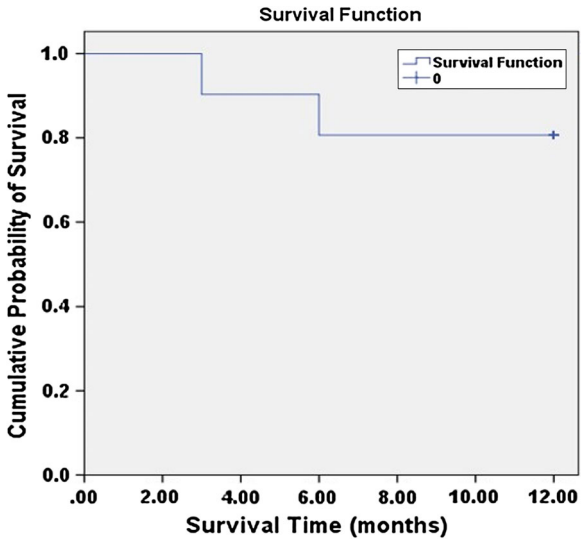

Fig. 4 Kaplan–Meier survival curve showing time to failure

two or more lines of BCVA, strabismus, bleb leak, blebitis, persistent corneal edema, endophthalmitis, or suprachoroidal hemorrhage.

DISCUSSION

Our exploratory prospective study has shown that combined phacoemulsification with XEN implantation was effective in lowering the IOP and the number of topical glaucoma medications in Chinese patients with primary glaucoma for at least 12 months, with a good safety profile.

We present novel data on the efficacy and safety of the XEN gel implant in Chinese eyes with primary glaucoma. To our knowledge, there are currently no published data on the clinical efficacy of the XEN gel implant in Chinese eyes or eyes with PACG. In our study, only one patient required further glaucoma surgery because of uncontrolled IOP despite maximum tolerated glaucoma medications. In the patients who did not require subsequent glaucoma surgery, there was a significant decrease in IOP by approximately 45% from preoperative unmedicated IOP and approximately 20% from preoperative medicated IOP, with a reduction in glaucoma medications by 1.3 medications.

Table 3 Postoperative complications after combined phacoemulsification and XEN implantation in Chinese eyes

Complication	Number (%)
Hyphema	1 (3.2)
Transient hypotony	4 (12.9)
Shallow anterior chamber	1 (3.2)
Choroidal detachment	0 (0)
Hypotonous maculopathy	0 (0)
Persistent hypotony	0 (0)
Cystoid macular oedema	1 (3.2)
Persistent cornea oedema	0 (0)
Implant exposure	0 (0)
Implant occlusion	1 (3.2)
Ptosis	4 (12.9)
Strabismus	0 (0)
Loss of $\geq$ 2 lines of best corrected visual acuity	0 (0)
Bleb leak	0 (0)
Blebitis	0 (0)
Endophthalmitis	0 (0)
Suprachoroidal hemorrhage	0 (0)

These results are similar to the findings of a multicenter study by Reitsamer et al., which included 202 eyes (96.2% Caucasian) with POAG [2]. They reported that XEN implantation was associated with a reduction in IOP by approximately 30% and a decrease in glaucoma medications by 1.5 at 24 months. The type or dose of antifibrotic therapy administered during surgery was not specified in the study protocol and 77% of the subjects received 10 μg of mitomycin C, while all the patients in our study received 20 μg of mitomycin C. To achieve similar surgical outcomes, it may be necessary to administer higher doses of antifibrotic therapy for Chinese patients compared to Caucasian patients though more studies are required to verify this. In a multicenter, retrospective study by Schlenker et al. [17], white ethnicity was correlated with surgical success in eyes that underwent trabeculectomy, but there was no significant difference in success rates between whites and non-whites in eyes that underwent XEN implantation. Racial differences in scleral flap scarring may have accounted for the difference in trabeculectomy success rates between whites and non-whites, while this was not relevant for eyes which underwent XEN implantation as a scleral flap was not created.

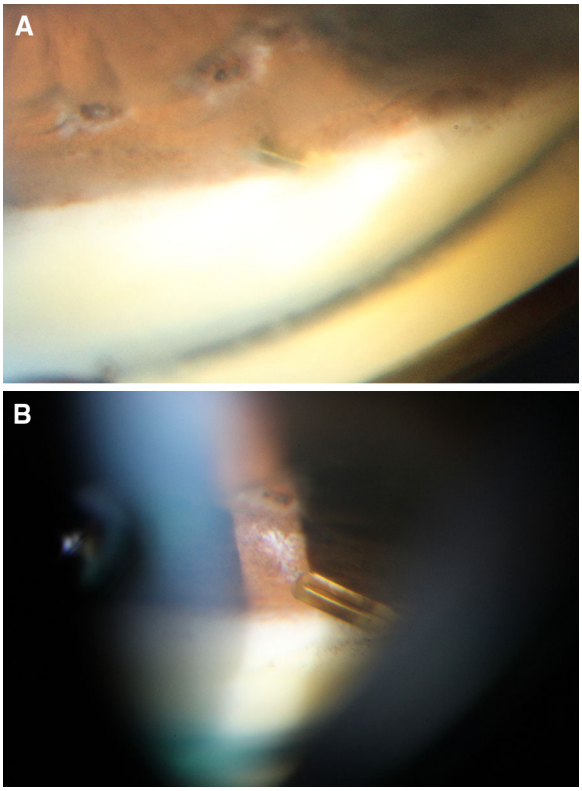

Fig. 5 Gonioscopy photographs showing iris occlusion of the XEN gel implant 1 week after combined phacoemulsification and XEN implantation (**a**) and resolution of implant occlusion after laser iridoplasty (**b**)

The surgical outcomes of XEN implantation in eyes with PACG have not been previously reported. In our study, eyes with PACG did not differ significantly from eyes with POAG in IOP or glaucoma medication reduction, or in the rate of success. Randomized controlled trials comparing cataract surgery alone with

combined cataract surgery and trabeculectomy in eyes with PACG showed that the combined procedure was more effective at reducing the number of medications, albeit with a higher rate of complications [18, 19]. Prolonged iridotrabecular contact in eyes with PACG results in trabecular damage and raised IOP even when the angles are open after cataract surgery. XEN implantation in such eyes would bypass the increased trabecular resistance by draining aqueous from the anterior chamber to the subconjunctival space, which may explain the high proportion of eyes that are medication-free in our study. The outcomes of other minimally invasive glaucoma surgical devices, such as the iStent trabecular micro-bypass stent, have also been reported in eyes with PACG. Hernstadt et al. showed that combined iStent implantation with cataract surgery was effective in lowering the IOP and the number of glaucoma medications for at least 12 months in an exploratory case series that included 37 eyes with primary angle closure disease [13]. While combined phacoemulsification and iStent implantation in eyes with PACG resulted in IOP in the mid-teens [13], the mean IOP in our study was in the low teens, suggesting that subconjunctival aqueous drainage may be able to achieve lower target IOP compared with trabecular bypass procedures.

Our findings suggest that combined phacoemulsification and XEN implantation had a good safety profile in Chinese eyes, with no sight-threatening complications. The most common postoperative complications were transient hypotony (12.9%) and ptosis (12.9%). Though the size and length of the XEN gel implant confers approximately 6–8 mmHg pressure resistance, aqueous flow around the implant in the early postoperative period can result in hypotony, which resolved spontaneously within 3 weeks in all the affected eyes. Only one eye (3.2%) developed a shallow anterior chamber in association with hypotony, which was also transient and recovered without further surgical interventions. To our knowledge, ptosis after XEN implantation has not been previously reported, though it is known to be associated with conventional glaucoma surgery, such as trabeculectomy and tube shunt implantation [20]. The mechanisms behind ptosis after XEN implantation are unclear, but could include traumatic disinsertion or damage of the levator aponeurosis from the lid speculum or lid edema [21, 22]. Patients with narrower vertical palpebral apertures have been shown to develop postoperative ptosis more frequently [22]. As the palpebral apertures of Chinese eyes are known to be smaller compared to Caucasian eyes, this could explain the higher incidence of ptosis after combined phacoemulsification and XEN implantation in our study. Postoperative implant occlusion by iris was uncommon in our study, and only occurred in one eye with PACG. In contrast, Hernstadt et al. reported that iStent occlusion by iris occurred in 27.0% of eyes with PACG after combined phacoemulsification and iStent implantation, because the anterior chamber angle remained crowded after cataract removal in eyes with plateau iris or a thick peripheral iris [13]. The intraocular length of the XEN gel implant is longer than the iStent trabecular micro-bypass stent, and it is positioned more anteriorly and further from the iris than the iStent; hence, postoperative occlusion of the XEN gel implant by iris occurs much less frequently than postoperative iStent occlusion by iris, even in eyes with PACG.

The strengths of our prospective study include the good compliance of the study subjects with the study protocol, with no patients being lost to follow-up, and the standardized surgical technique by a single experienced surgeon. However, our study had several limitations. First, the small sample size of this exploratory study could have resulted in inadequate statistical power for subgroup analyses. Second, the 1-year follow-up duration did not allow us to detect the longer-term complications of combined phacoemulsification and XEN implantation, e.g., blebitis, which have been reported in other studies [2, 16]. Third, it was not possible to determine the additional effect of XEN implantation in lowering the IOP compared with phacoemulsification alone, and a randomized study comparing the combined procedure with phacoemulsification alone is required in the future, especially in eyes with PACG. Lastly, information on the duration of

treatment with glaucoma eyedrops was not available, which could affect the outcome of subconjunctival surgeries.

CONCLUSION

This exploratory study showed that combined phacoemulsification and XEN implantation in Chinese eyes was effective in lowering the IOP and the number of glaucoma medications for at least 12 months, with a favorable safety profile. The postoperative outcomes of XEN implantation have not been previously reported in Chinese eyes or in eyes with PACG, and these results require verification in a larger study with a longer follow-up duration.

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Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, had full access to all of the data in this study, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Disclosures. Chelvin C. A. Sng is a consultant for Alcon, Allergan, and Santen and has also received research and travel funding from Glaukos and Allergan. Marcus Ang is a consultant for Allergan, Ziemer, Zeiss, and Johnson & Johnson. Paul T. K. Chew, Hla Myint Htoon, Katherine Lun and Preethi Jeyabal have nothing to declare.

Compliance with Ethics Guidelines. This study was approved by the National Healthcare Group Domain Specific Review Board. Informed consent was obtained from all subjects before recruitment into this study.

Data Availability. The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Lewis RA. Ab interno approach to the subconjunctival space using a collagen glaucoma stent. J Cat Ref Surg. 2014;40(8):1301–6.
2. Reitsamer H, Sng C, Vera V, et al. Two-year results of a multicenter study of ab interno gelatin implant in medically uncontrolled primary open-angle glaucoma. Graefes Arch Clin Exp Ophthalmol. 2019;257(5):983–96.
3. Quigley HA. Number of people with glaucoma worldwide. Br J Ophthalmol. 1996;80(5):389–93.
4. Tan C, Chew PT, Lum WL, Chee C. Trabeculectomy—success rates in a Singapore hospital. Singapore Med J. 1996;37(5):505–7.
5. Wong HT, Seah SK. Retrospective analysis of outcome of trabeculectomies for primary glaucoma. Asia-Pacific Ophthalmol. 1998;10:12–5.
6. Ng PW, Yeung BY, Yick DW, et al. Fornix-based trabeculectomy with Wise's suture technique in Chinese patients. Ophthalmology. 2000;107(12):2310–3.
7. Taylor SC. Skin of color: biology, structure, function, and implications for dermatologic disease (review). J Am Acad Dermatol. 2002;46(Suppl62):S41–62.
8. Lama PJ, Fechtner RD. Antifibrotics and wound healing in glaucoma surgery (review). Surv Ophthalmol. 2003;48(3):314–46.
9. Wong TY, Foster PJ, Hee J, et al. Prevalence and risk factors for refractive errors in adult Chinese in Singapore. Invest Ophthalmol Vis Sci. 2000;41(9):2486–94.
10. Koh V, Chen D, Aquino CM, et al. Success rates of 2-site phacoemulsification combined with fornix-based trabeculectomy using mitomycin C for primary angle-closure glaucoma and primary open-angle glaucoma in an Asian population. Jpn J Ophthalmol. 2017;61(3):245–52.
11. Jampel HD, Pasquale LR, Dibernardo C. Hypotony maculopathy following trabeculectomy with mitomycin C. Arch Ophthalmol. 1992;110(8):1049–50.

12. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol. 2002;86(2):238–42.

13. Hernstadt DJ, Cheng J, Htoon HM, et al. Case series of combined iStent implantation and phacoemulsification in eyes with primary angle closure disease: one-year outcomes. Adv Ther. 2019;36(4):976–86.

14. Canadian Ophthalmological Society. Evidence-based clinical practice guidelines for the management of glaucoma in the adult eye. Can J Ophthalmol. 2009;44(Suppl 1):S7–93.

15. Parrish RK 2nd, Minckler DS, Lam D, Pfeiffer N, Rojanapongpun P. Recommended methodology for glaucoma surgical trials. In: Shaarawy TM, Sherwood MB, Grehn F, editors. World Glaucoma Association guidelines on design and reporting of glaucoma surgical trials. Amsterdam: Kugler; 2009. p. 1–14.

16. Sng CC, Wang J, Hau S, et al. XEN-45 collagen implant for the treatment of uveitic glaucoma. Clin Exp Ophthalmol. 2018;46(4):339–45.

17. 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):1579–88.

18. Tham CC, Kwong YY, Leung DY, et al. Phacoemulsification versus combined phacotrabeculectomy in medically uncontrolled chronic angle closure glaucoma with cataracts. Ophthalmology. 2009;116(4):725–31 (31.e1–3).

19. Tham CC, Kwong YY, Leung DY, et al. Phacoemulsification versus combined phacotrabeculectomy in medically controlled chronic angle closure glaucoma with cataract. Ophthalmology. 2008;115(12):2167-83.e2.

20. Park AJ, Eliassi-Rad B, Desai MA. Ptosis after glaucoma surgery. Clin Ophthalmol. 2017;11:1483–9.

21. Kaplan LJ, Jaffe NS, Clayman HM. Ptosis and cataract surgery. A multivariant computer analysis of a prospective study. Ophthalmology. 1985;92(2):237–42.

22. Crosby NJ, Shepherd D, Murray A. Mechanical testing of lid speculae and relationship to postoperative ptosis. Eye (Lond). 2013;27(9):1098–101.